Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron 63 (2007) 3623–3658
Tetrahedron

Tetrahedron report number 795

Recent advances in organotrifluoroborates chemistry

Hélio A. Stefani,[a,b,*] Rodrigo Cella[b] and Adriano S. Vieira[a]

[a]*Departamento de Farmácia, Faculdade de Ciências Farmacêuticas, Universidade de São Paulo, São Paulo, SP, Brazil*
[b]*Instituto de Quimica, Universidade de São Paulo, São Paulo, SP, Brazil*

Received 15 December 2006
Available online 1 February 2007

Contents

1. Introduction . . . 3624
2. Preparation of organotrifluoroborates . . . 3624
   2.1. From organolithium or magnesium reagents . . . 3625
      2.1.1. Lithium exchange or Grignard's reaction . . . 3625
      2.1.2. *ortho*-Lithiation reaction . . . 3625
      2.1.3. Deprotonation reaction . . . 3625
   2.2. From hydroboration or borylation reaction . . . 3626
   2.3. From Baylis–Hillman adducts . . . 3627
   2.4. From allylic alcohols . . . 3628
   2.5. Preparation of cyclopropyltrifluoroborate . . . 3628
   2.6. From trimethylboroxine . . . 3629
3. Functionalization of organotrifluoroborate salts . . . 3630
   3.1. Nucleophilic substitution . . . 3630
   3.2. Oxidation . . . 3630
      3.2.1. Thioether oxidation . . . 3630
      3.2.2. Alcohol oxidation . . . 3631
   3.3. Epoxidation . . . 3631
   3.4. Olefination . . . 3631
      3.4.1. Wittig reaction . . . 3631
      3.4.2. Horner–Wadsworth–Emmons reaction . . . 3631
   3.5. *cis*-Dihydroxylation of olefins . . . 3631
   3.6. Metalation of aryltrifluoroborates . . . 3631
4. Applications of organotrifluoroborate salts . . . 3632
   4.1. Suzuki coupling reaction . . . 3632
      4.1.1. Synthesis of biphenyls and related systems . . . 3632
      4.1.2. Alkylation of aryl and heteroaryl halides . . . 3637
      4.1.3. Allylation and crotylation reactions . . . 3639
      4.1.4. Alkynylation of aryl and heteroaryl halides . . . 3639
      4.1.5. Alkenylation reaction . . . 3640
      4.1.6. Styrenes and related systems . . . 3641
      4.1.7. Stilbenes and related systems . . . 3642
      4.1.8. Dienes . . . 3643
      4.1.9. Enynes . . . 3643
      4.1.10. Enediynes . . . 3644
      4.1.11. Cascade Suzuki–Heck reaction . . . 3644
      4.1.12. Diels–Alder/cross-coupling reactions . . . 3644

* Corresponding author. Fax: +55 11 3815 4418; e-mail: hstefani@usp.br

0040–4020/$ - see front matter
doi:10.1016/j.tet.2007.01.061

4.1.13. α,β-Unsaturated carbonylic compounds . . . 3644
4.1.14. Ene-Allenes . . . 3645
4.2. Other metal-catalyzed reactions . . . 3645
4.2.1. Ketones . . . 3645
4.2.2. Cross-coupling reaction with Baylis–Hillman adducts . . . 3646
4.3. 1,2- and 1,4-Addition reactions . . . 3646
4.3.1. Addition to ketones, aldehydes, and esters . . . 3646
4.3.2. Amides . . . 3649
4.3.3. Imines and iminium species . . . 3650
4.4. Halogenation of organotrifluoroborates . . . 3651
4.5. Total synthesis . . . 3652
4.5.1. Oximidine II . . . 3652
4.5.2. Trityrosine and pulcherosine . . . 3652
4.5.3. (−)-Tetrahydrolipstatin . . . 3653
4.5.4. Cryptophycins . . . 3653
4.6. Ring-opening reactions . . . 3654
4.6.1. Epoxide ring-opening reactions . . . 3654
4.6.2. Lactone ring-opening reactions . . . 3654
4.7. Miscellaneous . . . 3655
4.7.1. Amines . . . 3655
4.7.2. Ethers . . . 3655
4.7.3. Chalcogen compounds . . . 3655
5. Conclusion . . . 3655
References and notes . . . 3656
Biographical sketch . . . 3658

1. Introduction

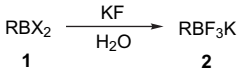
In recent years, organoboron compounds have become one of the most popular organometallic reagents for carbon–carbon bond formation. The great applicability (in place of other organometallic reagents) is due to some features of the organoboron compounds, e.g., (1) compatibility with many functional groups; (2) availability of reagents via hydroboration and transmetalation; (3) low toxicity; (4) their ultimate degradation into the environmentally friendly boric acid and in addition (5) the handling and removal of boron-containing byproducts are easier when compared to other organometallic reagents.

The most used organoboron compounds are boronic acids and boronate esters, but these classes of compounds have some drawbacks; they are unstable and highly sensitive to air and moisture, and are generally expensive. To solve these problems, organoboron reagents have been replaced by organotrifluoroborate salts. The latter compounds show greater nucleophilicity than their boronic acid or boronate ester analogues. They are crystalline solids, which are stable in air and moisture, and are easily prepared from inexpensive materials.

The availability of many publications in the literature clearly indicates the impact of organotrifluoroborates in organic synthesis in the last 10 years. In the beginning of 2005 Molander and Figueroa[1] reviewed the use of organotrifluoroborates with focus on their use in Suzuki–Miyaura coupling reactions. A more complete review was done by Darses and Genêt[2] in 2003. Since then, various groups have reported significant contribution in this area and our review aims to give an overview of the latest advances in the chemistry of organotrifluoroborate salts, from their preparation to their transformations and applications in organic synthesis.

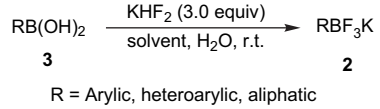
2. Preparation of organotrifluoroborates

Initially, the organotrifluoroborate salts **2** were obtained from the reaction of organodihaloboranes **1** with excess of aqueous KF (Scheme 1).[3] The dihaloorganoborane can be isolated or generated in situ from organostananes.



Scheme 1.

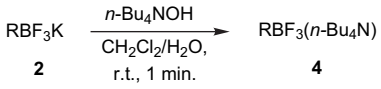
In 1995,[4] the use of potassium hydrogen difluoride (KHF_2) improved the methods to prepare organotrifluoroborates. With this reagent the use of organodihaloboranes (highly reactive and unstable compounds) was no longer necessary. Since then, the organotrifluoroborate salts **2** are obtained by the simple treatment of boronic acids and derivates **3** with an aqueous solution of KHF_2, Scheme 2;[5] some methods of preparation of these salts are shown.



Scheme 2.

The isolation and purification of potassium organotrifluoroborates are in many cases very easy and practical. Generally, it can be done by removal of reaction solvent followed by washing with hot acetone and crystallization in diethyl ether.

The treatment of potassium organotrifluoroborates **2** with tetra-*n*-butylammonium hydroxide affords tetra-*n*-butylammonium organotrifluoroborate salts **4** (Scheme 3).[6] This counterion exchange increases the solubility of the organotrifluoroborates in both polar and non-polar solvents and this fact has been shown to improve the cross-coupling yields.

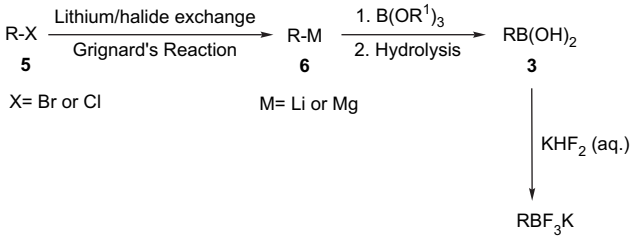


Scheme 3.

2.1. From organolithium or magnesium reagents

2.1.1. Lithium exchange or Grignard's reaction. The use of organometallic reagents is very common in the synthesis of boronic acids and derivatives.[7] Therefore, the organotrifluoroborates could easily be prepared from organohalides **5** by a sequence of lithium/halide exchange or magnesium insertion (Grignard's reaction), boronation, hydrolysis, and in situ treatment with KHF_2 (Table 1).

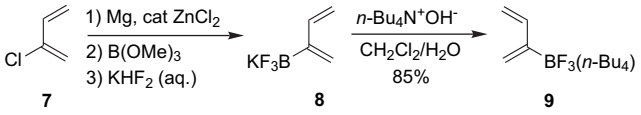
Table 1. Organotrifluoroborate salts **2** obtained from organometallic reagents **6**



Entry	R	X	M	Yield (%)	Ref.
1	1-Naphthyl	Br	Li	82	4
2	4-$CF_3C_6H_4$	Br	Li	91	4
3	3,5-Bis(CF_3)C_6H_3	Br	Li	68	4
4	4-$MeOC_6H_4$	Br	Li	85	5b
5	Mesytil	Br	Li	38	5b
6		Cl or Br	Mg	84–93	5b,8
7		Br	Li	25	8
8	CH_2X	Br or I	Li	78–89	9
9	$PhCH_2$	Cl	Mg	66	10
10		Br	Mg	76	11
11	2-Pyridyl	Br	Li	50	12
12	3-Pyridyl	Br	Li	90	12
13	2,6-Difluorophenyl	Br	Li	82	13
14	C_6F_5	Br	Mg	70–81	13
15	C_6F_5	Br	Li	62	13
16		Cl	Mg	78	14

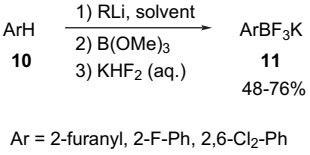
As can be seen in Table 1 several potassium organotrifluoroborate salts could be made in moderate to good yields by this method. When aryl halides are used, it is clear that the reaction tolerates both electron-withdrawing and electron-donating substituents without affecting the yield. When the *ortho*-positions are occupied the aryltrifluoroborates were obtained in low-to-good yields (entries 5 and 16, Table 1).

Recently, De and Welker[14] synthesized the 1,3-dienyl-2-trifluoroborate **8** (entry 16, Table 1) from 2-chloroprene **7**. As we will see, this compound was used in a Diels–Alder/cross-coupling reaction. They also prepared the corresponding tetra-*n*-butylammonium salt of the 1,3-dienyl-2-trifluoroborate **9** after treatment with *n*-Bu_4NOH (Scheme 4).



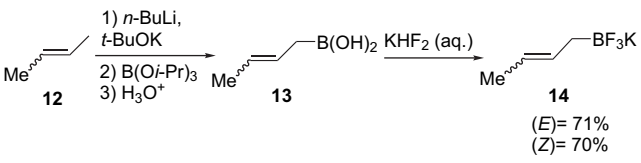
Scheme 4.

2.1.2. *ortho*-Lithiation reaction. Several aryltrifluoroborate salts **11** have been obtained from *ortho*-lithiation reactions (Scheme 5).[4] The *ortho*-lithiation reaction works by providing the alkyllithium with a point of coordination, increasing reactivity specifically in the location of the coordination site of the substrate, and hence directing the regioselectivity.[15] Thus, the functionalized aryltrifluoroborate **11** could be obtained as a unique regioisomer.



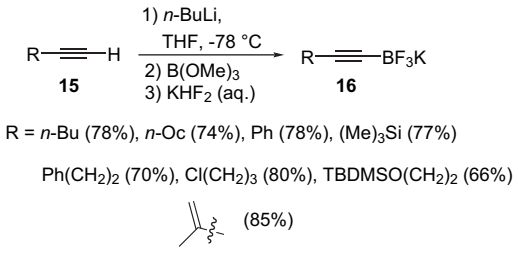
Scheme 5.

2.1.3. Deprotonation reaction. Potassium crotyltrifluoroborates **14** were synthesized from their corresponding boronic acids **13**.[11] The crotylboronic acids were readily prepared using the protocol already described (Scheme 6).[16] After formation of the crotylboronic acid **13**, the reaction was quenched with an aqueous solution of KHF_2 to afford the crotyltrifluoroborate salts **14** in good yield.



Scheme 6.

From the deprotonation of terminal alkynes **15**, normally with *n*-BuLi, followed by boronation reaction and treatment with aqueous KHF_2, potassium alkynyltrifluoroborate salts **16** can be obtained (Scheme 7).[5b,17] Surprisingly, alkynes

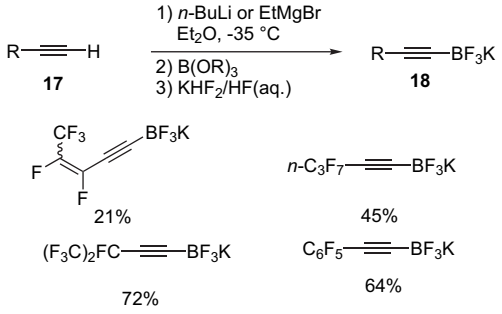


Scheme 7.

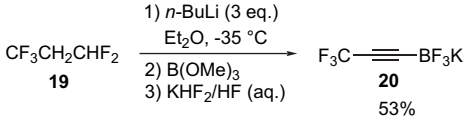
containing a trialkylsilyl group attached either at the carbon atom or oxygen atom were not removed, despite the use of a fluoride source.

Unfortunately, when functionalized alkynes bearing basic heteroatoms, cyano, and esters groups were employed, it was not possible to produce the corresponding trifluoroborate salts.[17]

Some potassium ((perfluoroorgano)ethynyl)trifluoroborates **18** have been obtained from deprotonation of (perfluoroorgano)ethynes **17** with *n*-BuLi or EtMgBr and subsequent reaction with trialkylboronates and KHF_2/aqueous HF in low-to-good yields (Scheme 8).[18] In this same report the authors described the preparation of other ((perfluoroorgano)ethynyl)trifluoroborate salts **20** by the reaction of 1,1,1,3,3-pentafluoropentane **19** with 3 equiv of *n*-BuLi (Scheme 9) and by treatment of the olefin *n*-$C_6F_{13}BrC{=}CH_2$ **21** with LDA (Scheme 10). In this latter case when LDA was replaced by 3 equiv of *n*-BuLi a different product **23** was obtained.

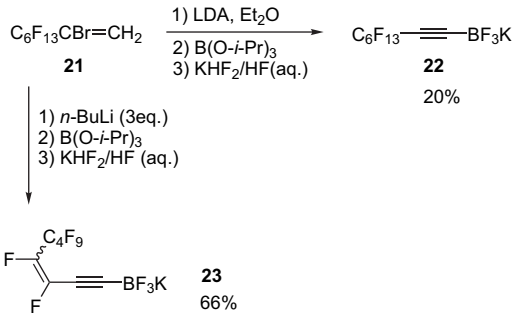


Scheme 8.

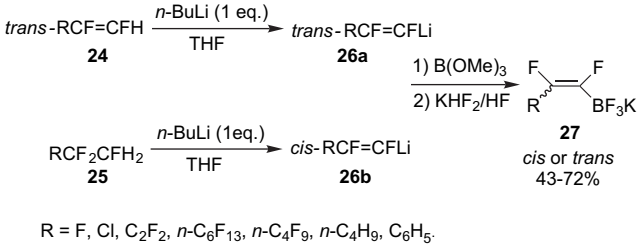


Scheme 9.

Potassium polyfluoroalk-1-enyltrifluoroborates **27** were prepared by the addition reaction of RCF=CFLi **26** to trimethylborate followed by the hydrolysis of the crude product with an aqueous solution of KHF_2 and HF 40% (Scheme 11).[19] The *trans*-RCF=CFLi **26a** is easily obtained from the corresponding alkenyl compounds **24**, while the *cis*-RCF=CFLi **26b** is prepared from the treatment of fluoroalkanes **25** with 2 equiv of *n*-BuLi.

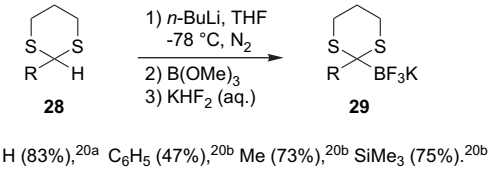


Scheme 10.



Scheme 11.

Potassium 1,3-dithianotrifluoroborate salts **29** could be prepared by deprotonation reaction of 1,3-dithianes **28** with *n*-BuLi followed by the addition of trimethylborate and an aqueous solution of KHF_2 (Scheme 12).[20]



Scheme 12.

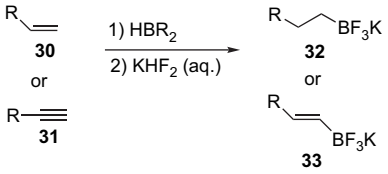
2.2. From hydroboration or borylation reaction

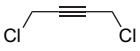
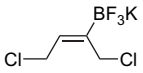
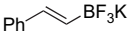
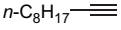
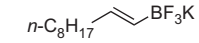
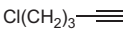
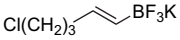
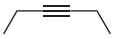
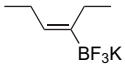
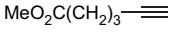
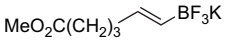
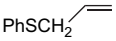
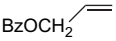
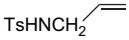
Addition of dialkylborane, dialcoxyborane or dihaloboranes to alkenes **30** or alkynes **31** gives alkylboron **32** or alkenylboron **33** compounds, respectively, in very high yields.[7] Normally, hydroboronation reactions are highly regio- and diastereoselective. Taking advantage of this classical method for organoboron compounds, several potassium alkyl and alkenyltrifluoroborate salts have been prepared in situ. A list of organotrifluoroborates obtained by hydroboration is given in Table 2.

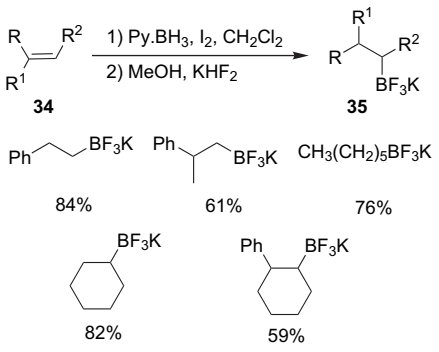
Recently, Clay and Vedejs[24] reported the use of pyridine borane as a hydroboration agent to obtain some potassium alkyltrifluoroborates **35** (Scheme 13). The reaction was carried out in dichloromethane in presence of iodine, followed by treatment with methanolic solution of KHF_2.

From the hydroboration of (+)-α-pinene **38** with DMAP·BH_3 **36** and catalytic amounts of iodine followed by treatment with a KHF_2 solution in methanol/water, it was possible to obtain the potassium isopinocampheyltrifluoroborate **41** in 80% yield (Scheme 14).[25]

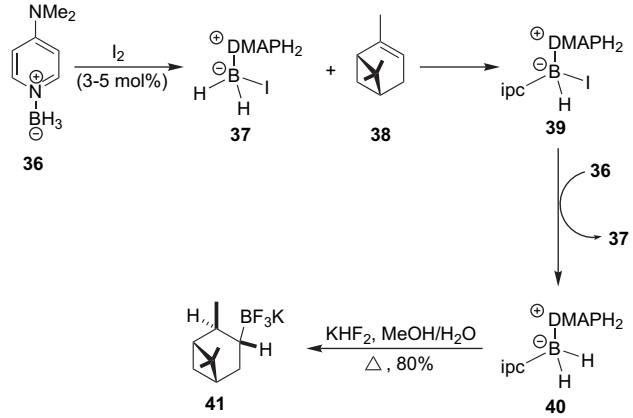
Table 2. Alkyl **32** and Alkenyltrifluoroborates **33** prepared by hydroboration



Entry	Substrate	Borane	Product	Yield (%)	Ref.
1		$HB(Ipc)_2$		45	5b
2		Cathecolborane		81	21
3		$Br_2BH\cdot SMe_2$		83	22
4		$Br_2BH\cdot SMe_2$		68	22
5		$Br_2BH\cdot SMe_2$		63	22
6		$Br_2BH\cdot SMe_2$		47	22
7		$Br_2BH\cdot SMe_2$	$PhS(CH_2)_3BF_3K$	75	23
8		Pinacolborane	$BzO(CH_2)_3BF_3K$	64	23
9		Pinacolborane	$TsHN(CH_2)_3BF_3K$	40	23

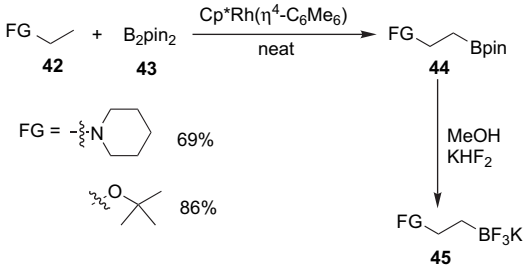


Scheme 13.



Scheme 14.

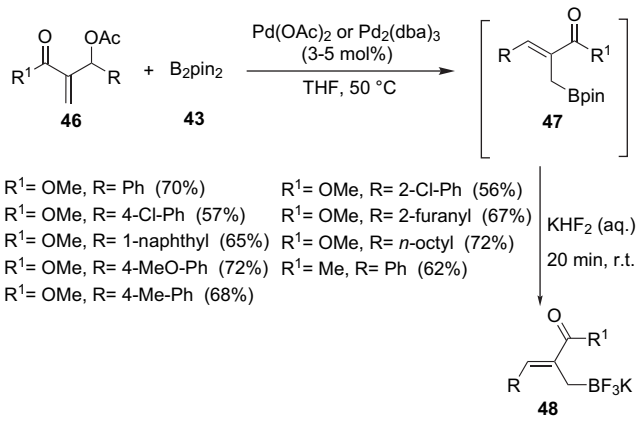
Hartwig and co-workers[26] reported the synthesis of alkyltrifluoroborates **45** from the rhodium-catalyzed terminal borylation of alkyl groups **42** using $B_2(pin)_2$ **43** [bis(pinacolato)-diborane] followed by addition of methanolic KHF_2 in the crude reaction solution (Scheme 15).



Scheme 15.

2.3. From Baylis–Hillman adducts

The allyltrifluoroborates were prepared by the cross-coupling reaction between acetates of Baylis–Hillman adduct **46** (methyl acrylate and methyl vinyl ketone) and $B_2(pin)_2$ **43** in presence of a palladium catalyst in THF. The unstable allylboronate pinacol esters **47** were readily converted into the corresponding potassium allyltrifluoroborate salts **48** by treatment with excess aqueous KHF_2 at room temperature (Scheme 16).[27]



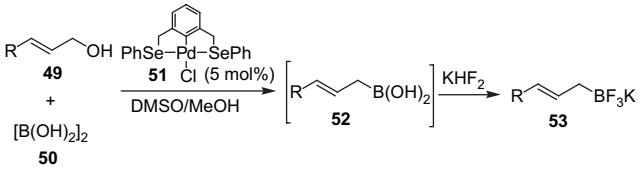
Scheme 16.

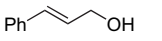
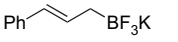
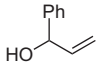
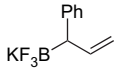
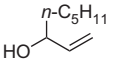
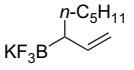
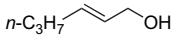
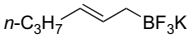
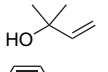
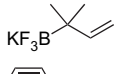
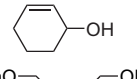
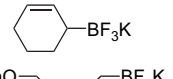
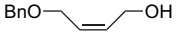
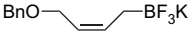
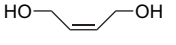
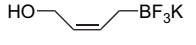
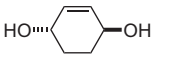
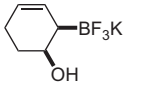
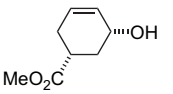
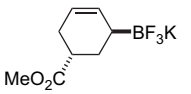
The reaction was *E*-stereoselective and applicable to Baylis–Hillman acetate adducts **46** derived from aryl, heteroaryl, and aliphatic aldehydes. All allyltrifluoroborates **48** were obtained in good yields.

2.4. From allylic alcohols

The transformation of allylic alcohols **49** into potassium allyltrifluoroborate salts **53** can be achieved via the reaction of allylic alcohols **49** with diboronic acid **50** in the presence of a selenide-based palladium complex **51** (Table 3).[28] The allyl boronic acids **52** were formed and these unstable compounds were treated with aqueous KHF_2 to afford their trifluoroborate derivatives.

Table 3. Potassium organotrifluoroborates **53** from allylic alcohols **49**



Entry	Substrates	Products	Yields (%)
1			92
2			86
3			90
4			94
5			98
6			92
7			87
8			74
9			87
10			82

The use of a DMSO/MeOH mixture as well as a selenide-based complex **51** is indispensable. When the reactions were performed in pure DMSO, a very slow reaction with low conversion of the allylic alcohol substrate occurred. It was observed that the catalyst is poorly soluble in MeOH. Commonly used palladium(0) sources were found to be inefficient as catalysts in this reaction.

The boronation reactions proceed with excellent regioselectivity and in excellent yields (Table 3). When a diol was used only the observed monoboronation occurred (entry 8, Table 3). When a cyclic diol was used (entry 9, Table 3) the reaction proceeded with allyl rearrangement and trans stereoselectivity. In the case of allylic alcohol containing an ester group (entry 10, Table 3) it was necessary to employ catalytic amounts of strong acids, such as *p*-toluenesulfonic acid to accelerate the boronation reaction.

The suggested mechanism probably involves the transformation of the hydroxyl group in a better leaving group, an allyl boronic ester (Scheme 17). Perhaps this esterification is facilitated by the inclusion of a methanol molecule in the six-membered ring transition-state **54** (TS) of the process. In the sequence, the cleavage of the B–B bond is also facilitated by coordination of the water molecule produced in the esterification.

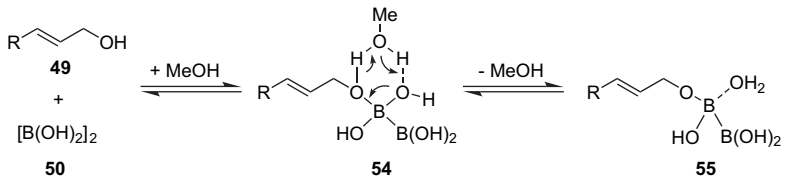
2.5. Preparation of cyclopropyltrifluoroborate

Alkenylboronic esters **56** are cyclopropanated by reaction with diazomethane, catalyzed by $Pd(OAc)_2$ (Scheme 18),[29] followed by in situ treatment with excess of aqueous KHF_2 to afford the stereodefined potassium cyclopropyl trifluoroborate **57** in excellent yields. It was observed that trifluoroborates generated from (*E*)-alkenylboronic esters **56a** have trans configuration and cis configuration when (*Z*)-alkenylboronic esters **56b** were used.

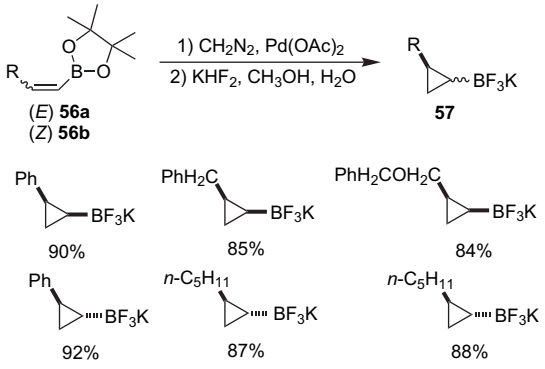
An efficient synthesis of 1,2,3-trisubstituted potassium cyclopropyl trifluoroborate salts **60** was achieved from allylic alcohols **58**.[30] The allylic alcohols **58** were treated with a *gem*-dizinc carbenoid, trimethylborate, and a solution of KHF_2 in methanol/water (Scheme 19). The reaction is general for (*Z*)-alkenes under the reaction conditions, however, the yield of (*E*)-alkenes was lower.

The proposed mechanism postulates the formation of the zwitterions **A**, which is in equilibrium with the borate ester **B** (Scheme 20). Cyclopropanation gives cyclopropylzinc **C**, followed by an intramolecular zinc–boron exchange, to give cyclopropylborinate **D** that would be hydrolyzed during the work-up.

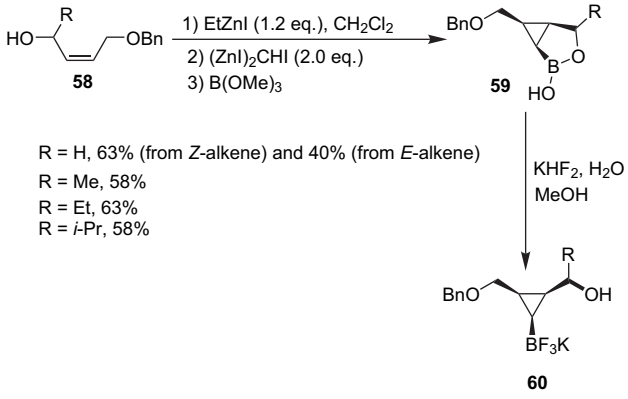
Enantiomerically pure cyclopropyl trifluoroborates **62** were synthesized via deprotection of their corresponding pure diastereomeric boronic esters **61** (Scheme 21) with a very high excess of KHF_2 (50 equiv) in MeOH/H_2O at 80 °C, affording the crystalline enantiomers in high yields (Scheme 21).[31] The essential boronic intermediates **61** were obtained by one-pot sequence hydroboration of benzyl-protected



Scheme 17.

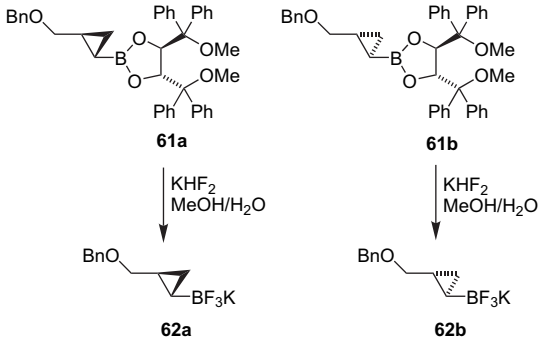


Scheme 18.



Scheme 19.

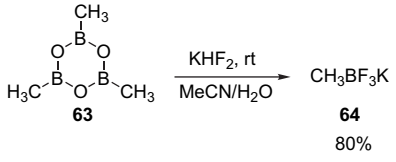
(Bn) propargylic alcohol followed by a cyclopropanation reaction.



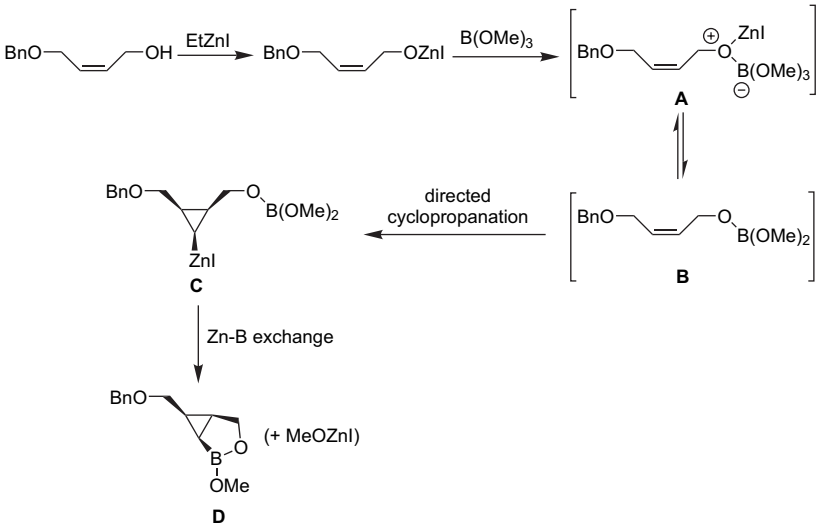
Scheme 21.

2.6. From trimethylboroxine

Potassium methyltrifluoroborate salt **64** was readily prepared from commercially available trimethylboroxine **63** by treatment with KHF_2 at room temperature in MeCN/H_2O solution (Scheme 22).[23]



Scheme 22.



Scheme 20.

3. Functionalization of organotrifluoroborate salts

The growing employment of organotrifluoroborates in organic chemistry has prompted the search of different ways to reach more functionalized organotrifluoroborates. In this area, the Molander's group has given the major contribution.

3.1. Nucleophilic substitution

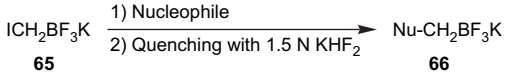
The preparation of various potassium organotrifluoroborates was achieved via direct nucleophilic substitution of potassium iodomethyltrifluoroborates **65**.[9] Preparation of starting material had already been described and the substitution reaction was carried out with a wide range of nucleophiles (Table 4), such as alkyl- and aryllithiums, Grignard's reagents, alkylamines, alkoxides, carbanions, dianions, and lithium arylthiolates.

Azide-containing potassium organotrifluoroborates **68** are obtained from the direct nucleophilic substitution of the haloalkyltrifluoroborates **67** with NaN_3 (Scheme 23).[32]

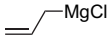
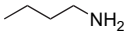
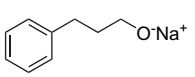
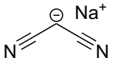
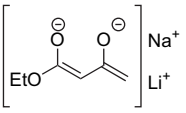
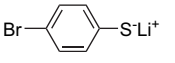
Some 1,4-disubstituted organo-[1,2,3]-triazol-1-yl-trifluoroborates **70** were produced through the 1,3-dipolar cycloaddition reaction of potassium azido-organotrifluoroborate **68** with various alkynes **69**, using CuI (10 mol %) as catalyst (Table 5). The 1,4-disubstituted organo-[1,2,3]-triazol-1-yl-trifluoroborates **70** were also obtained from their halogen salts **67** by a one-pot multicomponent reaction. In both cases the products were obtained in excellent yields.

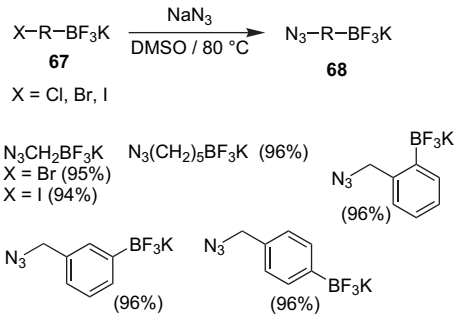
The one-pot synthesis of potassium organo-[1,2,3]-triazol-4-yl-trifluoroborates **73** was achieved directly from the

Table 4. Nucleophilic substitution reactions of potassium iodomethyltrifluoroborates



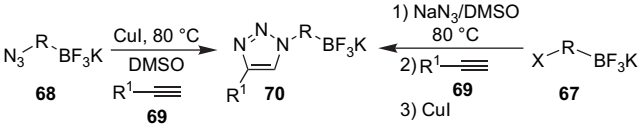
65 **66**

Entry	Nucleophile	Yield (%)
1		86
2		83
3		85
4		88
5		95
6		86
7		91
8		88
9	KCN	98
10		94



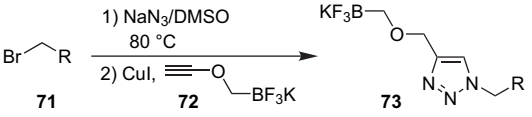
Scheme 23.

Table 5. 1,3-Dipolar cycloaddition reaction of potassium azido-organotrifluoroborate **68** with alkynes **69**



Entry	R	R^1	Yield (%)
1	CH_2	C_6H_5	90
2	CH_2	CH_2OH	85
3	CH_2	$C_6H_5SCH_2$	93
4	CH_2	Naphthyl	93
5	CH_2	CO_2Et	98
6	$(CH_2)_5$	C_6H_5	95
7	$(CH_2)_5$	CO_2Et	93

reaction of an alkyl bromide **71** with NaN_3 in DMSO followed by reaction with potassium prop-2-ynyloxymethyltrifluoroborate **72** in presence of CuI (Scheme 24).



R = 4-Me-C_6H_4 (91%)

R = 4-NO_2-C_6H_4 (87%)

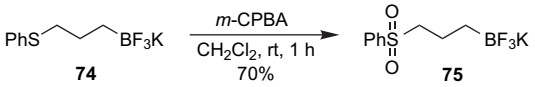
R = CO_2Et (94%)

Scheme 24.

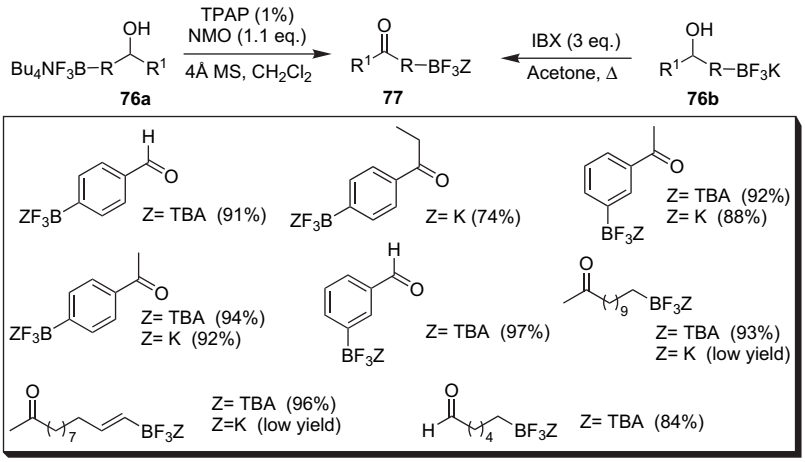
The reaction works well with benzyl bromide and electron-poor 4-nitrobenzyl bromide. However, ethyl bromoacetate and electron-rich 4-methylbenzyl bromide require longer reaction times or 30 mol % of CuI for the completion of the reaction.

3.2. Oxidation

3.2.1. Thioether oxidation. Potassium phenylsulfonylpropyltrifluoroborate **74** was prepared by a simple oxidation of its corresponding thioether-trifluoroborate **75** utilizing *m*-chloroperbenzoic acid (*m*-CPBA) in methylene chloride at room temperature (Scheme 25).[33] The trifluoroborate moiety remained intact even under oxidative conditions.



Scheme 25.



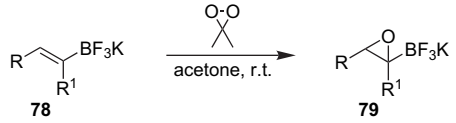
Scheme 26.

3.2.2. Alcohol oxidation. A general oxidation reaction of potassium and tetra-*n*-butylammonium (TBA) organotrifluoroborates **77** containing primary and secondary alcohols was described by Molander and Petrillo.[34] When the counterion was TBA the reaction was carried out in a TPAP/NMO system and when the counterion was potassium, IBX was used as an oxidizing agent (Scheme 26).

Other oxidation conditions, such as Swern, Dess–Martin periodinane, and TEMPO/bleach, were successfully employed and furnished the corresponding carbonyl trifluoroborate compounds. The conditions described above were chosen due to the simplicity in execution.

3.3. Epoxidation

Potassium vinyltrifluoroborate salts **78** were successfully transformed into their epoxide derivatives **79** by the reaction with dimethyldioxirane at room temperature (Scheme 27) with the concomitant retention of the trifluoroborate moiety.[33] The potassium epoxytrifluoroborates **79** were obtained in good yields as a white solid, completely stable in air.



Scheme 27.

The epoxidation with *m*-CPBA also affords the epoxides in excellent yields but the product crystallizes together with *m*-chlorobenzoic acid.

3.4. Olefination

3.4.1. Wittig reaction. A Wittig reaction was performed with organotrifluoroborates containing a carbonyl group **80** and ylide reagents **81**, leading to the vinyltrifluoroborate salts **82** (Scheme 28).[35] The reaction proved to be very diastereoselective. When nonstabilized ylides were employed the (*Z*) isomers were obtained in higher ratio. However, when stabilized ylides were used the (*E*) isomers were obtained almost exclusively.

3.4.2. Horner–Wadsworth–Emmons reaction. The Horner–Wadsworth–Emmons olefination was also studied employing functionalized potassium alkyl- and aryltrifluoroborates containing an aldehyde group **83** to prepare vinyltrifluoroborates **85** (Scheme 29).[35] By this approach the vinyltrifluoroborates were isolated as the tetra-*n*-butylammonium organotrifluoroborates to overcome the difficulty to separate the solid mixture from the excess phosphonate. Again, the olefination reaction demonstrated to be highly diastereoselective and the (*E*) isomers were obtained in major ratio.

3.5. *cis*-Dihydroxylation of olefins

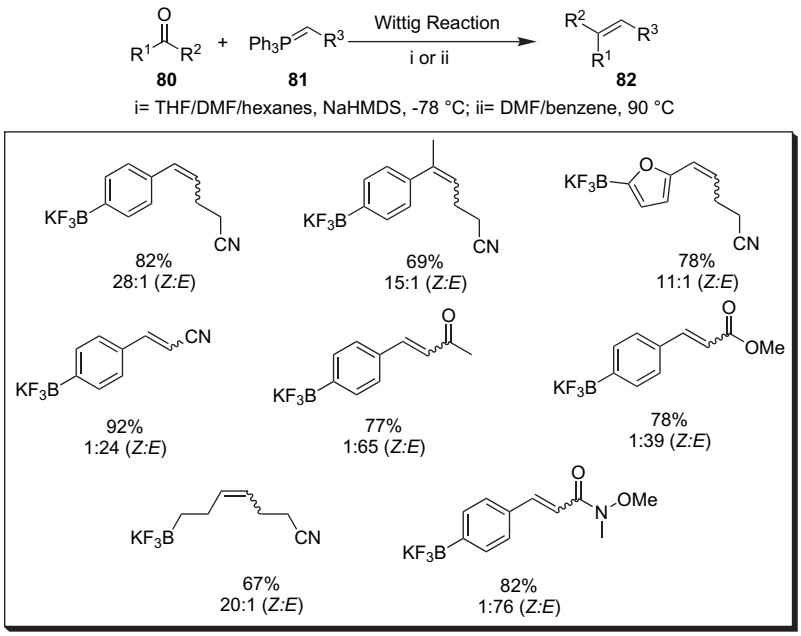
The *cis*-dihydroxylation of olefin-containing potassium organotrifluoroborates **86** proceeds smoothly using 1.3 mol % of OsO_4, *N*-methylmorpholine *N*-oxide (NMO) and acetone/*t*-BuOH/water solvent mixture at room temperature to give the diol **87** in moderate-to-excellent yields as a white solid and with retention of the valuable trifluoroborate moiety (Scheme 30).[36]

The dihydroxylation was successfully performed with 1,1-, 1,2-disubstituted, and trisubstituted olefins. Hydroxylation of potassium allyltrifluoroborate occurs under the same reaction condition.

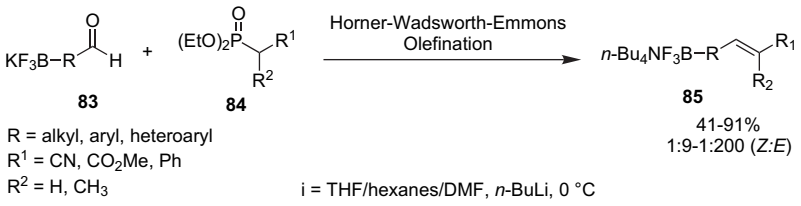
3.6. Metalation of aryltrifluoroborates

Lithium-halogen exchange reaction of potassium 4-bromophenyl trifluoroborates **88** followed by addition to aliphatic or aromatic aldehydes gave secondary alcohols (Scheme 31).[37]

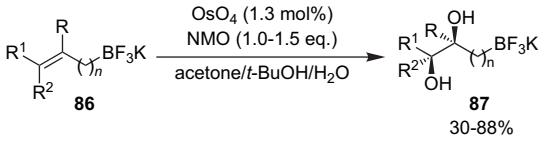
Ketones were also studied leading to tertiary alcohols in good yields. α,β-Unsaturated aldehydes lead only to the 1,2-addition product. Electrophiles such as iodine, trimethylsilyl chloride, and phenylisocyanate can be used as well. Control of the reaction time was crucial to achieve good yields.



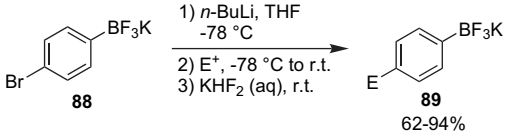
Scheme 28.



Scheme 29.



Scheme 30.



Scheme 31.

The reaction was general only to *para*-substituted potassium bromoaryl trifluoroborates.

4. Applications of organotrifluoroborate salts

4.1. Suzuki coupling reaction

The first palladium-catalyzed cross-coupling reaction of organoboron compounds with an organohalide was observed by Neghishi in 1978.[38] This reaction is now known as Suzuki or Suzuki–Miyaura coupling due to the strong efforts of Prof. Akira Suzuki and Prof. Norio Miyaura in the last three decades.[7c,39]

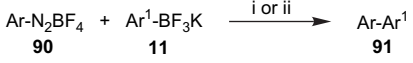
Recently, a number of synthesis and industrial applications employing the cross-coupling reaction of organoboron compounds with different types of organic electrophiles have become powerful tools for the construction of new organic compounds, and in these reactions, the use of organotrifluoroborates has increased in the last 10 years.

4.1.1. Synthesis of biphenyls and related systems. The aryl–aryl bond formation has become a most important tool of organic synthesis because these bonds are found in natural products as well as in numerous biologically active parts of pharmaceuticals and agrochemicals.

The first Suzuki–Miyaura cross-coupling reaction involving organotrifluoroborates was reported in 1997.[40] Arenediazonium tetrafluoroborates **90** were effective substrates in palladium-catalyzed cross-coupling reactions with aryltrifluoroborates **11** (Table 6).[5b] The aryltrifluoroborates proved to be more reactive than their corresponding organoboronic acids.

The reaction was not affected by electron-donating or electron-withdrawing groups in both partners (Table 6).

Table 6. Cross-coupling reaction of potassium aryltrifluoroborates **11** with arenediazonium tetrafluoroborates **90**

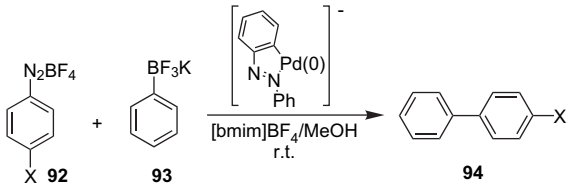


i = 1,4-dioxane, $Pd(OAc)_2$ (5 mol%);
ii = MeOH, $Pd_2(\mu\text{-}OAc)_2[P(o\text{-tolyl})_3]_2$ 5 mol%

Entry	Ar-	Ar^1-	Yield (%)
1	4-Me-C_6H_4	C_6H_5	88
2	4-NO_2-C_6H_4	4-F-C_6H_4	92
3	4-EtO_2C-C_6H_4	4-MeO-C_6H_4	93
4	4-F-C_6H_4	4-OHC-C_6H_4	67
5	2,6-$(Me)_2$-4-Br-C_6H_2	1-Naphthyl	21
6	2,4-$(MeO)_2$-C_6H_3	2,4-Dichloro-C_6H_3	Traces
7	3-PhC(O)-C_6H_4	3-Furanyl	86
8	4-Br-C_6H_4	3-NO_2-C_6H_4	60
9	4-TfO-C_6H_4	C_6H_5	66
10	4-I-C_6H_4	C_6H_5	41

However, this protocol was inefficient when both substrates are sterically hindered (entries 5 and 6, Table 6). The cross-coupling reaction was chemoselective as it was possible to selectively couple the diazonium moiety in presence of triflate, bromo, and iodo substituents (entries 8–10, Table 6).

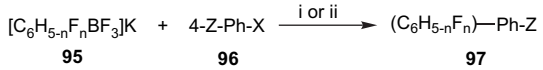
Substituted aryldiazonium salts **92** were also reacted with potassium phenyltrifluoroborate **93** in presence of catalytic azapalladacycle, using ionic liquid as reaction media, to afford the corresponding biaryls **94** in high yields (Scheme 32).[41]



X = OMe (78%), CO_2Et (82%), Br (79%), Cl (95%)

Scheme 32.

Frohn et al. reported the palladium-catalyzed cross-coupling reaction between (polyfluoroorgano)trifluoroborate salts **95** and aryl halides or benzenediazonium tetrafluoroborates **96** (Scheme 33).[42] The reaction involving diazonium salts afforded the (polyfluoro)biaryls **97** in lower yields than when the aryl halides were used. In the latter reactions the use of Ag_2O and a phosphine ligand, such as triphenylphosphine, was necessary.

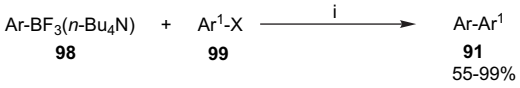


$C_6H_{5-n}F_n$ = C_6F_5, 2,3,4,5-C_6HF_4, 3,4,5-$C_6H_2F_3$,...
X = Br, I, N_2BF_4
Z = F, NO_2, MeO, H, Me, CO_2Et

i = $Pd(OAc)_2$/ 2 PPh_3, Ag_2O, K_2CO_3, toluene, 100 °C;
ii = $Pd(PPh_3)_4$, DME, 20 °C

Scheme 33.

A comparative study between the use of potassium aryltrifluoroborate salts and TBA aryltrifluoroborates was evaluated[6] and the TBA salts gave yields often 25–50% greater than their K^+ counterparts under the same conditions. The cross-coupling reaction of TBA aryltrifluoroborates **98** and aryl halides **99** afforded the biaryl systems **91** in excellent yields (Scheme 34). Electron-rich, electron-poor, and sterically hindered substituents in both substrates do not affect the reaction.



Ar = Ph, 3-NO_2-Ph, 4-Cl-Ph, 3-Cl-Ph, 3-furanyl, 3-pyridyl
Ar^1 = Ph, 4-NO_2-Ph, 4-MeO-Ph, 4-Cl-Ph, 3-NO_2-Ph, mesityl, 3-pyridyl
X = Br or I

i = $Pd(OAc)_2$ (5 mol %), dppb (5 mol %), Cs_2CO_3, DME/H_2O, 50 °C, 24 h

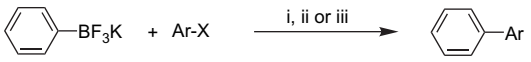
Scheme 34.

An extensive study concerning the cross-coupling reaction of potassium aryl- and heteroaryltrifluoroborates with aryl and heteroaryl halides or triflates in the Suzuki–Miyaura coupling explored in detail the formation of biaryl systems.[12,43]

A set of reactions employing potassium phenyltrifluoroborate **93** and electron-poor and electron-rich aryl halides **100** in presence of $Pd(OAc)_2$ (Table 7). Some electron-rich halides required the use of triphenylphosphine as a ligand. When aryl or heteroaryl triflates were employed, the use of PCy_3 as a ligand was essential.[43b]

The effect of electron-donating and electron-withdrawing groups in the trifluoroborate salts was also evaluated by reaction with 4-bromobenzonitrile **102** (Scheme 35). When electron-rich or even slightly electron-poor aryltrifluoroborates **11** were used excellent yields were obtained under ligandless conditions. However, when more electron-deficient trifluoroborates were employed under ligandless conditions, a high percentage of the trifluoroborate homocoupling product was observed. Thus, the use of a phosphine ligand proved to be necessary.

Table 7. Synthesis of biaryl compounds **101** by Suzuki–Miyaura cross-coupling reaction



i = $Pd(OAc)_2$ (0.5 mol%), K_2CO_3, MeOH or H_2O.
ii = $Pd(OAc)_2$ (0.5 mol%), PPh_3 (0.5 mol%), K_2CO_3, MeOH.
iii= $Pd(OAc)_2$ (5 mol%), PCy_3 (10 mol%), Cs_2CO_3, THF/H_2O

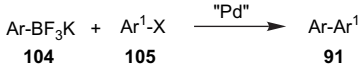
Entry	Ar	X	Yield (%)
1	4-NO_2-C_6H_4	Br, OTf	>99, 65
2	4-CF_3-C_6H_4	Br	79
3	4-CN-C_6H_4	Br	87
4	2-OHC-C_6H_4	Br	89
5	3-MeO_2C-C_6H_4	Br	87
6	4-HO_2C-C_6H_4	Br	96
7	4-MeO-C_6H_4	Br, OTf	95, 92
8	4-HO-C_6H_4	Br	82
9	4-NHAc-C_6H_4	Br	62
10	2-Me_2N-C_6H_4	Br	65
11	2,4-$(MeO)_2$-C_6H_3	Br	75
12	4-Cl-C_6H_4	OTf	82
13	1-Naphthyl	OTf	86

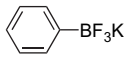
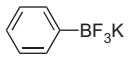
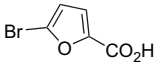
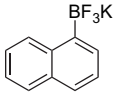
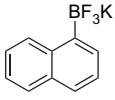
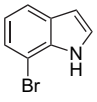
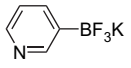
Scheme 35.

Next, *ortho*-substituted coupling partners were employed to assess steric effects in the process. The presence of one methyl group in the *ortho*-position of the trifluoroborate permitted the use of ligandless conditions for the couplings. However, when two methyls were situated *ortho* to the trifluoroborate group, the reaction required more time and did not reach completion under ligandless conditions.

Reaction of potassium heteroaryltrifluoroborates **104** and heteroaryl halides **105** generally occurs with moderate to high yields under ligandless conditions; some representative examples can be seen in Table 8. However, in all these reactions, the formation of the homocoupled product from the trifluoroborate, and even from the heteroaryl bromide, was observed, complicating the purification and reducing the yield. As in the case of coupling between aryltrifluoroborates with aryl halides, when electron-deficient heteroaryl coupling partners were used, the phosphine ligand was necessary to improve the yields.

Table 8. Cross-coupling reaction of aryltrifluoroborates with heteroaryl halides



Entry	Ar-BF_3K	Ar^1-X	Reaction condition[a]	Yield (%)
1			A	90
2			A	67
3			B	72
4			B	80
5			A	68
6			B	63
7			B	77
8			B	83
9			B	72
10			B	64

[a] Condition A: $Pd(OAc)_2$ (0.5–1 mol %), K_2CO_3 (3 equiv), MeOH or H_2O. Condition B: $PdCl_2(dppf)\cdot CH_2Cl_2$ (0.5–2 mol %), Et_3N (3 equiv), EtOH.

Interestingly, when the trifluoroborate group is α to the heteroatom in the furans and pyridines, the Suzuki reaction was not efficient, even when ligand conditions were used.

Usually, the cross-coupling Suzuki–Miyaura reaction to form aryl–aryl or aryl–heteroaryl bond is performed using aryl- or heteroaryl bromides or iodides. Recently, Barder and Buchwald[44] developed a methodology that employs aryl- or heteroaryl chlorides with aryl- and heteroaryltrifluoroborate salts using $Pd(OAc)_2$ and *S*-Phos (**A**) **110** as the supporting ligand (Scheme 36). The coupling reactions work well with electron-rich or hindered aryl chlorides.

Using the same methodology developed for the above reaction, a number of nitrogen- and sulfur-containing heteroaryl chlorides **113** were converted into the respective, arylheteroaryl compounds **114** in good yields (Scheme 37).

Another example[45] of cross-coupling reaction of a 3-pyridyltrifluoroborate **112** and an aryl chloride **115** was performed using PCy_3 as a ligand (Scheme 38), giving the product **116** in 85% yield.

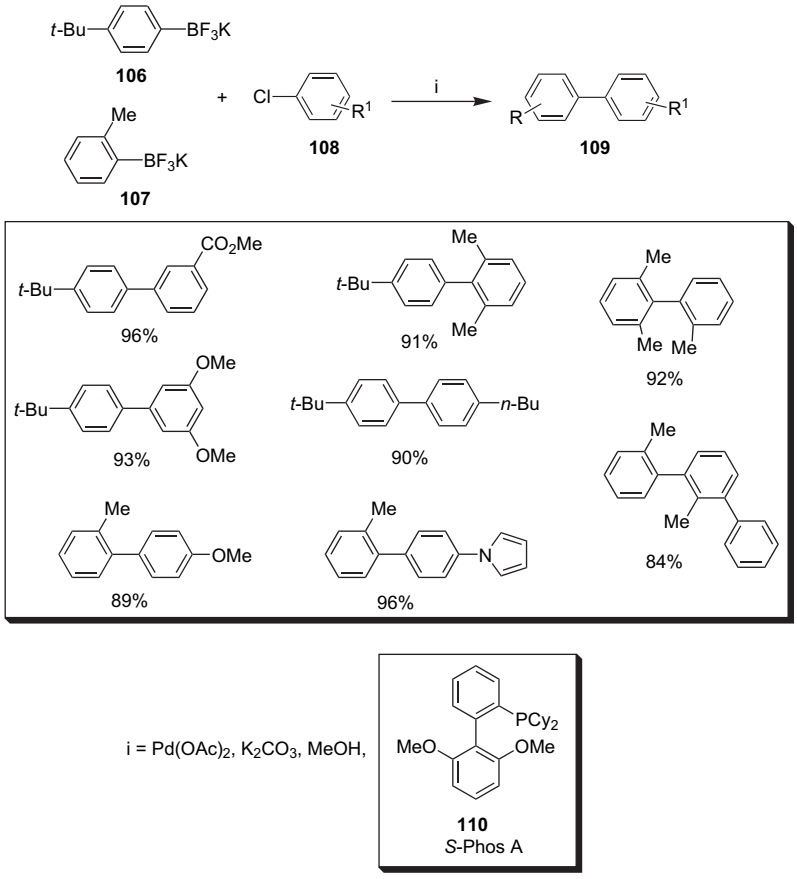
Recently,[46] a palladium-NHC (NHC=*N*-heterocyclic carbene) **119** catalyst has been employed in the Suzuki–Miyaura reaction between aryl chlorides **117** and aryltrifluoroborates **118** (Scheme 39).

Biarylic systems **91** were synthesized in aqueous media by a Suzuki reaction involving potassium aryltrifluoroborates **11** and aryl halides **99** in presence of poly(vinylpyrrolidone)-supported palladium metal **121** (Table 9).[47] This palladium source was recycled at least eight times without loss of activity via a simple decantation procedure.

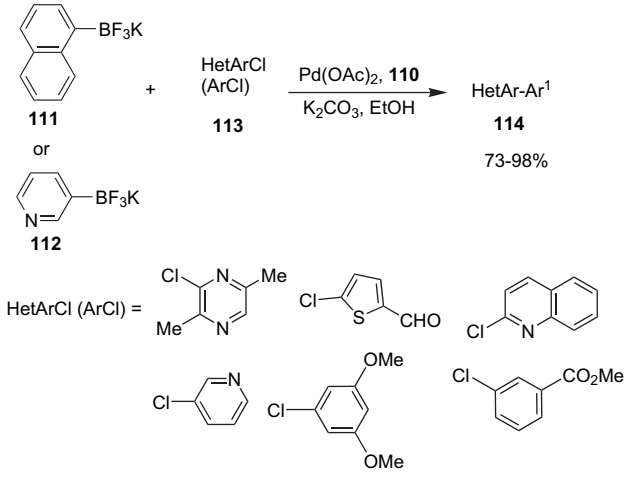
Electron-rich, electron-poor, and sterically hindered substituents in the aryl halide do not affect the reaction. Aryl iodides react with higher yields than aryl bromides.

The use of microwaves in organic chemistry has gained a great importance in the last years.[48] Taking advantage of this alternative energy source, Kabalka et al. have coupled aryltrifluoroborate **122** with aryl iodides[49] **123a** or aryl triflates[50] **123b** (Scheme 40). Aryl iodides are coupled in the presence of $PdCl_2(dppf)\cdot CH_2Cl_2$ and Hünig's base (*i*-Pr_2NEt) with excellent yields. However, the use of a phosphine ligand and a base was not necessary when aryl triflates were employed.

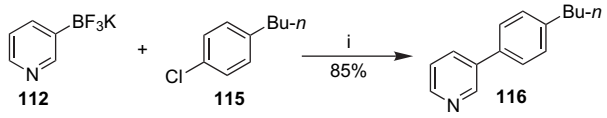
In both cases, the reaction tolerated the nature of the substituents on the aromatic ring. Reagents containing electron-poor, electron-rich, and sterically bulky substituents afforded the coupling products in moderate-to-excellent yields.



Scheme 36.

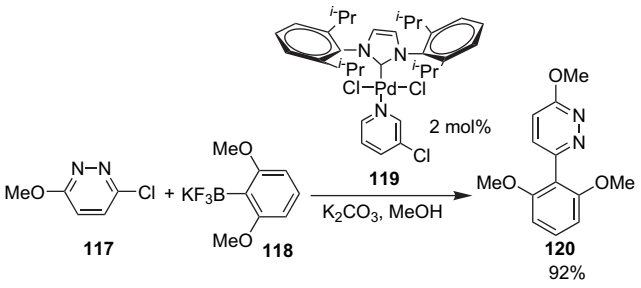


Scheme 37.



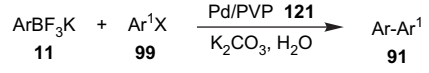
i = $[Pd_2(dba)_3]$ 1 mol%, PCy_3 2.3 mol%, K_3PO_4 (1.7 equiv), dioxane/H_2O, 100 °C.

Scheme 38.

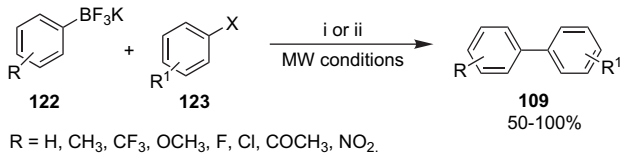


Scheme 39.

Table 9. Suzuki reaction between aryltrifluoroborates **11** and aryl halides **99** in aqueous media



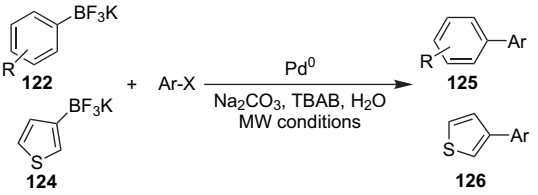
Entry	Ar	Ar^1X	Yield (%)
1	4-MeC_6H_4	C_6H_5I	96
2	4-MeC_6H_4	C_6H_5Br	78
3	4-MeC_6H_4	2-FC_6H_4I	93
4	4-MeC_6H_4	3-FC_6H_4I	90
5	C_6H_5	C_6H_5I	91
6	4-MeC_6H_4	4-$MeCOC_6H_4I$	95
7	4-MeC_6H_4	4-$MeCOC_6H_4Br$	82
8	C_6H_5	2-MeC_6H_4I	92



R = H, CH_3, CF_3, OCH_3, F, Cl, $COCH_3$, NO_2.
R^1 = H, NO_2,CN, $COCH_3$, CH_3, OCH_3, F, Cl.
i = $PdCl_2(dppf).CH_2Cl_2$ (2 mol%), *i*-Pr_2NEt (3 equiv), *i*-PrOH/H_2O (2:1), 10 min.
ii = $Pd(OAc)_2$ (0.6 mol%), EtOH/H_2O (1:1), 15 min.

Scheme 40.

The same source of energy was used to prepare biaryls from aryl-**122** and furyltrifluoroborates **124** and aryl- and heteroaryl halides **100** (Scheme 41) using ultra-low palladium concentration (2.5 ppm).[51] The reaction worked very well with a wide range of aryl bromides and iodides. However, when an aryl chloride was used the cross-coupling product was obtained in very low yield.

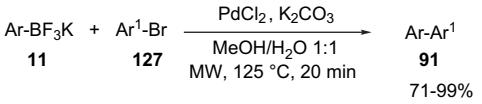


X = Cl, Br, I
R = H,OMe, Me, CF_3
Ar = 4-MeO-Ph, 4-Me-Ph, Ph, 3-CN-Ph, 4-HO-Ph, 4-NH_2-Ph 2-Me-Ph, 2-pyridyl, 2-furanyl, 4-MeOC-Ph

Scheme 41.

When electron-rich aryl bromides were reacted with potassium 3-thiophenetrifluoroborate **124** a decrease in the yield was observed, but the same reaction involving electron-poor substrates afforded good yields. The palladium source was an aqueous solution of elemental Pd stabilized by HCl. All reactions were completed within 5 min, using H_2O as the solvent and tetra-*n*-butylammonium bromide as a phase-transfer agent.

Recently, Harker and Crouch[52] described the synthesis of biaryls **91** by the Suzuki–Miyaura coupling of bromoarenes **127** with potassium aryltrifluoroborates **11** under microwave irradiation in a MeOH/H_2O solvent system (Scheme 42). The methodology works in the absence of phosphine ligands or phase-transfer catalyst.



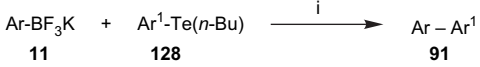
Ar^1 = 4-MeO-C_6H_4, 2-Me-C_6H_4, 4-CN-C_6H_4, 4-NO_2-C_6H_4, 4-MeC(O)-C_6H_4, 1-naphthyl
Ar^2 = C_6H_5, 3-thienyl

Scheme 42.

Organotellurium compounds have been used as the electrophilic reagent in several metal-catalyzed cross-coupling reactions such as Sonogashira, Negishi, and Heck.[53]

By taking advantage of the attractive features of potassium organotrifluoroborate salts **11** and the organotellurium compounds **128** as an alternative to the traditional aryl halides was recently reported the cross-coupling reaction between potassium aryltrifluoroborates and aryl tellurides catalyzed by palladium(0), affording biaryls **91** in good to excellent yields (Table 10).[54]

Table 10. Cross-coupling of aryl(*n*-butyl)tellurides **128** with potassium aryltrifluoroborates **11**

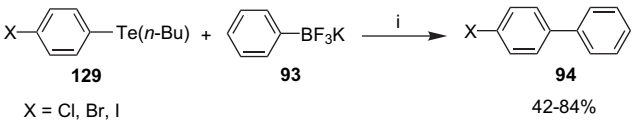


i = $Pd(PPh_3)_4$ (10 mol%), Et_3N (3 equiv), Ag_2O (2 equiv) MeOH, reflux

Entry	Ar	Ar^1	Yield (%)
1	C_6H_5	4-MeO-C_6H_4	82
2	C_6H_5	4-NO_2-C_6H_4	89
3	C_6H_5	2-Me-C_6H_4	74
4	C_6H_5	1-Naphthyl	79
5	C_6H_5	4-HO-C_6H_4	92
6	C_6H_5	4-MeO_2C-C_6H_4	83
7	C_6H_5	2-Furanyl	63
8	C_6H_5	3-Pyridyl	65
9	4-MeO-C_6H_4	1-Naphthyl	87
10	4-MeO-C_6H_4	4-Cl-C_6H_4	75
11	2-Furanyl	4-Cl-C_6H_4	52
12	3-MeO-C_6H_4	4-Cl-C_6H_4	80

The reaction tolerates both electron-withdrawing, electron-donating substituents and even *ortho*-substitution in both substrates, affording the corresponding biphenyl compound in good yield. However, this method was less effective for the reaction involving heteroarylic substrates.

In the same report was shown a study on the relative reactivity of the tellurium moiety compared to usual halides in the cross-coupling reaction (Scheme 43). The general order of relative reactivity observed was Te>I>Br≫Cl. The same order was observed in other Suzuki cross-coupling reactions involving different unsaturated tellurium species as will be shown in this review.

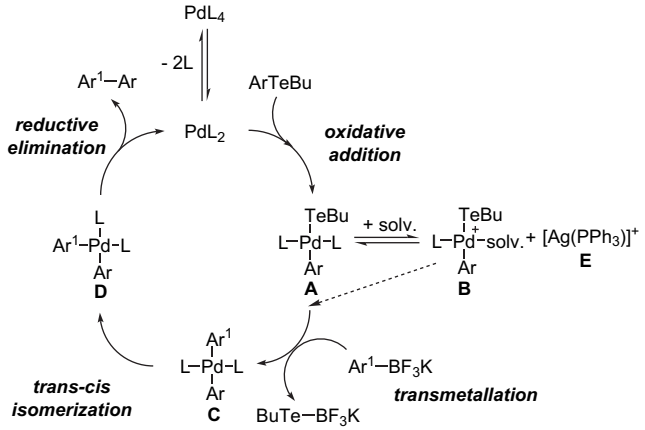


X = Cl, Br, I
i = $Pd(PPh_3)_4$ (10 mol%), Et_3N (3 equiv), Ag_2O (2 equiv), MeOH, reflux

Scheme 43.

By observations made using electrospray ionization mass spectrometry technique (ESI-MS) a catalytic cycle was proposed for this reaction (Scheme 44). In this proposed cycle, the aryl telluride oxidatively adds to the PdL_2 species leading to the tellurated palladium intermediate **A** that can exchange one ligand by a solvent molecule yielding the detected species **B**. In the transmetalation step of the catalytic cycle, both species **A** or **B** can react with the aryltriflouroborate where the tellurium moiety would be combined with the borate as its aryl group is transferred to palladium, forming the detected bis-arylated palladium intermediate **C**. The labile trans intermediate **C** should isomerize to the cis intermediate **D**, which suffers reductive elimination readily

since its abundance in the solution is very low. In this way the biarylic product is formed regenerating the starting zerovalent palladium catalyst.



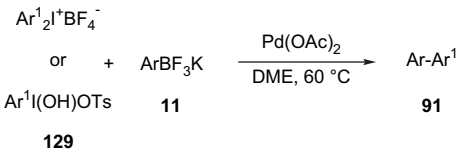
Scheme 44.

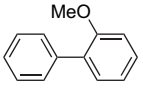
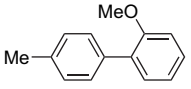
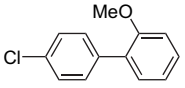
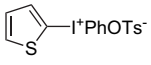
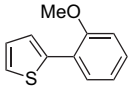
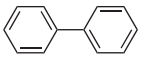
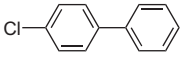
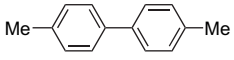
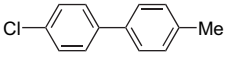
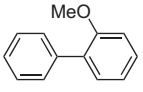
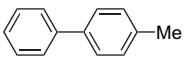
Xia and Chen[55] reported the use of hypervalent iodine species **129** (iodonium salts) as another alternative to the traditional Suzuki reaction (Table 11). Diaryliodonium tetrafluoroborate and hydroxyl(tosyloxy)iodobenzene (Koser's reagent) coupled with potassium aryltrifluoroborates **11** in presence of 5 mol % $Pd(OAc)_2$ to afford the biaryl systems **91** in excellent yields.

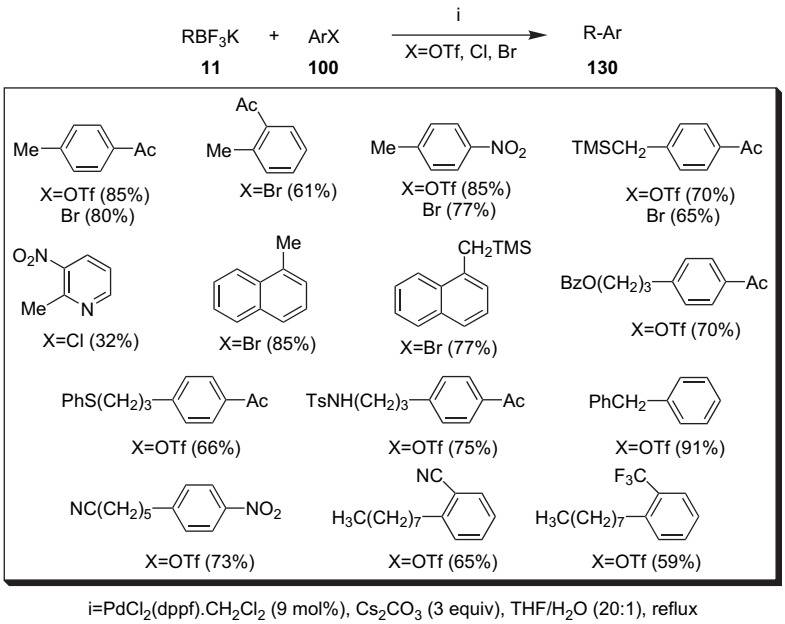
4.1.2. Alkylation of aryl and heteroaryl halides. Alkylation of aryl and heteroaryl halides or triflates was performed through the cross-coupling reaction of different aryl triflates and halides **100** and potassium alkyltrifluoroborate salts **11** using $PdCl_2(dppf)\cdot CH_2Cl_2$ and Cs_2CO_3 under reflux in THF/H_2O (Scheme 45).[23] Aryl triflates proved to be as reactive as aryl bromides. The reaction works better with *para*-aryl substrates than with *ortho*-aryl derivatives, probably due to steric effects. The reaction was tolerant with various functionalities such as cyano, ketone, ester, amide, and nitro groups despite the aqueous basic conditions.

It is well established that the reaction of 3-halopropylboranes with base leads to the synthesis of cyclopropanes.[56] However, it was observed that the cross-coupling reaction of potassium 3-chloropropyltrifluoroborate **131** with 4-acetylphenyltriflate **132** works well despite the basic conditions used (Scheme 46).[23]

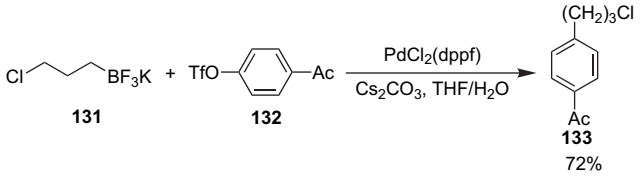
Table 11. Cross-coupling of hypervalent iodine **129** with potassium aryltrifluoroborates **11**



Entry	Iodonium salt	$ArBF_3K$	$Ar\text{-}Ar^1$	Yield (%)
1	$Ph_2I^+BF_4^-$	$2\text{-}MeOC_6H_4BF_3K$		87
2	$(4\text{-}MeC_6H_4)_2I^+BF_4^-$	$2\text{-}MeOC_6H_4BF_3K$		84
3	$(4\text{-}ClC_6H_4)_2I^+BF_4^-$	$2\text{-}MeOC_6H_4BF_3K$		81
4		$2\text{-}MeOC_6H_4BF_3K$		83
5	$Ph_2I^+BF_4^-$	$PhBF_3K$		99
6	$(4\text{-}ClC_6H_4)_2I^+BF_4^-$	$PhBF_3K$		92
7	$(4\text{-}MeC_6H_4)_2I^+BF_4^-$	$4\text{-}MeC_6H_4BF_3K$		95
8	$(4\text{-}ClC_6H_4)_2I^+BF_4^-$	$4\text{-}MeC_6H_4BF_3K$		89
9	PhI(OH)OTs	$2\text{-}MeOC_6H_4BF_3K$		87
10	PhI(OH)OTs	$4\text{-}MeC_6H_4BF_3K$		94

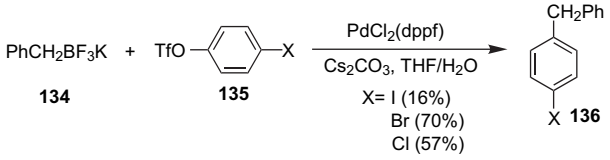


Scheme 45.



Scheme 46.

The reaction demonstrated a very highly selective coupling C–X bond in 4-bromo-, 4-chloro-, and 4-iodophenyltriflate **135** (Scheme 47).[11] In the case of 4-iodophenyltriflate the yield was lower due to the homocoupling reaction of the iodide.

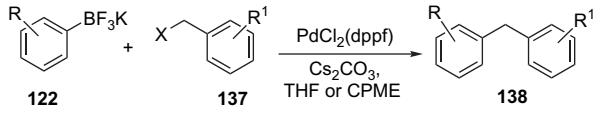


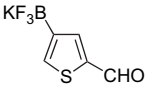
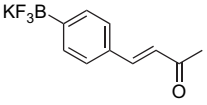
Scheme 47.

Recently, Molander and Elia[57] described the synthesis of diarylmethanes **138** by the palladium-catalyzed Suzuki–Miyaura cross-coupling of benzyl halides **137** with potassium aryltrifluoroborates **122** (Table 12).

Among the tested systems, the use of $PdCl_2(dppf)\cdot CH_2Cl_2$ with Cs_2CO_3 (3 equiv) in THF/H_2O or CPME/H_2O afforded the best conversion of the desired product **138**, requiring the lowest catalyst loading. The use of ethereal solvents affords the highest isolated yields with minimal homocoupling byproduct. The reaction was tolerant to a broad variety of functionality and it works well with both electron-rich and electron-poor substrates.

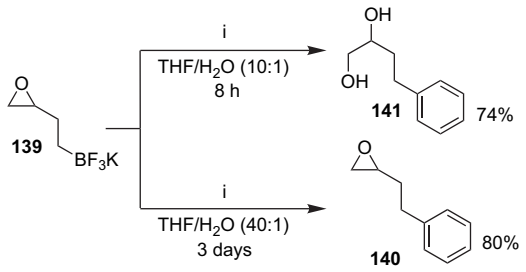
Table 12. Coupling of potassium aryltrifluoroborates **122** with benzyl halides **137**



Entry	$ArCH_2X$	$ArBF_3K$	Yield (%)
1	$C_6H_5CH_2Br$	$C_6H_5BF_3K$	84
2	$C_6H_5CH_2Cl$	4-$MeOC_6H_4BF_3K$	91
3	$C_6H_5CH_2Br$	4-$MeOC_6H_4BF_3K$	86
4	$C_6H_5CH_2Br$	2,6-$(Me)_2C_6H_3BF_3K$	82
5	$C_6H_5CH_2Br$	4-$CF_3C_6H_4BF_3K$	87
6	$C_6H_5CH_2Br$	4-$OHCC_6H_4BF_3K$	87
7	$C_6H_5CH_2Br$	3-$O_2NC_6H_4BF_3K$	69
8	$C_6H_5CH_2Br$		72
9	$C_6H_5CH_2Br$		70
10	4-$MeOC_6H_4CH_2Cl$	$C_6H_5BF_3K$	78

A Suzuki–Miyaura reaction was performed using the oxiranylethyltrifluoroborate **139** and 4-cyanophenyl bromide **102** in a THF/H_2O solvent system (Scheme 48).[33] The product formed in this reaction was totally dependent on the amount of water. The Suzuki product **140** was obtained in 80% yield, when a very small amount of water was used. However, when using a higher percentage of water the product observed was a diol **141** resulting from a cross-coupling/ring-opening type reaction.

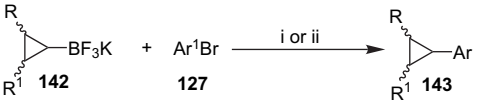
Potassium cyclopropyl trifluoroborates 1,2-disubstituted[29] and 1,2,3-trisubstituted[30] **142** were successfully employed in cross-coupling reaction with aryl bromides **127** in the



i = 4-cyanophenyl bromide **102**, $PdCl_2(dppf).CH_2Cl_2$ (9 mol%), Cs_2CO_3, reflux.

Scheme 48.

presence of a palladium catalyst, affording the substituted aryl cyclopropanes in good yields (Scheme 49). In both cases, the configuration of stereodefined potassium cyclopropyltrifluoroborate salts was preserved after the cross-coupling reaction **143**.

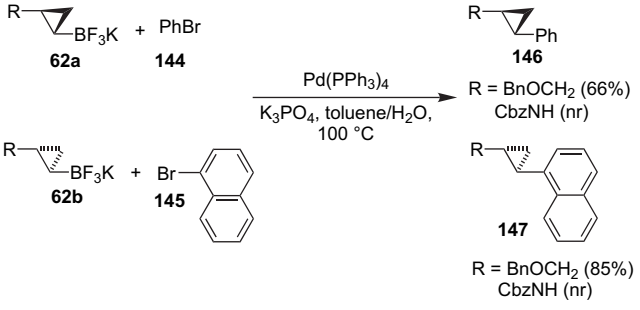


R = Ph, $PhCH_2$, n-C_5H_{11}, $BnOCH_2$
R^1 = H, CH_2OH, $CH_3(OH)CH$
Ar^1 = 4-MeCO-Ph, 4-Ph-Ph, 4-CN-Ph, 4-NO_2-Ph, 2-MeO-Ph

i = $Pd(PPh_3)_4$ (2 mol%), toluene/H_2O, K_3PO_4 .H_2O, reflux.
ii = $Pd(OAc)_2$ (3 mol%), 2-biphenyldicyclophexylphosphine, toluene/H_2O, K_3PO_4, 100 °C

Scheme 49.

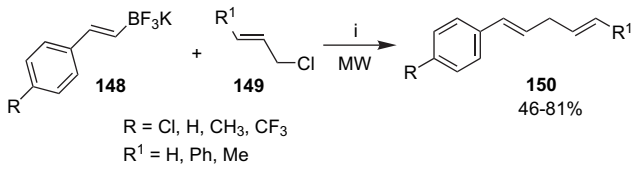
Using a similar methodology as described above, two examples of enantiomerically pure cyclopropyl trifluoroborates **62** were coupled with aryl bromides (Scheme 50).[31] When amine derivatives of this cyclopropyl trifluoroborates were used no reaction was observed.



Scheme 50.

4.1.3. Allylation and crotylation reactions. A microwave-enhanced Suzuki cross-coupling reaction between vinyltrifluoroborates **148** and allyl chlorides **149** (Scheme 51) was shown by Kabalka and co-workers.[58] In the study to determine the best conditions, interestingly, it was found that allyl chloride produces better results than other allyl halides.

1,4-Pentadienes **152** were synthesized by a Suzuki cross-coupling reaction of allyl- and cinnamyl acetates **151** with

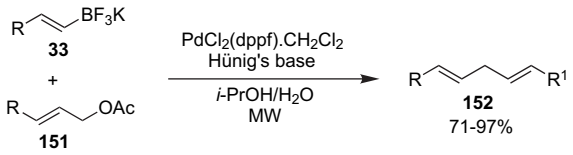


R = Cl, H, CH_3, CF_3
R^1 = H, Ph, Me

i = $PdCl_2(dppf).CH_2Cl_2$ (2 mol%), i-PrOH/H_2O, Hünig's base

Scheme 51.

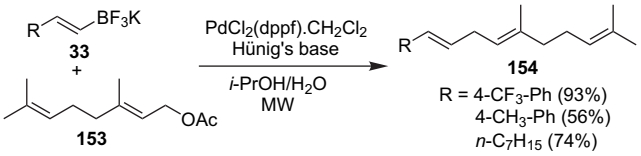
various potassium vinyl- and arylvinyltrifluoroborates **33** under microwave irradiation (Scheme 52).[59] The coupling reactions are stereoselective since the E isomers are the only observed products, and also regioselective.



R = Ph, 4-CF_3-Ph, 4-CH_3-Ph, 4-Cl-Ph, n-C_7H_{15}
R^1 = H, Ph

Scheme 52.

Geranyl acetate **153** was also employed as allylating agent to produce a variety of 1,4,7-trienes **154** in moderate-to-excellent yields under the same conditions (Scheme 53).



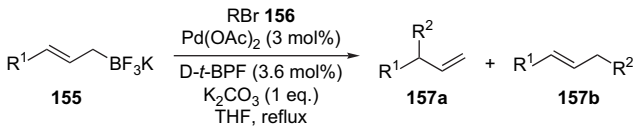
Scheme 53.

Recently, Yamamoto et al.[60] described a high γ-selective cross-coupling reaction of potassium allyltrifluoroborate salts **155** with aryl and 1-alkenyl bromides **156** (Table 13). In this reaction, the yields and regioselectivities of the coupling position were highly sensitive to phosphine ligands employed, and the product formation was very slow in the absence of a base. The reaction proceeded in reflux of THF in the presence of K_2CO_3 as a base and catalyst generated in situ from $Pd(OAc)_2$ and 1,1′-bis-(di-t-butylphosphino)ferrocene, affording the products in very good regioselectivities (>99/1 in favor of the alkene **157a**) and good yields.

4.1.4. Alkynylation of aryl and heteroaryl halides. Aryl- and heteroaryl acetylenes **158** were synthesized by the reaction of potassium alkynyltrifluoroborates **16** with aryl- and heteroaryl bromides and triflates **100** containing various functionalities such as cyano, aldehyde, amine, ketone, hydroxyl groups, and carboxylic acids.[17] Some representative examples are shown in Table 14. After a study of reactivity of various electrophiles with the potassium alkynyltrifluoroborate **16** was established a new reactivity order: OTf>Br>I≈Cl.

The reaction works well with activated heteroaryl chlorides **113** to provide the functionalized heteroaryl alkyne **160** in

Table 13. γ-Selective cross-coupling reaction of aryl and 1-alkenyl bromides **156** with potassium allyltrifluoroborate salts **155**



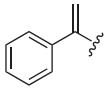
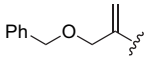
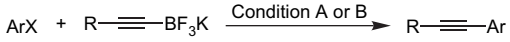
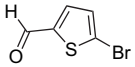
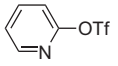
Entry	R^1	R^2	Yield (%)
1	H	3-MeO_2C-C_6H_4	38
2	CH_3	4-H_2N-C_6H_4	80
3	CH_3	4-BzHN-C_6H_4	96
4	CH_3	4-CH_3O-C_6H_4	90
5	CH_3	2,6-$(CH_3)_2$-C_6H_3	87
6	CH_3	2-MeO_2C-C_6H_4	92
7	CH_3	4-CN-C_6H_4	77
8	CH_3		75
9	CH_3		66
10	CH_3		65
11	c-C_6H_{11}	3-MeO_2C-C_6H_4	98

Table 14. Cross-coupling reaction of aryl halides and triflates **100** with potassium alkynyltrifluoroborates **16**

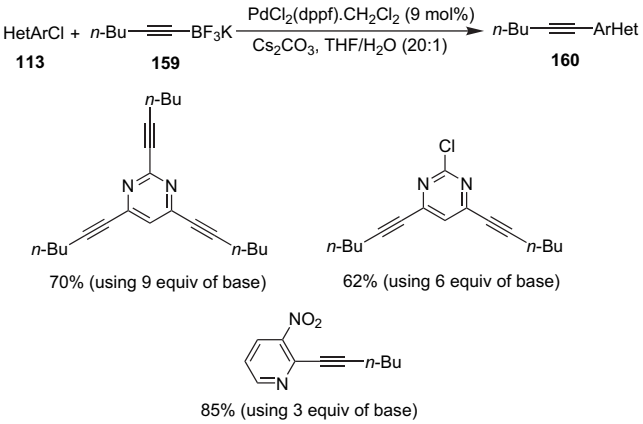


Entry	ArX	R	Reaction conditions[a]	Yield (%)
1	4-CN-Ph-Br	*n*-Bu	A	98
2	4-HO-Ph-Br	*n*-Bu	A, B	48, Traces
3	4-Me_2N-Ph-Br	*n*-Bu	A, B	61, 33
4	4-HO_2C-Ph-Br	*n*-Bu	A	73
5		*n*-Bu	A, B	46, 97
6		*n*-Bu	A, B	47, 88
7		*n*-Bu	B	31
8	4-MeOC-Ph-OTf	*n*-Bu	B	87
9	4-NO_2-Ph-OTf	*n*-Bu	B	98
10	4-CN-Ph-Br	Ph	A	69
11	4-CN-Ph-Br	$Cl(CH_2)_3$	A	85
12	4-CN-Ph-Br	TBDMSO$(CH_2)_2$	A	88
13	4-CN-Ph-Br	TMS	A	60

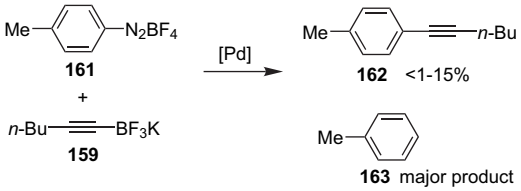
[a] Condition A: $PdCl_2(dppf)\cdot CH_2Cl_2$ (9 mol %), Cs_2CO_3 (3 equiv), THF/H_2O (20:1), reflux, 12 h. Condition B: $PdCl_2(dppf)\cdot CH_2Cl_2$ (9 mol %), Cs_2CO_3 (3 equiv), THF(anhydrous), reflux, 12 h.

good yields (Scheme 54).[17] When the 2,4,6-trichloropyrimidine was used the trisubstituted product was obtained by the use of 9 equiv of base, while the 2,4-disubstituted was obtained when 6 equiv of base were employed.

Genêt and co-workers[5b] reported that the cross-coupling reaction of alkynyltrifluoroborates **159** and toluenediazonium tetrafluoroborates **161** works in a very small scale (Scheme 55). The major product **163** observed resulted from decomposition of benzenediazonium.

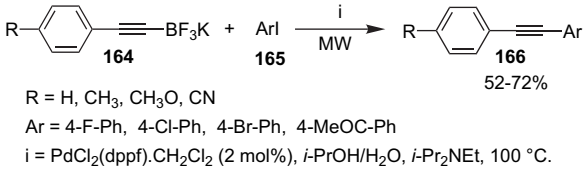


Scheme 54.



Scheme 55.

Potassium alkynyltrifluoroborate salts **164** have cross-coupled with aryl iodides **165** under microwave irradiation in presence of a palladium catalyst to afford aryl alkynes **166** in good yields (Scheme 56).[61]



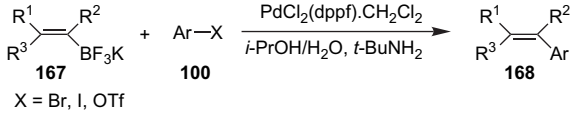
Scheme 56.

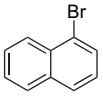
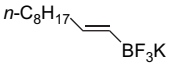
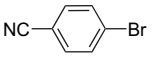
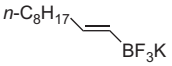
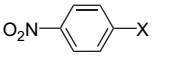
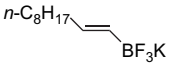
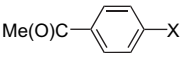
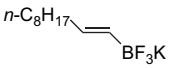
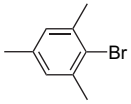
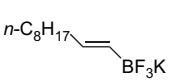
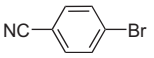
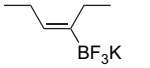
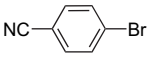
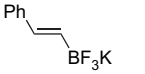
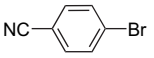
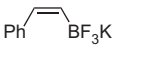
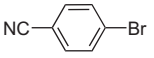
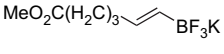
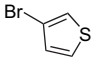
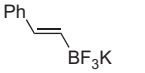
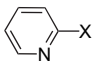
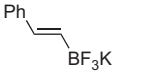
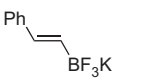
4.1.5. Alkenylation reaction. A efficient coupling reaction of different aryl halides and triflates **100** with potassium alkenyltrifluoroborates **167** was carried out in presence of $PdCl_2(dppf)\cdot CH_2Cl_2$, *i*-PrOH/$H_2O$ as solvent and *t*-$BuNH_2$ as a base (Table 15).[22] The reaction of potassium alkenyl trifluoroborates with heteroaryl halides was also studied; applying the same conditions used in the aryl halide and aryl triflate cross-coupling, good yields were obtained in most cases.

In an extension of this study, the cross-coupling reactions were carried out between potassium aryl- and heteroaryltrifluoroborates **11** and alkenyl bromides **169** (Table 16).[62] The reaction was catalyzed by $Pd(PPh_3)_4$ or in some cases by $PdCl_2(dppf)\cdot CH_2Cl_2$, in presence of K_2CO_3 as a base, and toluene/H_2O (2.6:1) as solvent mixture, affording the aryl olefins **168** in good to excellent yields.

In both reports the obtained results indicated the stereospecificity and the compatibility with the presence of various functional groups, such as aldehydes, ketones, nitro, ciano,

Table 15. Suzuki reaction involving potassium alkenyltrifluoroborates **167** and aryl halides **100**



Entry	Electrophile	Nucleophile	Yield (%)
1			78
2			87
3			71 (X=Br), 76 (X=OTf)
4			69 (X=Br), 60 (X=OTf), 65 (X=I)
5			38
6			70
7			80
8			86
9			33
10			80
11			70 (X=Br), 41 (X=OTf)
12			70

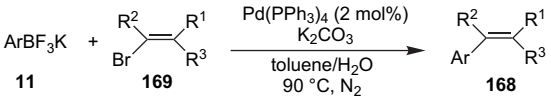
enones, and silyl ether protecting groups. The reaction was demonstrated to be tolerant of substitution patterns in both coupling partners.

4.1.6. Styrenes and related systems. Styrene units are synthetically useful intermediates in the formation of new polymeric materials, and these structures are widely encountered in various natural products.

Genêt et al.[5b,63] proved that potassium vinyltrifluoroborate **170** is an efficient vinylating agent of arenediazonium compounds **171** (Table 17). The reaction was tolerant of a wide range of substituents in the arenediazonium and highly chemoselective since bromide, iodide, and triflate substituents do not participate in the coupling reaction.

The cross-coupling reaction involving arenediazonium salts **171** and potassium vinyltrifluoroborate **170** was catalyzed by an azapalladacycle complex (0.1 mol %) at room temperature using an ionic liquid as reaction media to afford the coupled product in high yield (Scheme 57).[41]

Table 16. Suzuki reaction involving potassium aryltrifluoroborates **11** and alkenyl bromides **169**



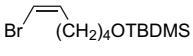
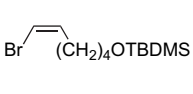
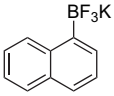
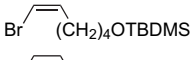
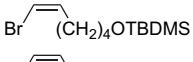
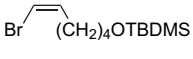
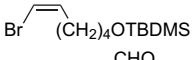
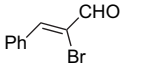
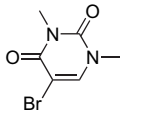
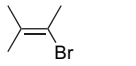
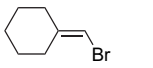
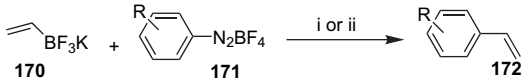
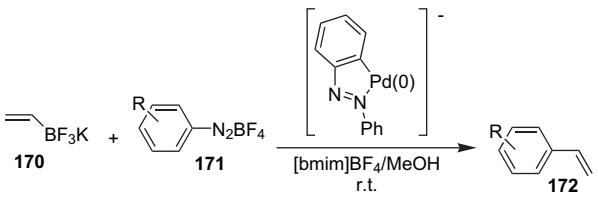
Entry	Alkenyl bromide	$ArBF_3K$	Yield (%)
1		$PhBF_3K$	97
2			>99
3		2-Me-$PhBF_3K$	91
4		2,6-$(Me)_2$-$PhBF_3K$	82
5		4-OHC-$PhBF_3K$	89
6		3-Thiophenyl-BF_3K	>99
7		$PhBF_3K$	94
8		$PhBF_3K$	88
9		4-OHC-$PhBF_3K$	94
10		3-OHC-$PhBF_3K$	85

Table 17. Cross-coupling reaction of potassium vinyltrifluoroborate **170** with arenediazonium compounds **171**



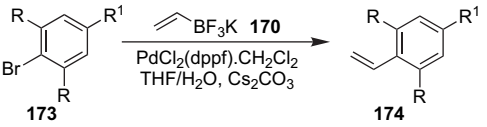
Entry	R	Yield (%)
1	4-PhC(O)	86
2	3-PhC(O)	81
3	4-MeO	81
4	2-Me	78
5	4-NO_2	84
6	4-EtO_2C	88
7	4-HO_2C	72
8	4-Br	70
9	4-TfO	75
10	3-I	76

The vinylation of hindered aryl bromides **173** was achieved using an excess of potassium vinyltrifluoroborates **170** in the presence of $PdCl_2(dppf)\cdot CH_2Cl_2$, cesium carbonate as a base and THF/H_2O as solvent mixture (Scheme 58).[64] Despite good yield obtained when benzyl 3,5-bis(benzyloxy)-4-bromobenzoate in the optimization of the reaction



Scheme 57.

conditions, the vinylation of other examples studied afforded the coupled product in low to medium yields and the reactions required long reaction times (2–7 days).

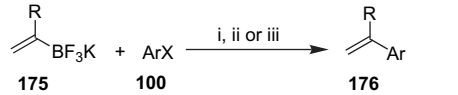


R = OBn; R^1= CO_2Bn (87%)
R = R^1 = Me (32%)
R = OMe; R^1 = CO_2Et (53%)

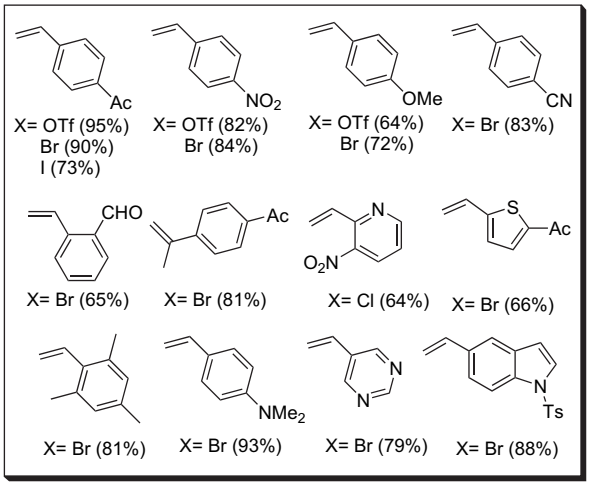
Scheme 58.

An inconvenience in this reaction is the formation of the reduced product (bromide replaced by hydrogen), however, it could be eliminated by use of 5 equiv of the vinyltrifluoroborate salt **170**.

In a very extensive study, Molander et al.[8,65] showed that palladium-catalyzed cross-coupling reactions of potassium vinyltrifluoroborates **175** with aryl or heteroaryl halides and triflates **100** afford functionalized styrenes **176** in good to excellent yields (Scheme 59). The reaction was tolerant to many functional groups, such as ketone, nitro, ether, aldehydes, and nitrile.



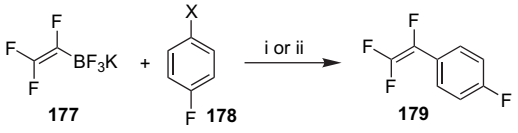
i = $PdCl_2$(dppf).CH_2Cl_2 (2 mol%), Et_3N, *i*-PrOH or MeOH
ii = $PdCl_2$ (2 mol%), PPh_3 (6 mol%), Cs_2CO_3, THF/H_2O
iii = $PdCl_2$ (2 mol%), RuPhos (6 mol%), Cs_2CO_3, THF/H_2O



Scheme 59.

It was observed that electronic and steric effects of the substituents in the ring do not affect the yield reactions, however, the time reaction was affected: electron-deficient rings react faster than electron-rich rings.

The first example of a cross-coupling reaction using a perfluoroalkenylboron reagent was reported in 2002 by Frohn and co-workers.[42a] The perfluorinated analog of potassium vinyltrifluoroborate **177** reacted with the arenediazonium tetrafluoroborates **178** in low yield, 40% (Scheme 60). In a posterior report,[42b] the use of aryl iodide increased the yield to 76%.



X = N_2BF_4 (40%)
I (76%)

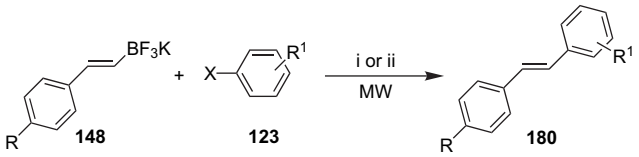
i = $Pd(PPh_3)_4$, dioxane.
ii = $Pd(OAc)_2$, PPh_3, Ag_2O, K_2CO_3, toluene.

Scheme 60.

4.1.7. Stilbenes and related systems. Stilbenes are a very important class of compounds that exhibit many biological activities, e.g., antineoplastic, antimicrobial, multi-drug-resistant, antiangiogenesis, cytotoxic, and inhibit cell proliferation. Due to these facts the synthesis of stilbene structures has attracted considerable attention of the organic chemists.[66]

Recently, (*E*)- and (*Z*)-stilbenes were prepared by the Suzuki–Miyaura cross-coupling reaction involving potassium organotrifluoroborates under microwave[51,61] or ultrasound[67] irradiation.

Using microwave irradiation it was possible to prepare various (*E*)-stilbenes **180** using substituted bromo[51] or iodobenzenes[61] **123** and (*E*)-styryltrifluoroborate salts **148** catalyzed by elemental palladium or $PdCl_2(dppf)\cdot CH_2Cl_2$ (Scheme 61).



61-99%

X = Br or I
R = CF_3, Cl, CH_3
R^1 = COMe, Me, F, Cl

i = Pd^0, Na_2CO_3, TBAB, H_2O.
ii = $PdCl_2$(ddpf).CH_2Cl_2 (2 mol%), *i*-PrOH-H_2O, *i*-Pr_2NEt.

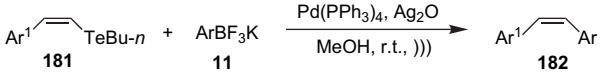
Scheme 61.

Interestingly, Kabalka et al.[61] reported that under their reaction conditions the reactions are stereoselective, while in the report of Leadbeater and co-workers[51] the stilbenes were obtained in an *E*, *Z* alkene mixture.

The ultrasound-assisted cross-coupling reaction between the (*Z*)-styryl *n*-butyltellurides **181** and potassium aryltrifluoroborate salts **11** catalyzed by $Pd(PPh_3)_4$ in the presence of

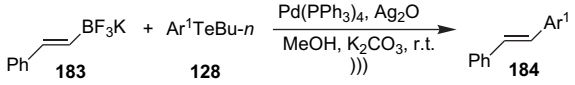
Ag_2O afforded the (*Z*)-stilbenes **182** in good yields (Table 18).[67] The (*E*)-stilbenes **184** were synthesized in good to excellent yields from the cross-coupling reaction between the potassium (*E*)-styryltrifluoroborate **183** and *n*-butyl(aryl)-tellurides **128** (Table 19). In the latter case it was necessary to use K_2CO_3 as a base to improve the yield.

Table 18. Synthesis of (*Z*)-stilbenes **182** from the cross-coupling reaction of (*Z*)-styryl *n*-butyltellurides **181** with potassium aryltrifluoroborates **11**



Entry	Ar^1	Ar	Yield (%)
1	C_6H_5	C_6H_5	82
2	C_6H_5	4-Cl-C_6H_4	70
3	C_6H_5	4-MeO-C_6H_4	60
4	C_6H_5	4-Me-C_6H_4	78
5	C_6H_5	2-Me-C_6H_4	62
6	C_6H_5	1-Naphthyl	70
7	4-Me-C_6H_4	C_6H_5	76
8	4-Br-C_6H_4	C_6H_5	78

Table 19. Synthesis of (*E*)-stilbenes **184** from the cross-coupling reaction of potassium (*E*)-styryltrifluoroborate **183** with *n*-butyl(aryl)tellurides **128**

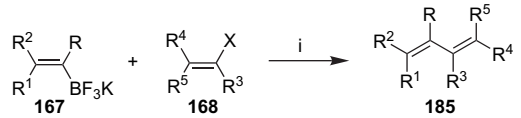


Entry	Ar^1	Yield (%)
1	C_6H_5	90
2	1-Naphthyl	87
3	4-MeO-C_6H_4	75
4	2-Me-C_6H_4	91
5	4-MeO_2C-C_6H_4	72
6	4-Br-C_6H_4	91
7	4-I-C_6H_4	71
8	3-Pyridyl	69

The reaction is stereoselective and relatively insensitive to the nature of the substituents in both substrates. The cross-coupling reaction was very chemoselective and once again the tellurium moiety proved to be more reactive than halide atoms.

4.1.8. Dienes. The synthesis of dienes has represented one of the long-standing challenges in organic synthesis owing to their presence in biologically active compounds. To offer more approaches, some methodologies to synthesize dienes using potassium organotrifluoroborates were developed.

(*E*,*E*)-, (*E*,*Z*)-, (*Z*,*E*)-, or (*Z*,*Z*)-conjugated dienes **185** were stereospecifically produced by Suzuki–Miyaura cross-coupling reaction of alkenyltrifluoroborates **167** with a variety of alkenyl bromides **168** (stereodefined reagents) bearing various functionalities and substitution patterns (Scheme 62).[68]

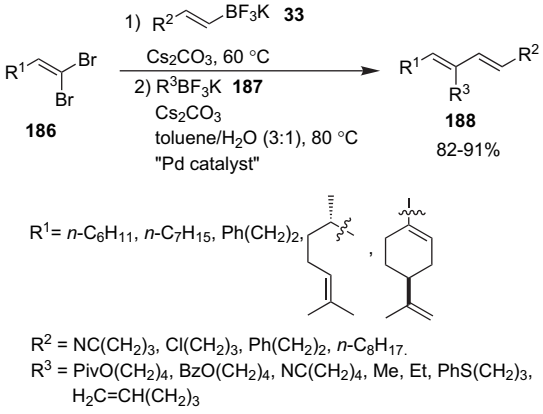


i = $Pd(OAc)_2$ / PPh_3 (2 eq.), Cs_2CO_3 (3 eq.), THF/H_2O (10:1), 70 °C.

Scheme 62.

Despite the presence of a fluoride source, alkenyl bromides bearing silyl ethers, such as TES, TBDMA, and TIPS did not loose the silyl groups during the cross-coupling reaction.

The same authors reported the sequential and stereoselectively coupling reaction of 1,1′-dibromoalkenes **186** with alkenyl **32** and alkyltrifluoroborates **187** leading to trisubstituted conjugated dienes **188** in excellent yields (Scheme 63).[69] In all cases, just one stereoisomer of the desired product was obtained.



Scheme 63.

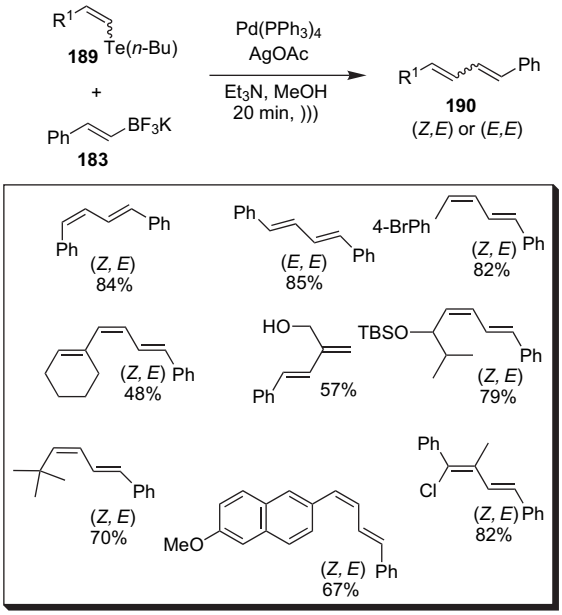
Functionalized potassium alkyltrifluoroborate salts **187** were effective substrates for the reaction conditions developed. However, methyl-, ethyl-, and 4-pentenyltrifluoroborates required higher temperature (90 °C) and the change of $Pd(PPh_3)_4$ catalyst to the $PdCl_2(dppf)\cdot CH_2Cl_2$ complex.

The use of unsaturated tellurium species was previously[54] demonstrated to be a very advantageous option to the traditional halides in the Suzuki–Miyaura reactions using organotrifluoroborates as nucleophilic partners.

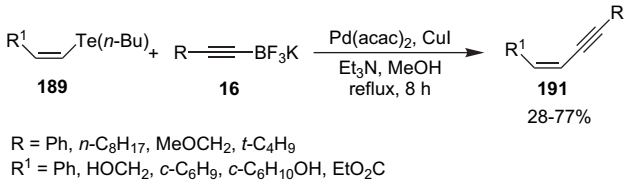
The ultrasound-assisted synthesis of stereodefined dienes was reported using the coupling reaction of vinylic tellurides **189** and β-styryltrifluoroborate salt **183** affording 1,3-dienes **190** in moderate to good yields (Scheme 64).[70] The presence of functionalities was well tolerated and the silyl group attached to a hydroxyl remains intact.

4.1.9. Enynes. The synthesis of 1,3-enynes via Suzuki–Miyaura reaction of vinylic tellurides **189** and potassium alkynyltrifluoroborate salts **16** in the presence of $Pd(acac)_2$, CuI, Et_3N as a base and MeOH as solvent afforded the product **191** in moderate to good yields (Scheme 65).[71] The stereochemical outcome of the reaction shows that it proceeds in a stereoconservative way, resulting in only the (*Z*)-enyne.

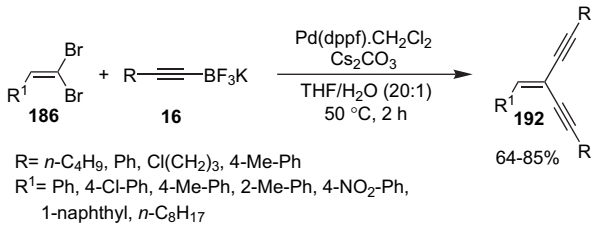
The presence of functional groups such as –OH, $–OCH_3$, $EtO_2C–$, and conjugated double and triple C–C bond was tolerated. However, when vinylic tellurides bearing nitrogenated groups, such as $(Et)_2NCH_2–$ or morpholine were used, no reaction was observed. A probable explanation would be the suggested coordination of the nitrogen and tellurium atoms with the palladium forming a stable six-membered ring complex.[72]



Scheme 64.



Scheme 65.



Scheme 66.

4.1.10. Enediynes. Enediynes have extensive application in non-linear optics (NLO), macrocyclic ligands, optical switches, and the synthesis of polycyclic aromatic hydrocarbons (PAHs). Other application of enediyne structures is in the pharmaceutical chemistry; they are highly potent antibiotic and antineoplastic agents. However, the methods to prepare enediynes are limited.

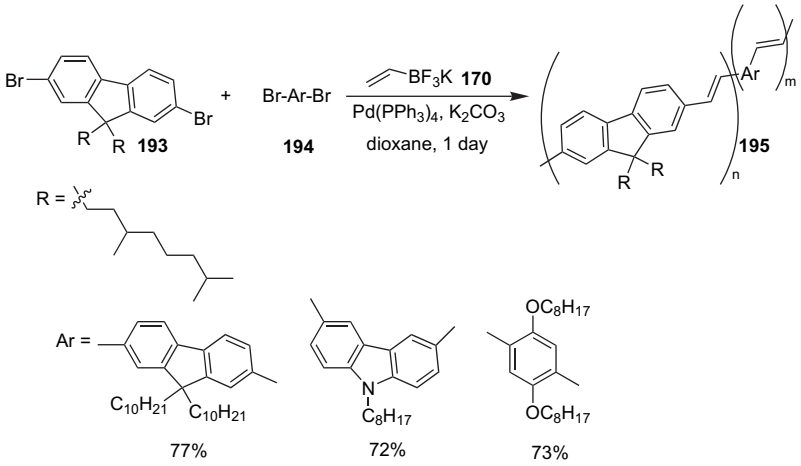
One more alternative to synthesize these compounds was developed through the reaction of 1,1-dibromo-1-alkenes **186** with potassium alkynyltrifluoroborates **16** (Scheme 66).[73] No special differences in the reactivity with respect to the electronic and steric effects on the substituents were observed.

4.1.11. Cascade Suzuki–Heck reaction. Nobile and coworkers[74] reported the synthesis of some poly(phenylenevinylenes) (PVPs) **195** by a cascade Suzuki–Heck reaction involving reaction of potassium vinyltrifluoroborate **170** with aryl dibromide compounds **194** (Scheme 67).

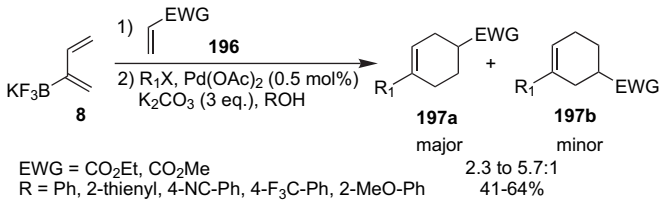
4.1.12. Diels–Alder/cross-coupling reactions. The potassium 1,3-dienyl-2-trifluoroborates **8** and the corresponding TBA salts were submitted to a series of tandem Diels–Alder/cross-coupling reactions without isolation and characterization of the boron intermediates (Scheme 68).[14] The trifluoroborate diene **8** was heated in presence of the dienophile **196**, $Pd(OAc)_2$, K_2CO_3, and refluxed in EtOH or MeOH.

The sequence seems to be useful for unsubstituted, electron-donating, or electron-withdrawing substituted phenyl halides and heteroaromatic halides. The regioselectivity of the reaction was affected by the substituents in the aryl halides. Comparison between the yields of the reaction of the tetra-*n*-butylammonium salt and the trifluoroborate does not indicate relevant difference.

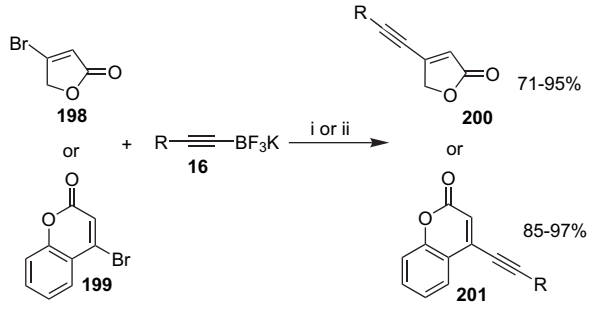
4.1.13. α,β-Unsaturated carbonylic compounds. 4-Bromo-2(*H*)-furanones **198** and 4-bromocoumarins **199** were transformed to their corresponding alkynyl compounds **200** and **201** with excellent yields by palladium-catalyzed Suzuki–Miyaura reaction (Scheme 69).[75]



Scheme 67.

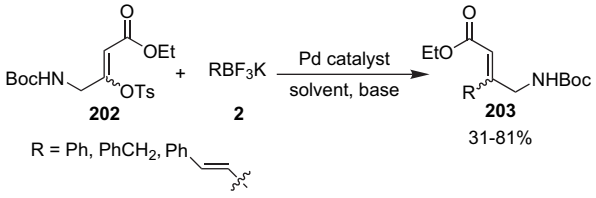


Scheme 68.



Scheme 69.

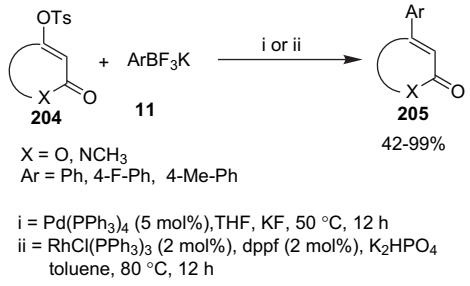
Enol tosylates are emerging as important alternatives to enol triflates and vinyl halides in Pd-catalyzed cross-coupling reactions. Taking advantage of this fact, Steinhuebel and co-workers[76] have reported the Suzuki–Miyaura cross-coupling reaction of (*E*)- and (*Z*)-enol tosylates **202** with potassium organotrifluoroborates **2** catalyzed by palladium, affording the product **203** in moderate to good yields (Scheme 70).



Scheme 70.

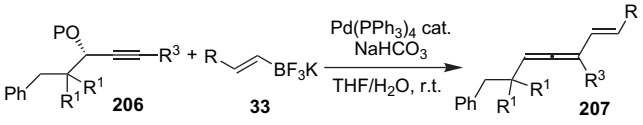
Wu and co-workers[77] reported the palladium-catalyzed cross-coupling reaction involving alkenyl tosylates **204** (coumarins or quinoline derivatives) and potassium aryltrifluoroborates **11** (Scheme 71). The coupled products **205** were produced in good yields. Recently,[78] the same authors reported the first example of a rhodium-catalyzed Suzuki–Miyaura reaction between the same substrates described above (Scheme 71).

4.1.14. Ene-Allenes. Allenes are becoming increasingly important as synthetic targets, both in natural products and in other biologically active compounds. In this way, various chiral ene-allenes **207** were synthesized by an analogous Suzuki–Miyaura reaction with alkenyl trifluoroborates **33** and propargylic carbonates and phosphates **206** (Table 20).[79]



Scheme 71.

Table 20. Suzuki–Miyaura reaction of alkenyl trifluoroborates **33** and propargylic carbonates and phosphates **206**



Entry	R	R^1	P	R^3	Yield (%)
1	Ph	Me	CO_2Me	n-C_8H_{17}	84
2	Ph	H	CO_2Me	H	70
3	H	H	$P(O)(OEt)_2$	$(CH_2)_3CN$	56
4	Ph	Me	CO_2Me	$(CH_2)_3CN$	76
5	H	Me	CO_2Me	$(CH_2)_3CN$	71
6	H	Me	CO_2Me	$(CH_2)_4OH$	63
7	H	Me	CO_2Me	$(CH_2)_4N(Bn)_2$	53
8	H	Me	CO_2Me	$(CH_2)_3CHO$	19
9	H	H	CO_2Me	$(CH_2)_4OTBS$	74
10	$(CH_2)_3Cl$	Me	CO_2Me	H	69
11	H	Me	CO_2Me	$(CH_2)_4SPh$	73
12	n-C_8H_{17}	H	CO_2Me	$(CH_2)_3SO_2Ph$	60

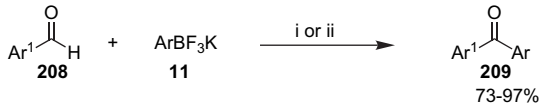
Many functional groups were tolerated by the reaction such as nitrile, protected and unprotected alcohols, amines, chlorides, and sulfur-containing substrates. Other classes of trifluoroborates were investigated, such as aryl, alkynyl, and alkyl, but only the aryltrifluoroborate coupled to generate the allene in the optimized conditions of the reaction, leading to the product in 26% yield and 80% ee.

The authors suggested that the observed racemization was probably due to an initial rapid formation of allene possessing high ee followed by a prolonged period in which little or no additional product was formed and racemization of the product occurred.

4.2. Other metal-catalyzed reactions

4.2.1. Ketones. The conversion of aldehydes into ketones is a very important process in organic synthesis. A recent report[80] presented a catalytic cross-coupling reaction of aryltrifluoroborates **11** with arylaldehydes **208** to afford

a great variety of diaryl ketones **209** (Scheme 72). The Heck-type reaction was catalyzed by a rhodium catalyst ($[Rh(CH_2CH_2)_2Cl]_2$) in presence of a phosphine.



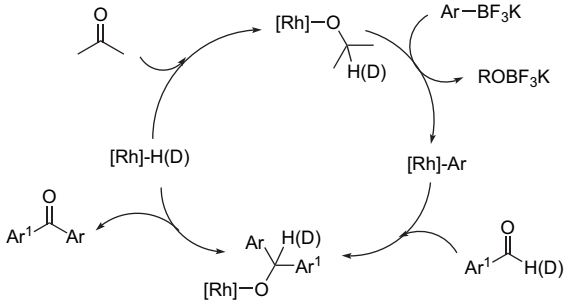
Ar = Ph, 3-Br-Ph, 3-F_3C-Ph, 2-Me-Ph, mesityl.
Ar^1 = 4-MeO-Ph, 2-MeO-Ph, 4-F-Ph, 3-HO-Ph, 2-furanyl, 2-thienyl, 4-HO-3-MeO-Ph.

i = $[Rh(CH_2CH_2)_2Cl]_2$ (1.5 mol%), P(*t*-Bu)$_3$, toluene/acetone/water, 80 °C.
ii = $[Rh(CH_2CH_2)_2Cl]_2$ (1.5 mol%), P(*t*-Bu)$_3$, 1,4-dioxane/acetone, 80 °C.

Scheme 72.

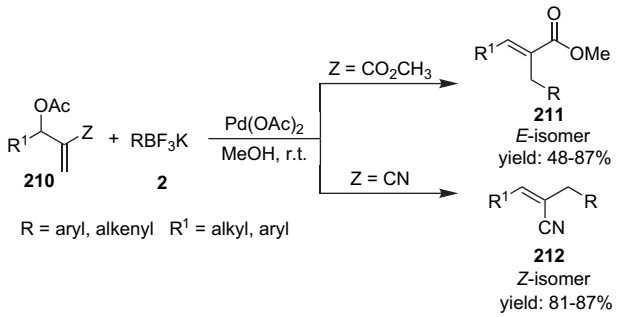
Good to excellent yields were obtained with several substitution patterns on the reaction partners. The coupling of heterocyclic aldehydes works well, but aliphatic aldehydes failed to react under these conditions.

The authors proposed a mechanism, which seems to involve a transmetalation of the organometallic reagent to rhodium(I) complex, followed by insertion of the aldehyde into the aryl-rhodium(I). β-Hydride elimination from the generated alkoxorhodium(I) complex, which would release diaryl ketones and a rodhium(I) hydride species is depicted in Scheme 73.



Scheme 73.

4.2.2. Cross-coupling reaction with Baylis–Hillman adducts. The cross-coupling reaction of potassium organotrifluoroborates **2** with acetates of Baylis–Hillman adducts **210** was developed using palladium catalyst and methanol as the solvent at room temperature (Scheme 74).[81] The reaction proceeds readily in moderated to excellent yields in the presence of $Pd(OAc)_2$ and no additional base or ligand is required.

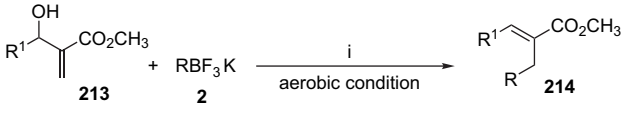


R = aryl, alkenyl R^1 = alkyl, aryl

Scheme 74.

3-Acetoxy-2-methylenealkanoates react with a variety of potassium organotrifluoroborates to provide (*E*)-2-substituted 2-alkenoates **211**. The reaction of 3-acetoxy-2-methylenealkanenitriles provides (*Z*)-2-substituted alk-2-enenitriles **212**. In all cases studied, the stereoselectivity was found to be >98:2. The reaction seems to be general to potassium trifluoroborates including aryl, heteroaryl, and even sterically hindered trifluoroborate salts.

In the presence of a rhodium complex, inactivated Baylis–Hillman adducts **213** react regioselectively with potassium organotrifluoroborates **2**, affording stereodefined trisubstituted alkenes **214** in good yields (Scheme 75).[82] This highly efficient reaction, in aerobic conditions, low temperature, and in absence of phosphine ligands, is believed to proceed via a 1,4-addition/β-hydroxy elimination mechanism.



R = aryl, alkenyl
R^1 = CH_3, *i*-C_4H_9, *n*-C_9H_{19}, C_6H_5, 1-$C_{10}H_7$

E/Z ratio: 96/4 - 99/1
yield: 44-98 %

i = $[Rh(cod)Cl]_2$ (0.05 - 1.5 mol%), $PhCH_3/CH_3OH$, 70 °C

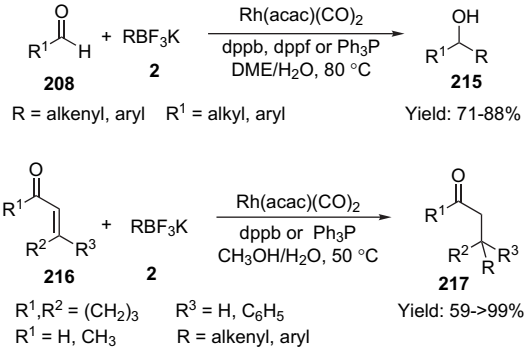
Scheme 75.

The presence of a protic solvent was essential to achieve high conversion of the starting Baylis–Hillman adduct. Among the binary mixtures evaluated, a toluene/methanol mixture proved to be suitable, achieving high yields and isomeric ratios (99/1) in favor of the (*E*) isomer.

4.3. 1,2- and 1,4-Addition reactions

4.3.1. Addition to ketones, aldehydes, and esters. The 1,2- and 1,4-additions of organometallic reagents to unsaturated carbonyl compounds are some of the most important and versatile reactions in organic synthesis.[83] Trivalent organoboronic acids can efficiently add to unsaturated substrates in the presence of catalytic amounts of rhodium catalysts.[84]

In the presence of phosphine ligands, asymmetric versions have been developed. Batey et al.[85] demonstrated that potassium organotrifluoroborates **2** participated in rhodium-catalyzed 1,2- and 1,4-additions to aldehydes **208** and enones **216** (Scheme 76).



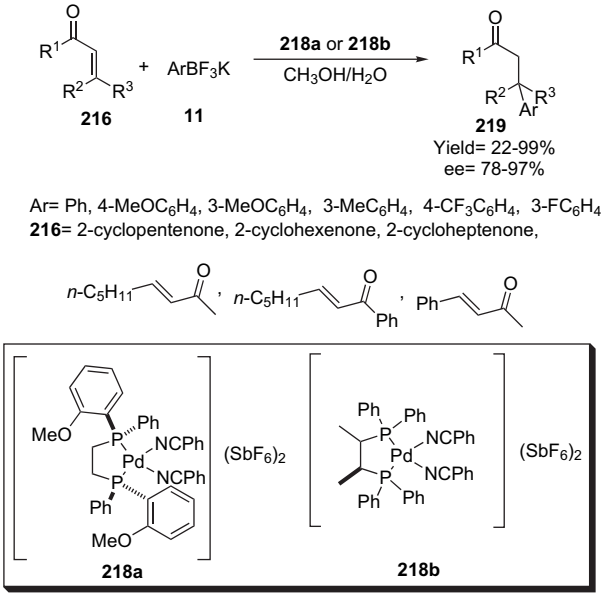
R = alkenyl, aryl R^1 = alkyl, aryl Yield: 71-88%

R^1,R^2 = $(CH_2)_3$ R^3 = H, C_6H_5
R^1 = H, CH_3 R = alkenyl, aryl Yield: 59->99%

Scheme 76.

In this work, good yields of 1,2- and 1,4-addition adducts **215** and **217** were obtained in the presence of catalytic amounts of $Rh(acac)(CO)_2$ and a bidentate ligand. Moreover, it is important to note that the reaction proceeded faster and with higher yields when organotrifluoroborates were used in the place of the corresponding boronic acids under identical conditions. The greater reactivity of organotrifluoroborates in this rhodium-catalyzed reaction presumably reflects the more facile transmetalation to form the active Rh-R species.

Recently, Miyaura and co-workers[86] reported a palladium-catalyzed 1,4-addition of aryltrifluoroborates **11** to enones **216** (Scheme 77). The reaction was carried out in presence of dicationic palladium(II) complexes **218a** or **218b** and the addition products **219** were obtained in good yields and high enantioselectivities exceeding 95% ee.



Scheme 77.

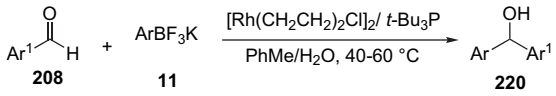
A recent study reported the synthesis of carbinol derivatives **220** via rhodium-catalyzed addition of potassium organotrifluoroborates **11** to aldehydes **208** (Table 21).[87] The addition products were obtained in high yields under mild aqueous conditions.

The reaction was demonstrated to accommodate both electron-rich and electron-poor aldehydes. In this methodology the reaction is compatible with the presence of various functionalities.

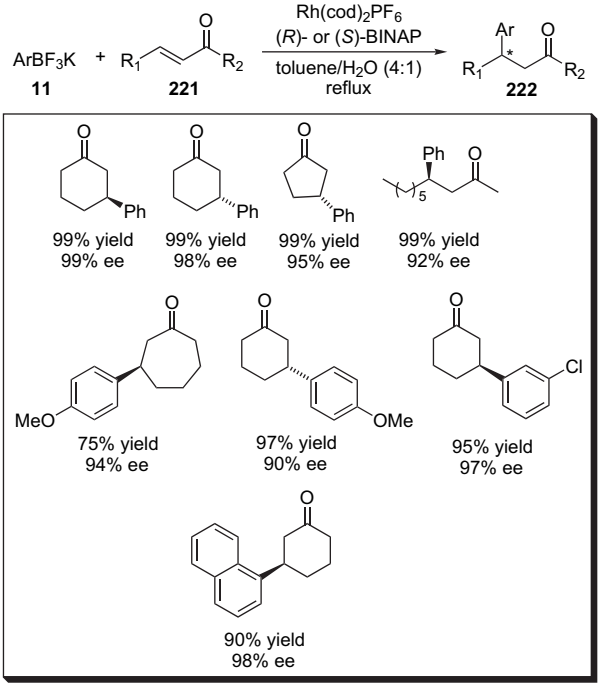
Genêt et al.[88] demonstrated that potassium aryltrifluoroborates **11** can be used to generate β-aryl carbonyl compounds **222** through the enantioselective, rhodium-catalyzed conjugate addition to enones (Scheme 78). It was observed that in some cases the reduction of potassium aryltrifluoroborate into the corresponding arene is a competitive process.

The use of (*R*)-BINAP affords preferentially the (*R*)-enantiomer, while (*S*)-BINAP affords the (*S*)-enantiomer. The enantioselectivity of the reaction proved to be dependent on the temperature and the solvent.

Table 21. Synthesis of carbinol via rhodium–catalyzed addition of potassium organotrifluoroborates **11** to aldehydes **208**

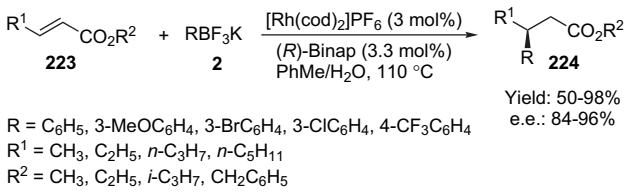


Entry	Ar	Ar^1	Yield (%)
1	C_6H_5	4-$MeOC_6H_4$	97
2	C_6H_5	4-$NO_2C_6H_4$	96
3	4-$MeOC_6H_4$	4-$CF_3C_6H_4$	96
4	C_6H_5	4-BrC_6H_4	94
5	4-ClC_6H_4	4-FC_6H_4	95
6	C_6H_5	2-$MeOC_6H_4$	99
7	C_6H_5	3-HOC_6H_4	99
8	C_6H_5	2-Furanyl	96
9	3-Thienyl	4-FC_6H_4	97
10	1-Naphthyl	2-Thienyl	71



Scheme 78.

Under the same reaction conditions described above, Genêt and co-workers[89] reported the first use of potassium organotrifluoroborates **2** in a rhodium-catalyzed asymmetric 1,4-addition to α,β-unsaturated esters **223**, extending the scope of this reaction (Scheme 79).

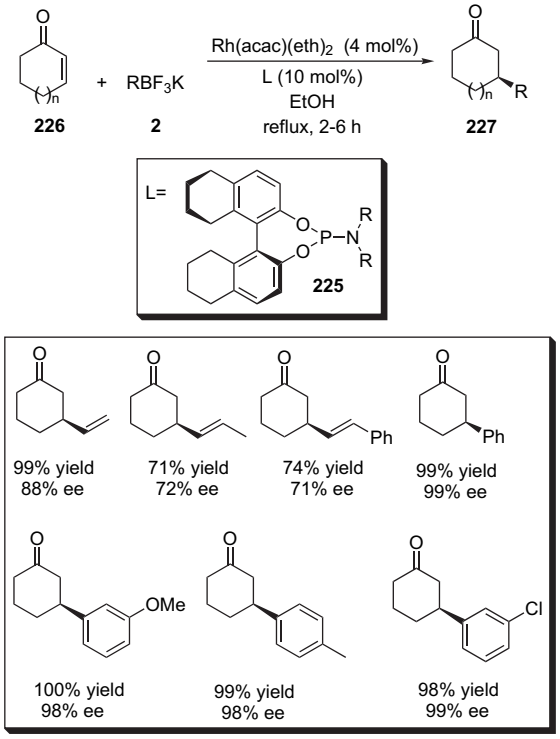


Scheme 79.

Using standard conditions, that is, cationic rhodium complex in the presence of (*R*)-BINAP as chiral ligand in a biphasic

solvent (toluene/water), the authors showed that the 1,4-addition reaction of potassium organotrifluoroborates with α,β-unsaturated esters **223** proceeds smoothly, affording the expected adduct in high yields and good to excellent enantiomeric excesses.

Recently,[90] the use of phosphoramidite ligands in the rhodium-catalyzed asymmetric conjugate addition of potassium organotrifluoroborates to enones was reported (Scheme 80).



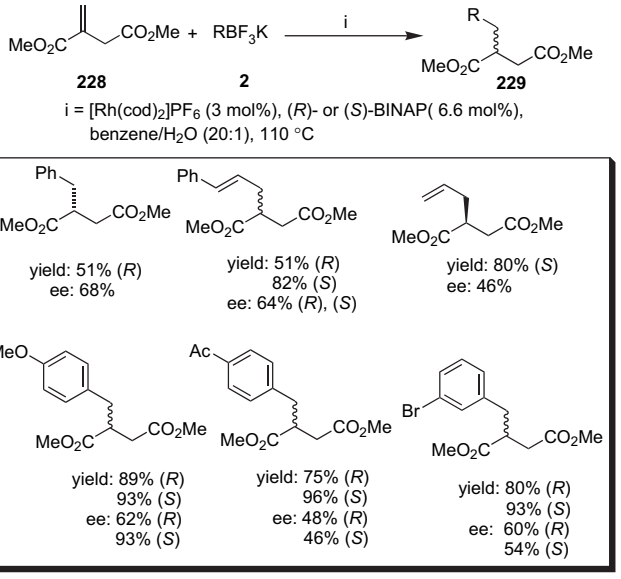
Scheme 80.

By screening of a homologous series of phosphoramidite ligands **225**, using the monodentate ligand combination approach, the authors discovered a highly efficient catalyst for the asymmetric conjugated addition of alkenyltrifluoroborates (up to 88% ee) and aryltrifluoroborates (up to 99% ee) to enones **226**.

By this methodology a library of chiral monodentate phosphoramidite ligands was rapidly obtained and screened in asymmetric C–C bond forming reactions using an automated parallel protocol.

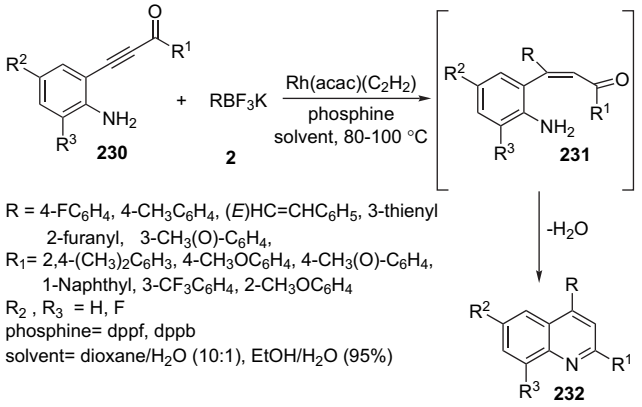
The rhodium-catalyzed tandem conjugate addition–protonation of potassium organotrifluoroborates **2** to dimethyl itaconate **228** in the enantioselective synthesis of 2-substituted succinic esters **229** was reported by Moos et al. (Scheme 81).[91]The products **229** were obtained in excellent yield and reproducible enantioselectivity. High temperature is essential for enantioselectivity; attempts to lower the reaction temperature resulted in racemic mixtures.

Recently Marinelli et al.[92] reported the synthesis of quinolines **232** by the sequential rhodium-catalyzed regioselective addition of potassium aryl- and vinyl trifluoroborates to



Scheme 81.

β-(2-aminophenyl)-α,β-ynones **230** followed by nucleophilic attack of the amino group onto the carbonyl (Scheme 82).

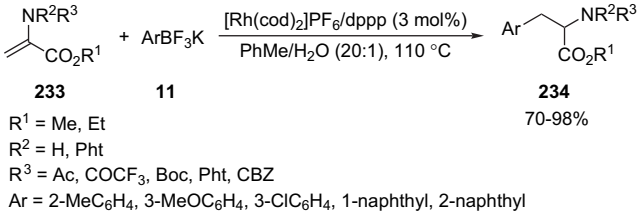


Scheme 82.

The quinolines **232** were isolated in moderate to high yields, and the methodology tolerates both electron-withdrawing and electron-donating substituents on the α,β-ynone and organotrifluoroborate moieties.

α-Amino acids are important building blocks, particularly for combinatorial chemistry and drug discovery. The synthesis of α-amino acids involving carbon–carbon bond formation by Michael addition to dehydroamino acid derivatives is a methodological alternative that has only been explored to limited extent.

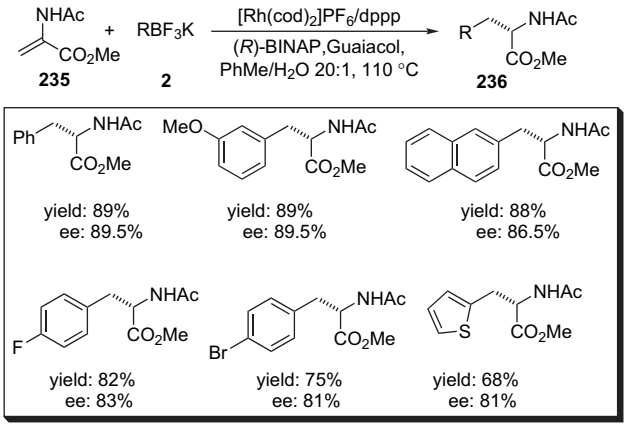
Recently, Genêt et al.[93] reported the development of a highly effective rhodium-catalyzed 1,4-addition of aryltrifluoroborates **11** to dehydroamino esters **233** (Scheme 83). The authors selected cationic $[Rh(cod)_2]PF_6$ as a rhodium source because it has proven to be highly effective in carbometalation processes of organotrifluoroborates with enones[88] and esters[89] (Scheme 83).



Scheme 83.

Under these conditions, the 1,4-addition reaction allowed the formation of various alanine derivatives in good to high yields (up to 98%); however, no enantioselectivity was observed.

In another study,[94] the same authors described the enantioselective tandem conjugate addition of organotrifluoroborates **2** to *N*-acylamidoacrylate **235** mediated by a chiral rhodium catalyst in presence of a chiral ligand together with in situ protonation by using an achiral phenol derivative. This methodology furnished a variety of amino acids derivatives **236** in good to excellent yields (Scheme 84).

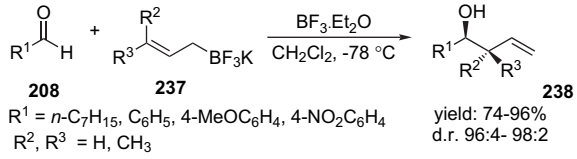


Scheme 84.

The highest ee values were obtained using (*R*)-BINAP as the chiral ligand, guaiacol as a proton source, and toluene as the solvent. A great variety of aryl alanine derivatives were obtained in good yield by this tandem carbometalation–enantioselective protonation process. Enantioselectivity ranging from 81% to nearly 90% ee was generally obtained.

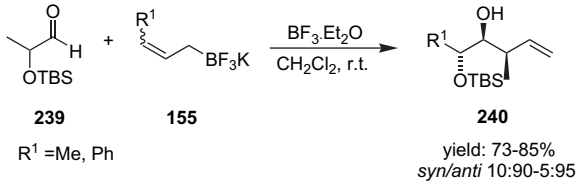
The addition of crotyl and allylorganometallics to carbonyl compounds is of great importance in organic and combinatorial syntheses. Carbonylic compounds react with a variety of allylmetal compounds to give homoallylic alcohols.[95] Batey and co-workers[11,96] reported the addition of potassium allyl- and crotyltrifluoroborates **237** to aldehydes **208** in presence of Lewis acids to afford the homoallylic alcohols **238** (Scheme 85).

Generally, high yields were obtained with a wide variety of aliphatic and aromatic aldehydes in very fast reactions. The crotylation reaction was demonstrated to be very diastereoselective, where the *syn* diastereoisomer was preferentially obtained with potassium (*Z*)-crotyltrifluoroborates and the *anti* product was obtained when (*E*)-crotyltrifluoroborates were employed.



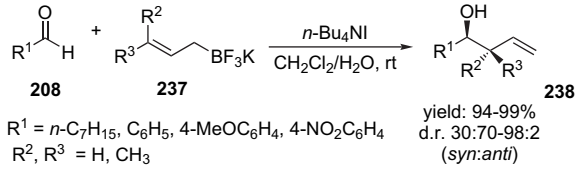
Scheme 85.

High diastereoselectivity was also observed in the allylation of aldehydes bearing an α- or β-stereogenic center.[95] When the (*Z*)-crotyl reagent was added to α-TBSO-substituted aldehydes **239**, the *anti* product **240** was obtained in *anti*/*syn* 90:10 to 95:5 ratio (Scheme 86). However, the diastereoselectivity was lower when (*E*)-crotyltrifluoroborate was used.



Scheme 86.

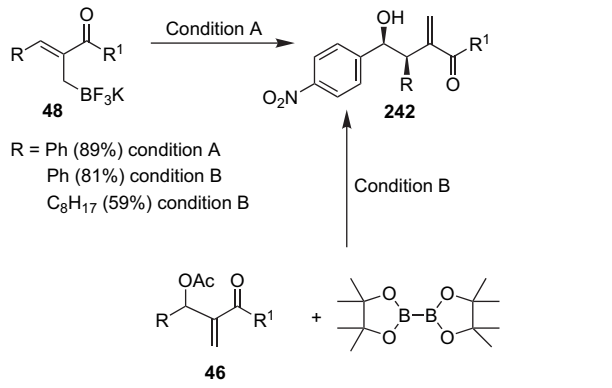
The allylation and crotylation of aldehydes **208** can also be conducted in aqueous biphasic medium (CH_2Cl_2/H_2O) in the presence of a phase-transfer catalyst (PTC), without necessity of a Lewis acid (Scheme 87).[97,98] The yields and the diastereoselectivity of the reaction under these conditions were comparable with the results of Lewis acid-catalyzed protocols,[11,95] with slight improvement.



Scheme 87.

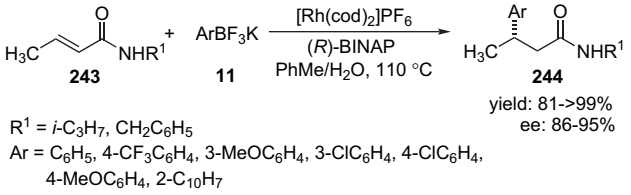
The (*E*)-2-alkoxy-3-substituted allyltrifluoroborate salts **48** can be converted into homoallylic alcohols in high yields and excellent diastereoselectivity by reaction with 4-nitrobenzaldehyde **241** in the presence of tetra-*n*-butylammonium iodide (Scheme 88).[27] A multicomponent reaction was also tested involving allylboration of reaction of the 4-nitrobenzaldehyde in the presence of $BF_3 \cdot Et_2O$ (30 mol %) at room temperature without isolation of the boron intermediate, furnishing the corresponding homoallylic alcohol **242** in good yield.

4.3.2. Amides. Potassium aryltrifluoroborates **11** can be used to generate chiral β-arylamides **244** via rhodium-catalyzed asymmetric 1,4-addition to α,β-unsaturated amides **243** (Scheme 89).[99] Using cationic rhodium complex as



Scheme 88.

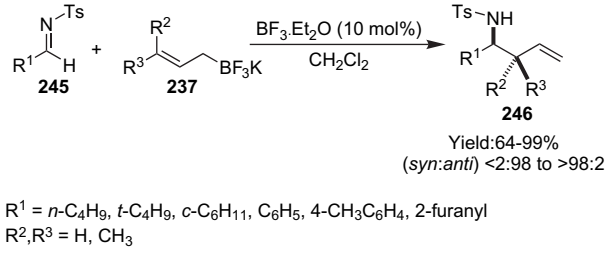
catalyst precursor, $[Rh(cod)_2]PF_6$, in the presence of (*R*)-BINAP as chiral ligand in a biphasic solvent mixture (toluene/water), high yields and enantiomeric excesses were achieved.



Scheme 89.

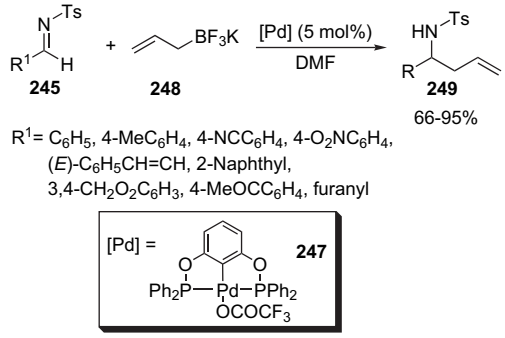
In the present reaction, addition of base did not show any influence on conversion, whereas it generally resulted in a dramatic decrease in enantioselectivity.

4.3.3. Imines and iminium species. Homoallylic amines **246** were prepared in high yields and excellent diastereoselectivity via allylation and crotylation of aliphatic, aromatic, and heterocyclic *N*-tosylimines **245**, employing potassium (*Z*)- and (*E*)-crotyltrifluoroborate **237** in presence of $BF_3 \cdot Et_2O$ (Scheme 90).[100] The use of (*Z*)- or (*E*)-crotyltrifluoroborates led, respectively, to the *anti* or *syn* products.



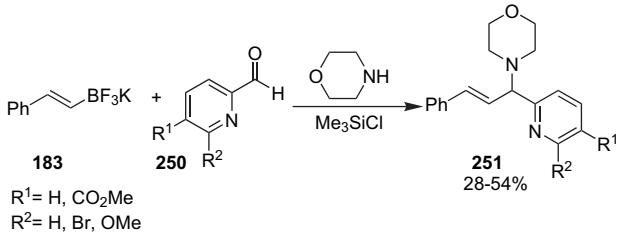
Scheme 90.

Recently, Szabó et al.[101] reported the synthesis of homoallylic amines **249** by the palladium pincer-complex **247** catalyzed allylation of tosylimines **245** by potassium trifluoro(allyl)borates **248** (Scheme 91). By this methodology a wide range of functionalized tosylimines can be allylated in good to excellent yields and under mild reaction conditions. The reaction was compatible with functional groups, such as ketone, nitro, acetals, and nitrile.



Scheme 91.

Mannich reaction is one of the most versatile methods to obtain secondary and/or tertiary amines by a three-component reaction. When one of these three components is an organoboron compound, the reaction is called Petasis reaction.[102] The first example of Petasis reaction involving organotrifluoroborates was described in 2000.[103] The reaction between heterocyclic aldehydes **250**, morpholine, and (*E*)-styryltrifluoroborate **183** in presence of trimethylsilyl chloride afforded the corresponding vinylamines **251** in low yields (Scheme 92).



Scheme 92.

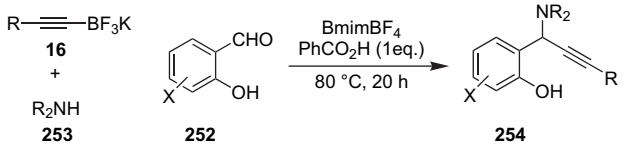
Propargylamines **254** were efficiently prepared by the reaction of potassium alkynyltrifluoroborate **16**, aldehyde **252**, and a secondary amine **253** in the presence of benzoic acid, using an ionic liquid such as butylmethylimidazolium tetrafluoroborate ($BmimBF_4$) (Table 22).[104] Interestingly, when a silyl group was attached to the alkyne, this group was removed under the reaction conditions (entry 10, Table 22).

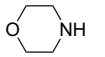
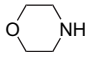
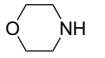
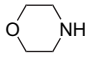
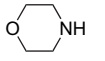
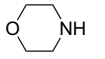
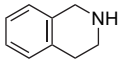
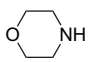
The proposed mechanism suggests that initial formation of an iminium ion **B** is followed by coordination of the borate species with the phenolate oxygen, forming an intermediate **C**, which produces the propargylamine **D** (Scheme 93).

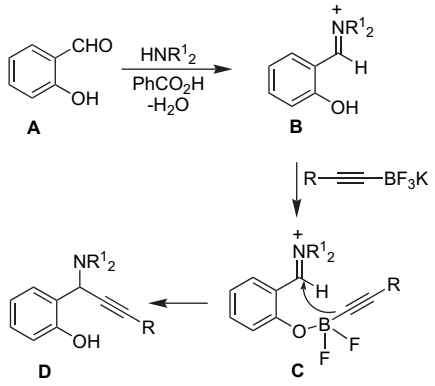
Tertiary amines **255** were prepared in good yields by the three-component Petasis reaction using potassium organotrifluoroborate salts **2**, aldehydes **208**, and secondary amines **253** in the presence of $BF_3 \cdot Et_2O$ (Scheme 94).[105]

It was observed, in general, that electron-rich aryls, heteroaryls, and vinyltrifluoroborates were successful nucleophiles, giving the desired products **255** in good yield,

Table 22. Petasis reaction involving potassium alkynyltrifluoroborates **16**



Entry	R	Amine	X	Yield (%)
1	*n*-C_4H_9	$(PhCH_2)_2NH$	H	81
2	*n*-C_4H_9		H	76
3	*n*-C_4H_9		3-Me	63
4	*n*-C_4H_9		5-Cl	53
5	C_6H_5		5-NO_2	79
6	C_6H_5	$(PhCH_2)_2NH$	H	81
7	4-MeC_6H_4		5-NO_2	78
8	*t*-C_4H_9		H	72
9	1-Cyclohexenyl		H	58
10	Me_3Si		H	55



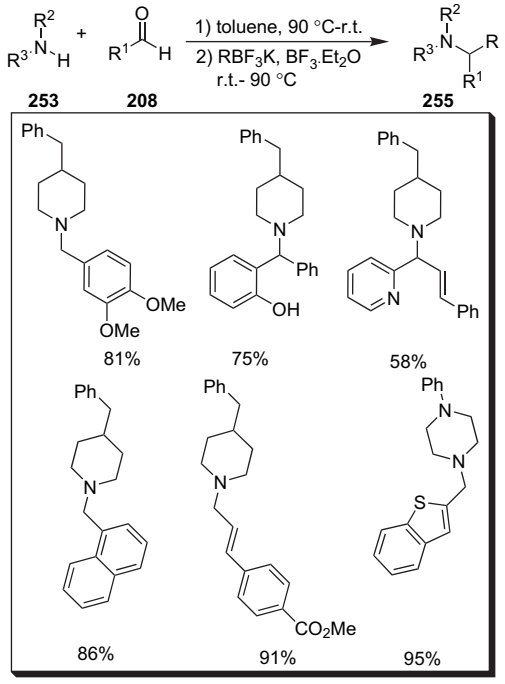
Scheme 93.

while electron-poor aryltrifluoroborates resulted in low yield, making addition of catalytic or stoichiometric acetic acid necessary to increase the yield. The authors also verified that only aldehydes containing α or *ortho* activating groups underwent this reaction.

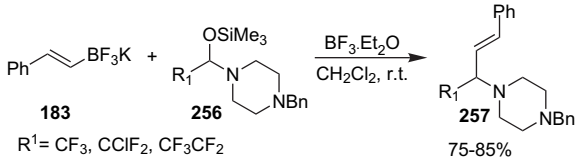
Hemiaminal derivates of fluoroaldehydes **256** were employed as an iminium source to react with (*E*)-styryltrifluoroborate salt **183** in the presence of $BF_3 \cdot Et_2O$ as Lewis acid to afford α-substituted α-(fluoroalkyl)amines **257** in good yield (Scheme 95).[106]

4.4. Halogenation of organotrifluoroborates

Aromatic, vinyl, and alkynyl halides are very important and useful tools in organic synthesis, as well as in medicinal and pharmaceutical research. The main method to obtain organic halides is the use of organometallic reagents, but their use is



Scheme 94.



Scheme 95.

somewhat restricted due to the high reactivity and toxic properties of many of the reagents. In this context, potassium organotrifluoroborate salts have proven to be versatile intermediates in organic synthesis.

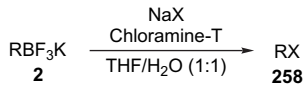
Aryl- and heteroaryltrifluoroborates can be rapidly converted into aryl and heteroaryl iodides regioselectively under mild conditions using sodium iodide in the presence of Chloramine-T to afford the products in good to excellent yields (entries 1–4, Table 23).[107] The method tolerates a wide variety of functional groups, and sterically hindered aryltrifluoroborates readily react at room temperature.

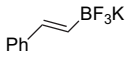
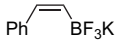
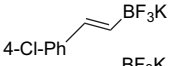
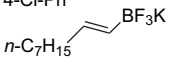
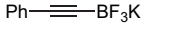
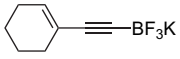
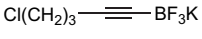
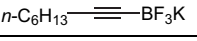
Under similar conditions vinyl- and alkyltrifluoroborates can also be iodinated in excellent yields, extending the scope of this reaction (entries 5–12, Table 23).[108] The method tolerates a wide variety of functional groups and affords the products in excellent yields.

The stereochemistry of the alkene is retained, which provides ready access to a variety of (*E*)- and (*Z*)-vinyl iodides. The reaction is also suitable for the preparation of 1-iodoalkynes. This was the first report of alkynylboron derivatives being used as precursors to iodoalkynes.

The same authors have reported[109] that by simple change of NaI for NaBr in the protocol described above, it is possible to obtain aryl, alkenyl, and alkynyl bromides **258** (Table 23).

Table 23. Halogenation of organotrifluoroborates **2**



Entry	RBF_3K **2**	X	Yield (%)	Ref.
1	$C_6H_5BF_3K$	I, Br	90, 76	107, 109
2	4-$MeOC_6H_4BF_3K$	I, Br	94, 87	107, 109
3	2,6-$(Me)_2C_6H_3BF_3K$	I, Br	84, 83	107, 109
5	3-ThienylBF_3K	I, Br	83, 65	107, 109
6		I, Br	85, 92	108, 109
7		I, Br	95, 89	108, 109
8		I, Br	90, 90	108, 109
10		I, Br	91, 72	108, 109
11		I, Br	96, 87	108, 109
13		I, Br	94, 78	108, 109
14		I, Br	94, 79	108, 109
15		I, Br	95, 79	108, 109

All the features observed in the iodination apply to the bromination, such as good yields, retention of stereochemistry, and mild reaction conditions.

The halogens have great potential in radiopharmaceutical design because of their ready availability and chemical reactivity. The preparation of high specific activity, no-carrier-added radiohalogenated agents has become increasingly important in nuclear medicine imaging.

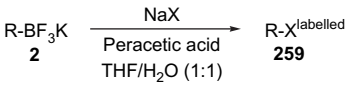
Recently, the use of organotrifluoroborates as precursors to radioiodinated agents was reported by Kabalka and Mereddy.[110] The authors describe a rapid, facile, and high yield synthesis of high specific activity iodine-123 labeled aryl and vinyl iodides (entries 1–8, Table 24) and alkynyl iodides (entries 9–12, Table 24)[111] from the corresponding organotrifluoroborates.

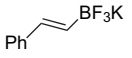
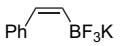
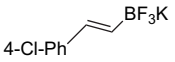
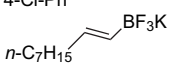
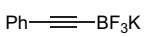
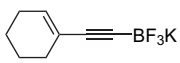
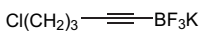
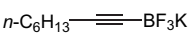
The iodination of aryltrifluoroborates containing electron-donating substituents is rapid and efficient, whereas those containing electron-withdrawing groups require longer reaction times. The presence of a nitro group effectively inhibits the reaction. Iodination of vinyltrifluoroborates proceeds with retention of stereochemistry, providing ready access to a variety of (*E*)- and (*Z*)-vinyl iodides. The radiochemical purity of the products was typically >98% and the overall radiochemical yields generally exceeded 75%.

A straightforward radiobromination procedure for the construction of radiobrominated alkenyl and alkynyl bromides using organotrifluoroborates was recently reported by Kabalka et al. (entries 5–12, Table 24).[112]

Bromination of alkenyl trifluoroborates proceeds with retention of configuration, providing ready access to a variety of (*E*) and (*Z*) alkenyl bromides. The radiochemical purity of the products typically exceeds 98% and the overall radiochemical yields are good.

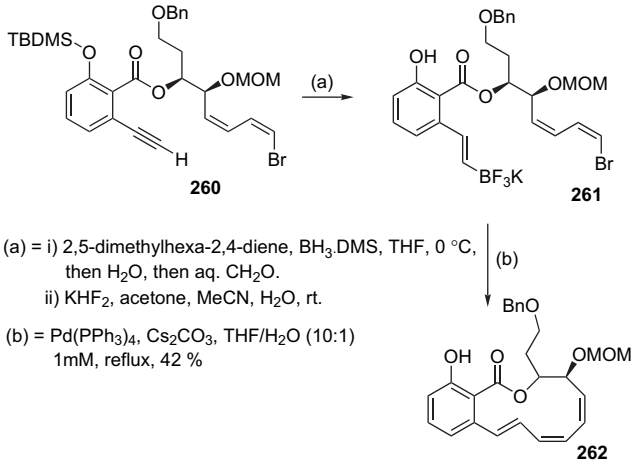
Table 24. Radiohalogenation of potassium organotrifluoroborates **2**



Entry	RBF_3K **2**	X	Yield (%)	Ref.
1	$C_6H_5BF_3K$	^{123}I	75	110
2	4-$MeOC_6H_4BF_3K$	^{123}I	88	110
3	2,6-$(Me)_2C_6H_3BF_3K$	^{123}I	79	110
4	3-ThienylBF_3K	^{123}I	62	110
5		^{123}I, ^{76}Br	83, 70	110, 112
6		^{123}I, ^{76}Br	78, 69	110, 112
7		^{123}I, ^{76}Br	86, 65	110, 112
8		^{123}I, ^{76}Br	58, 48	110, 112
9		^{123}I, ^{76}Br	92, 80	111, 112
13		^{123}I, ^{76}Br	90, 64	111, 112
14		^{123}I, ^{76}Br	91, 76	111, 112
15		^{123}I, ^{76}Br	88, 81	111, 112

4.5. Total synthesis

4.5.1. Oximidine II. Oximidine II exhibits an important selective cytotoxicity at ng/mL levels for *ras* and *src* oncogene transformed cells. The biological inhibition was found to affect the cell cycle at the G1 phase. In the synthesis of the intermediary **262** necessary to obtain the oximidine II was proposed a macrolactonization route, involving an initial intermolecular cross-coupling reaction between the vinyl bromide and the potassium vinyltrifluoroborate **261** (Scheme 96).[113] The corresponding potassium vinyltrifluoroborate was generated by the selective hydroboration of the terminal alkyne using Snieckus' reagent, *i*-PP_2BH. The resulting organoborane was converted directly into the corresponding potassium trifluoroborate **261**, isolated in virtually quantitative yields.



Scheme 96.

4.5.2. Trityrosine and pulcherosine. Cross-linked tyrosine oligomers are present in many natural peptides and proteins.

They are associated with some diseases and disorders, such as Alzheimer's and Parkinson's diseases, atherosclerosis and cataract formation. Due to these facts the synthesis of these compounds becomes a target of attention of several organic and medicinal chemists.

Recently, Hutton et al.[114] reported the synthesis of two trimers of tyrosines **263** and **264** (Fig. 1) and it was based in the Suzuki cross-coupling reaction involving organotrifluoroborates.

The crucial step to obtain the trityrosine **263** was the palladium-catalyzed cross-coupling reaction of 3,5-diiodo-*L*-tyrosine derivative **266** with 2 equiv of the tyrosine trifluoroborate **265** in THF/H_2O to afford the protected trityrosine **267** in 67% yield (Scheme 97).

Potassium tyrosine-3-trifluoroborate salt was synthesized in quantitative yield from the corresponding pinacol boronate derivative by treatment with potassium hydrogen difluoride.

Using the same approach the pulcherosine **264** was prepared. The treatment of bromo-isodityrosine derivative **268** with tyrosine trifluoroborate **265**, triethylamine, and $PdCl_2(dppf)\cdot CH_2Cl_2$ in *i*-PrOH/H_2O mixture as solvent afforded the protected pulcherosine **269** in a moderate yield, 32% (Scheme 98).

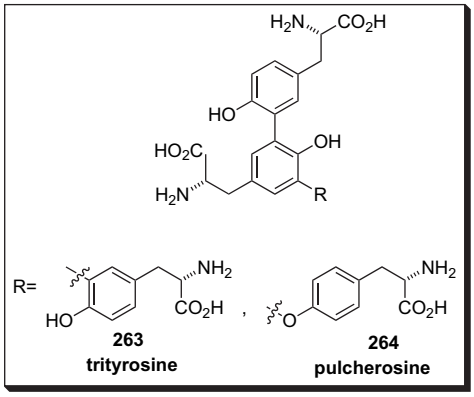
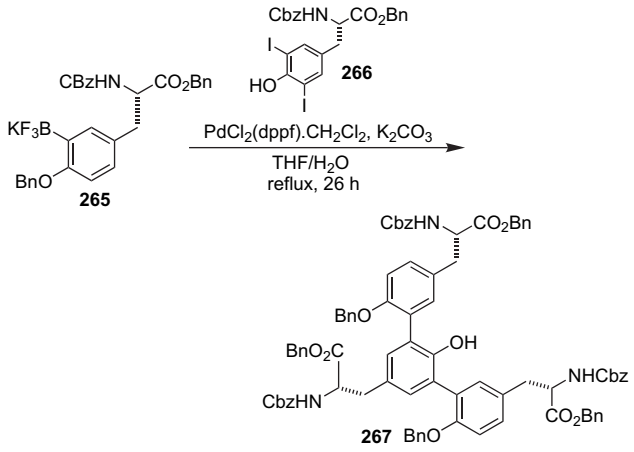


Figure 1. Tyrosine oligomers.



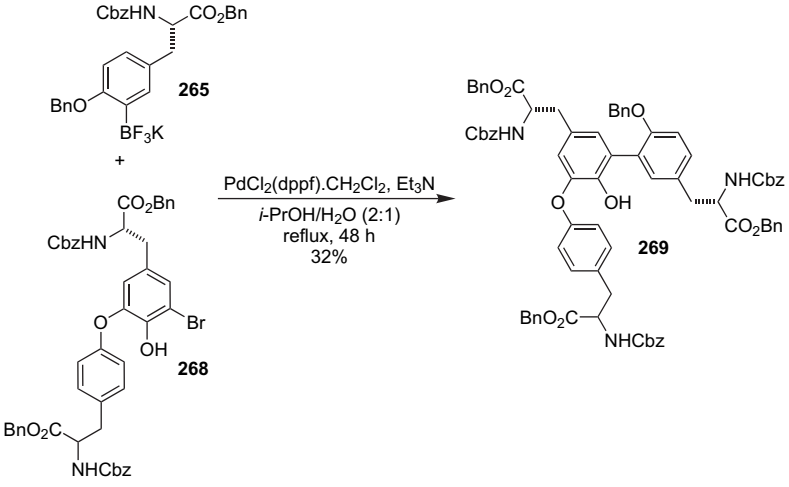
Scheme 97.

4.5.3. (−)-Tetrahydrolipstatin. Tetrahydrolipstatin **273**, the saturated form of lipstatin, works as a trigliceryde mimic and is a potent and irreversible inhibitor of pancrease lipase, a consequence of an irreversible reaction with the β-lactone.

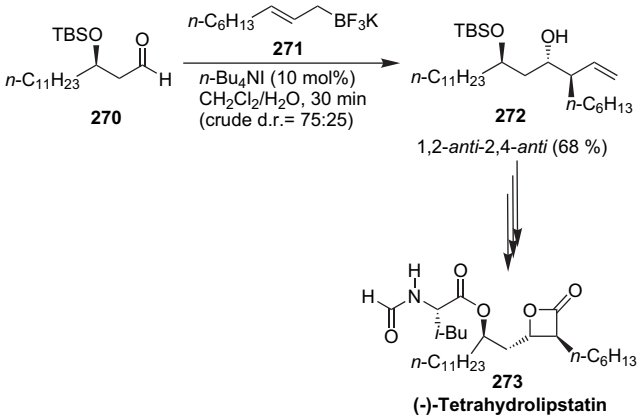
Several total syntheses of this target were done and recently a new approach employing an organotrifluoroborate was reported using the addition of potassium (2*E*)-nonenyltrifluoroborate **271** to a β-substituted aldehyde **270** in the presence of *n*-Bu_4NI in a biphasic medium (CH_2Cl_2/H_2O). This reaction provided a 3:1 mixture of 1,2-*anti*–2,4-*anti* and 1,2-*anti*–2,4-*syn* diastereomers **272** (Scheme 99).[98]

4.5.4. Cryptophycins. Cryptophycin **274** (Fig. 2) is a family of natural, synthetic, and semi-synthetic macro- and acyclic depsipeptides that have attracted considerable attention recently due to their clinical potential and pharmacological properties. These features, and the low natural abundance of cryptophycins have made them a target for total synthesis.

Lautens and Maddess[115] reported the application of bis-homoallylic alcohols **276**, obtained by the enantioselective allylation of in situ formed β,γ-unsaturated aldehydes using the potassium allyltrifluoroborate (Scheme 100),[116] for the synthesis of the fragment A **277** of cryptophycins. In this



Scheme 98.



Scheme 99.

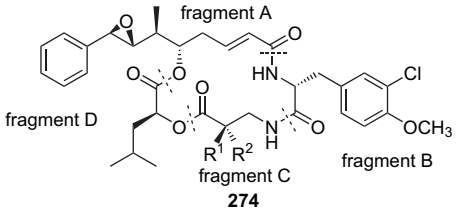
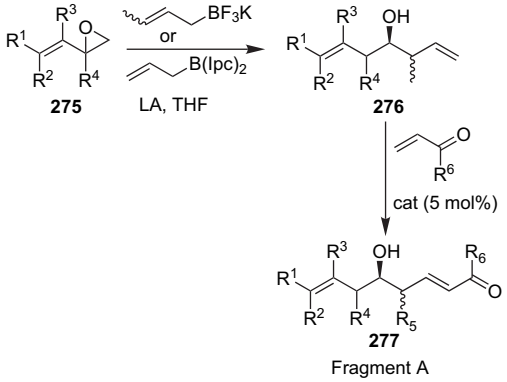


Figure 2. Cryptophycins.

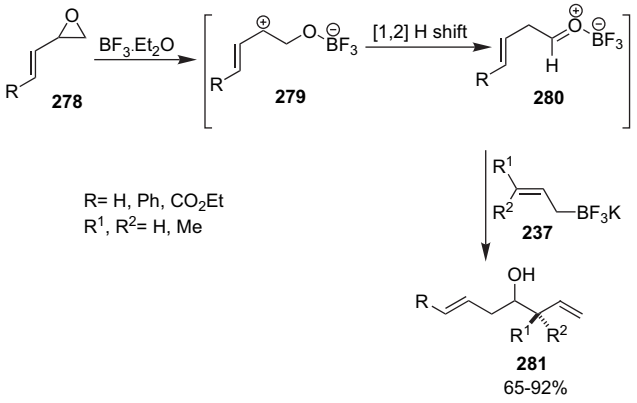
work, the bishomoallylic alcohols were subjected to modified Grubs cross-metathesis conditions, affording the respective products in moderate to good yields.



Scheme 100.

4.6. Ring-opening reactions

4.6.1. Epoxide ring-opening reactions. Allyl and crotyltrifluoroborates **237** were added to 2-vinyloxiranes **278** to afford secondary alcohols **281** in good yields (Scheme 101).[116] The reaction was mediated by $BF_3 \cdot Et_2O$ to generate the intermediate **280**, by a typical epoxide rearrangement.

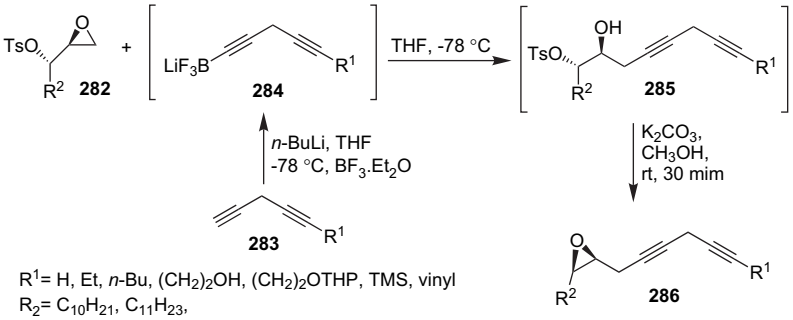


Scheme 101.

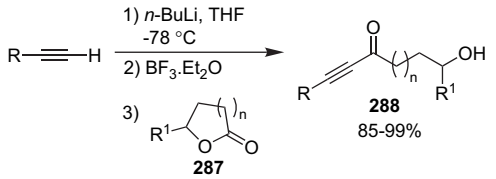
The crotylation reaction proved to be very diastereoselective. As in the case reported by Batey and co-workers,[11,98] the *syn* diastereoisomer was obtained with potassium (*Z*)-crotyltrifluoroborates and the *anti* product was obtained when (*E*)-crotyltrifluoroborates were employed.

Zhang and Che[117] described the regioselective addition of lithium alkynyltrifluoroborate **284**, generated in situ by the reaction of $BF_3 \cdot Et_2O$ with the alkynyl lithium, to epoxy tosylates **282**, affording the ring-opened intermediate **285**, which is used directly in the next ring-closure reaction to give the respective internal chiral epoxide bearing a 1,4-diyne or 1,4-enyne unit **286** (Scheme 102).

4.6.2. Lactone ring-opening reactions. Koutek et al.[118] described the synthesis of functionalized α-alkynones **288** by the regioselective ring-opening reaction of five-, six-, and seven-membered lactones **287** with lithium alkynyltrifluoroborates, which are generated in situ by the addition of $BF_3 \cdot OEt_2$ to alkynyllithiums (Scheme 103). By this method, several hydroxy substituted α-alkynones **288** were obtained in high yields, and the reaction was practically insensitive to structural variations in the evaluated substrates.



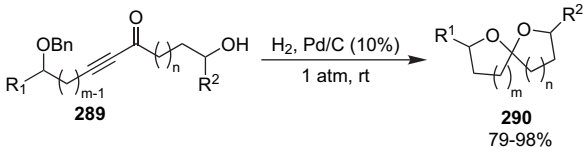
Scheme 102.



R= C_6H_5, $(CH_2)_2OBn$, CH(Me)OBn, *n*-Bu, $CH_2CH(Me)OBn$, $CH_2CH(Me)OTBDPS$
R^1= H, Me
n= 1, 2, 3

Scheme 103.

Using this methodology, a two step synthesis of spiroketal **290** was carried out.[119] The hydroxyl α-alkynones **289** were submitted to a palladium-catalyzed hydrogenation/spirocyclization reaction sequence (Scheme 104).

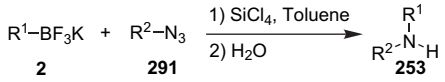


Scheme 104.

4.7. Miscellaneous

4.7.1. Amines. Secondary amines **253** were prepared by treating the organotrifluoroborate **2** with azido compounds **291** in presence of a Lewis acid (Table 25).[120]

Table 25. Synthesis of secondary amines **253**



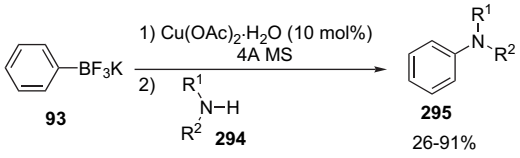
Entry	R^1	R^2	Yield (%)
1	C_6H_5	$PhCH_2$	82
2	C_6H_5	*n*-C_5H_{11}	70
3	C_6H_5	H	73
4	*c*-C_6H_{11}	$PhCH_2$	70
5	*n*-C_6H_{13}	$PhCH_2$	85
6	(*S*)-*n*-$C_6H_{13}CH(Me)$	$PhCH_2$	75

The chiral pyrrolidine **293** was synthesized by an intramolecular reaction of an alkyltrifluoroborate bearing an azide group **292** (Scheme 105).[105] The reaction was realized in presence of $SiCl_4$ and the product was obtained in 77% yield and 98% ee.

i = toluene/acetonitrile, $SiCl_4$, 22 °C, 10 h

Scheme 105.

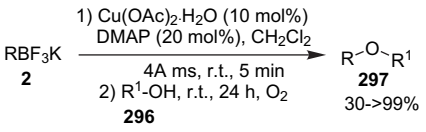
Quach and Batey[121] described the synthesis of arylamines **295** by the cross-coupling reaction of potassium aryltrifluoroborate salt **93** with primary and secondary aliphatic amines and anilines **294** in presence of $Cu(OAc)_2 \cdot H_2O$ (Scheme 106). In this method, the use of a base or a ligand was not necessary, and a wide range of functional groups was tolerated on both the cross-coupling partners.



R^1 = alkyl, aryl
R^2 = H, alkyl

Scheme 106.

4.7.2. Ethers. Ethers **297** were prepared by a copper-catalyzed coupling reaction of potassium organotrifluoroborate **2** salts with primary and secondary alcohols **296** under neutral conditions at room temperature (Scheme 107).[122]



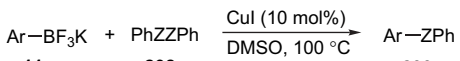
R = Ph, 4-$MeOC_6H_4$, 3-ClC_6H_4, 4-AcC_6H_4, 3-thienyl, *E*-styryl
R^1 = alkyl, aryl.

Scheme 107.

Various alcohols **296** such as phenols, aliphatic, allylic, and internal propargylic alcohols undergo cross-coupling, and a variety of functionalities are permitted. The reaction appears to be quite sensitive to steric effects around the hydroxyl group. Thus, secondary aliphatic alcohols suffer a decrease in yield, whereas tertiary alcohols did not react under these conditions.

Regarding the nature of the organotrifluoroborate salts, it was observed that electron-rich aryltrifluoroborates give the best results, whereas electron-deficient salts did not couple.

4.7.3. Chalcogen compounds. Unsymmetrical diarylselenides and tellurides **299** were produced in good yield from the reaction of potassium aryltrifluoroborates **11** with diphenyl diselenide and ditelluride **298**, respectively, in presence of a catalytic amount of cuprous iodide (10 mol %) using DMSO as solvent (Scheme 108).[123]



Ar= 4-Me Z=Se (88%)
Ar= 4-MeO Z=Se (92%)
Ar= 4-Me Z=Te (67%)

Scheme 108.

5. Conclusion

This review has presented the recent progress in the organotrifluoroborate chemistry. These compounds offer enormous

scope to synthetic organic chemists for the synthesis of target molecules. Many new methodologies are continuously developing in this field. In general, they are more reactive and stable than their boronic acid or ester correspondents.

Their preparation, isolation, and purification protocols are very easy and employ inexpensive reagents. New interesting achievements in organotrifluoroborates chemistry can be expected in the nearest future.

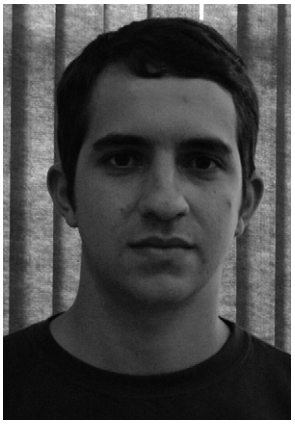
References and notes

1. Molander, G. A.; Figueroa, R. *Aldrichim. Acta* **2005**, *38*, 49.
2. Darses, S.; Genêt, J.-P. *Eur. J. Org. Chem.* **2003**, 4313.
3. (a) Chambers, R. D.; Clark, H. C.; Willis, C. J. *J. Am. Chem. Soc.* **1960**, *82*, 5298; (b) Pawelke, G.; Heyder, F.; Bürger, H. *J. Organomet. Chem.* **1979**, *178*, 1; (c) Bir, G.; Schacht, W.; Kaufmann, D. *J. Organomet. Chem.* **1988**, *340*, 267.
4. Vedejs, E.; Chapman, R. W.; Fields, S. C.; Lin, S.; Schrimpf, M. R. *J. Org. Chem.* **1995**, *60*, 3020.
5. (a) Vedejs, E.; Fields, S. C.; Hayashi, R.; Hithccock, S. R.; Powell, D. R.; Schrimpf, M. R. *J. Am. Chem. Soc.* **1999**, *121*, 2460; (b) Darses, S.; Michaud, G.; Genêt, J.-P. *Eur. J. Org. Chem.* **1999**, 1875.
6. Batey, R. A.; Quach, T. D. *Tetrahedron Lett.* **2001**, *42*, 9099.
7. (a) Brown, H. C. Product Number Z40,094-7; *Organic Syntheses Via Boranes*; Aldrich Chemical: Milwaukee, WI, 1997; Vol. 1; (b) Brown, H. C.; Zaidlewicz, M. Product Number Z40,095-5; *Organic Syntheses Via Boranes*; Aldrich Chemical: Milwaukee, WI, 2001; Vol. 2; (c) Suzuki, A.; Brown, H. C. Product Number Z51,430-6; *Organic Syntheses Via Boranes*; Aldrich Chemical: Milwaukee, WI, 2003; Vol. 3.
8. Molander, G. A.; Rivero, M. R. *Org. Lett.* **2002**, *4*, 107.
9. Molander, G. A.; Ham, J. *Org. Lett.* **2006**, *8*, 2031.
10. Molander, G. A.; Ito, T. *Org. Lett.* **2001**, *3*, 393.
11. Batey, R. A.; Thadani, A. N.; Smil, D. V. *Tetrahedron Lett.* **1999**, *40*, 4289.
12. Molander, G. A.; Biolatto, B. *J. Org. Chem.* **2003**, *68*, 4302.
13. Frohn, H.-J.; Franke, H.; Fritzen, P.; Bardin, V. V. *J. Organomet. Chem.* **2000**, *598*, 127.
14. De, S.; Welker, M. E. *Org. Lett.* **2005**, *7*, 2481.
15. Clayden, J. *Organolithiums: Selectivity for Synthesis*; Pergamon: Oxford, 2002.
16. Rousch, W. R.; Ando, K.; Powers, D. B.; Palkowitz, A. D.; Halterman, R. L. *J. Am. Chem. Soc.* **1990**, *112*, 6339.
17. Molander, G. A.; Katona, B. W.; Machrouhi, F. *J. Org. Chem.* **2002**, *67*, 8416.
18. Bardin, V. V.; Adonin, N. Y.; Frohn, H.-J. *Organometallics* **2005**, *24*, 5311.
19. (a) Frohn, H.-J.; Bardin, V. V. *Z. Anorg. Allg. Chem.* **2001**, *627*, 2499; (b) Bardin, V. V.; Frohn, H.-J. *Z. Anorg. Allg. Chem.* **2002**, *628*, 721.
20. (a) Stefani, H. A.; Cella, R.; Zukerman-Schpector, J.; Caracelli, I. *Z. Kristallogr.* **2006**, *221*, 167; (b) Unpublished results from our laboratory.
21. Petasis, N. A.; Yudin, A. K.; Zavialov, I. A.; Prakash, G. K. S.; Olah, G. A. *Synlett* **1997**, 606.
22. Molander, G. A.; Bernardi, C. R. *J. Org. Chem.* **2002**, *67*, 8424.
23. Molander, G. A.; Yun, C.-S.; Ribagorda, M.; Biolatto, B. *J. Org. Chem.* **2003**, *68*, 5534.
24. Clay, J. M.; Vedejs, E. *J. Am. Chem. Soc.* **2005**, *127*, 5766.
25. Shapland, P.; Vedejs, E. *J. Org. Chem.* **2006**, *71*, 6666.
26. Lawrence, J. D.; Takahashi, M.; Bae, C.; Hartwig, J. F. *J. Am. Chem. Soc.* **2004**, *126*, 15334.
27. Kabalka, G. W.; Venkataiah, B.; Dong, G. *J. Org. Chem.* **2004**, *69*, 5807.
28. Olsson, V. J.; Sebelius, S.; Selander, N.; Szabo, K. J. *J. Am. Chem. Soc.* **2006**, *128*, 4588.
29. Fang, G.-H.; Yan, Z.-J.; Deng, M.-Z. *Org. Lett.* **2004**, *6*, 357.
30. Charette, A. B.; Mathieu, S.; Fournier, J.-F. *Synlett* **2005**, 1779.
31. Hohn, E.; Pietruszka, J.; Solduga, G. *Synlett* **2006**, 1531.
32. Molander, G. A.; Ham, J. *Org. Lett.* **2006**, *8*, 2767.
33. Molander, G. A.; Ribagorda, M. *J. Am. Chem. Soc.* **2003**, *125*, 11148.
34. Molander, G. A.; Petrillo, D. E. *J. Am. Chem. Soc.* **2006**, *128*, 9634.
35. Molander, G. A.; Figueroa, R. *J. Org. Chem.* **2006**, *71*, 6135.
36. Molander, G. A.; Figueroa, R. *Org. Lett.* **2006**, *8*, 75.
37. Molander, G. A.; Ellis, N. M. *J. Org. Chem.* **2006**, *71*, 7491.
38. Negishi, E. *Aspects of Mechanism and Organometallic Chemistry*; Brewster, J. H., Ed.; Plenum: New York, NY, 1978; p 285.
39. For review: (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457; (b) Kotha, S.; Lahiri, K.; Kashinath, D. *Tetrahedron* **2002**, *58*, 9633.
40. Darses, S.; Genêt, J.-P.; Brayer, J.-L.; Demoute, J.-P. *Tetrahedron Lett.* **1997**, *38*, 4393.
41. Gallo, V.; Mastrorilli, P.; Nobile, C. F.; Paolillo, R.; Taccardi, N. *Eur. J. Inorg. Chem.* **2005**, 582.
42. (a) Frohn, H.-J.; Adonin, N. Y.; Bardin, V. V.; Starichenko, V. F. *J. Fluorine Chem.* **2002**, *117*, 115; (b) Frohn, H.-J.; Adonin, N. Y.; Bardin, V. V.; Starichenko, V. F. *Tetrahedron Lett.* **2002**, *43*, 8111.
43. (a) Molander, G. A.; Biolatto, B. *Org. Lett.* **2002**, *4*, 1867; (b) Molander, G. A.; Petrillo, D. E.; Landzberg, N. R.; Roana, J. C.; Biolatto, B. *Synlett* **2005**, 1763.
44. Barder, T. E.; Buchwald, S. L. *Org. Lett.* **2004**, *6*, 2649.
45. Kudo, N.; Perseghini, M.; Fu, G. C. *Angew. Chem., Int. Ed.* **2006**, *45*, 1282.
46. O'Brien, C. J.; Kantchev, E. A. B.; Valente, C.; Hadei, N.; Chass, G. A.; Lough, A.; Hopkinson, A. C.; Organ, M. G. *Chem.—Eur. J.* **2006**, *12*, 4743.
47. Wang, L.; Li, P.-H. *Chin. J. Chem.* **2006**, *24*, 770.
48. For review of microwave use: (a) Leadbeater, N. E. *Chem. Commun.* **2005**, 2881; (b) Lidström, P.; Tierney, J. P.; Wathey, B.; Westman, J. *Tetrahedron* **2001**, *57*, 9225.
49. Kabalka, G. A.; Al-Masum, M. *Tetrahedron Lett.* **2005**, *46*, 6329.
50. Kabalka, G. W.; Zhou, L.-L.; Naravane, A. *Tetrahedron Lett.* **2006**, *47*, 6887.
51. Arvela, R. K.; Leadbeater, N. E.; Mack, T. L.; Kormos, C. M. *Tetrahedron Lett.* **2006**, *47*, 217.
52. Harker, R. L.; Crouch, R. D. *Synthesis* **2007**, *25*.
53. For review: (a) Zeni, G.; Braga, A. L.; Stefani, H. A. *Acc. Chem. Res.* **2003**, *36*, 731; (b) Zeni, G.; Ludtke, D. S.; Panatieiri, R. B.; Braga, A. L. *Chem. Rev.* **2006**, *106*, 1032; (c) Petragnani, N.; Stefani, H. A. *Tetrahedron* **2005**, *61*, 1613.
54. Cella, R.; Cunha, R. L. O. R.; Reis, A. E. S.; Pimenta, D. C.; Klitzke, C. F.; Stefani, H. A. *J. Org. Chem.* **2006**, *71*, 244.
55. Xia, M.; Chen, Z.-C. *Synth. Commun.* **1999**, *29*, 2457.
56. (a) Hawthorne, M. F.; Dupont, J. A. *J. Am. Chem. Soc.* **1958**, *80*, 5830; (b) Brown, H. C.; Rhodes, S. P. *J. Am. Chem. Soc.* **1969**, *91*, 2149.

57. Molander, G. A.; Elia, M. D. *J. Org. Chem.* **2006**, *71*, 9198.
58. Kabalka, G. W.; Dadush, E.; Al-Masum, M. *Tetrahedron Lett.* **2006**, *47*, 7459.
59. Kabalka, G. W.; Al-Masum, M. *Org. Lett.* **2006**, *8*, 11.
60. Yamamoto, Y.; Takada, S.; Miyaura, N. *Chem. Lett.* **2006**, *35*, 704.
61. Kabalka, G. W.; Al-Masum, M.; Mereddy, A. R.; Dadush, E. *Tetrahedron Lett.* **2006**, *47*, 1133.
62. Molander, G. A.; Fumagalli, T. *J. Org. Chem.* **2006**, *71*, 5743.
63. Darses, S.; Michaud, G.; Genêt, J.-P. *Tetrahedron Lett.* **1998**, *39*, 5045.
64. Carter, R. R.; Wyatt, J. K. *Tetrahedron Lett.* **2006**, *47*, 6091.
65. Molander, G. A.; Brown, A. R. *J. Org. Chem.* **2006**, *71*, 9681.
66. For review of stilbene synthesis see: Ferré-Filmon, K.; Delaude, L.; Demonceau, A.; Noels, A. F. *Coord. Chem. Rev.* **2004**, *248*, 2323.
67. Cella, R.; Stefani, H. A. *Tetrahedron* **2006**, *62*, 5656.
68. Molander, G. A.; Felix, L. A. *J. Org. Chem.* **2005**, *70*, 3950.
69. Molander, G. A.; Yokoyama, Y. *J. Org. Chem.* **2006**, *71*, 2493.
70. Cella, R.; Orfão, A. T. G.; Stefani, H. A. *Tetrahedron Lett.* **2006**, *47*, 5075.
71. Stefani, H. A.; Cella, R.; Dorr, F. A.; Pereira, C. M. P.; Zeni, G.; Gomes, M., Jr. *Tetrahedron Lett.* **2005**, *46*, 563.
72. (a) Khalid, A.; Khandelwal, B. L.; Singh, A. K.; Singh, T. P.; Padmanabhan, B. *J. Coord. Chem.* **1994**, *31*, 19; (b) Singh, H. B.; Sudha, N.; Butcher, R. T. *Inorg. Chem.* **1993**, *31*, 1431.
73. Kabalka, G. W.; Dong, G.; Venkataiah, B. *Tetrahedron Lett.* **2005**, *46*, 763.
74. Grisorio, R.; Mastrorilli, P.; Nobile, C. F.; Romanazzi, G.; Suranna, G. P. *Tetrahedron Lett.* **2005**, *46*, 2555.
75. Kabalka, G. W.; Dong, G.; Venkataiah, B. *Tetrahedron Lett.* **2004**, *45*, 5139.
76. Steinhuebel, D.; Baxter, J. M.; Palucki Davies, I. W. *J. Org. Chem.* **2005**, *70*, 10124.
77. Wu, J.; Zhang, L.; Xia, H.-G. *Tetrahedron Lett.* **2006**, *47*, 1525.
78. Wu, J.; Zhang, L.; Luo, Y. *Tetrahedron Lett.* **2006**, *47*, 6747.
79. Molander, G. A.; Sommers, E. M.; Baker, S. R. *J. Org. Chem.* **2006**, *71*, 1563.
80. Pucheault, M.; Darses, S.; Genêt, J.-P. *J. Am. Chem. Soc.* **2004**, *126*, 15356.
81. Kabalka, G. W.; Venkataiah, B.; Dong, G. *Org. Lett.* **2003**, *5*, 3803.
82. Navarre, L.; Darses, S.; Genêt, J.-P. *Adv. Synth. Catal.* **2006**, *348*, 317.
83. (a) Krause, N.; Hoffmann-Röder, A. *Synthesis* **2001**, 171; (b) Sibi, M. P.; Manyem, S. *Tetrahedron* **2000**, *56*, 8033.
84. (a) Fagnou, K.; Lautens, M. *Chem. Rev.* **2003**, *103*, 169; (b) Hayashi, T. *Synlett* **2001**, 879; (c) Hayashi, T.; Takahashi, M.; Takaya, Y.; Ogasawara, M. *J. Am. Chem. Soc.* **2002**, *124*, 5052; (d) Amengual, R.; Michelet, V.; Genêt, J.-P. *Tetrahedron Lett.* **2002**, *43*, 5905; (e) Amengual, R.; Michelet, V.; Genêt, J.-P. *Synlett* **2002**, 1791.
85. Batey, R. A.; Thadani, A. N.; Smil, D. V. *Org. Lett.* **1999**, *1*, 1683.
86. Nishikat, T.; Yamamoto, Y.; Miyaura, N. *Chem. Lett.* **2005**, *34*, 720.
87. Pucheault, M.; Darses, S.; Genêt, J.-P. *Chem. Commun* **2005**, 4714.
88. (a) Pucheault, M.; Darses, S.; Genêt, J.-P. *Tetrahedron Lett.* **2002**, *43*, 6155; (b) Pucheault, M.; Darses, S.; Genêt, J.-P. *Eur. J. Org. Chem.* **2002**, 3552.
89. Navarre, L.; Pucheault, M.; Darses, S.; Genêt, J.-P. *Tetrahedron Lett.* **2005**, *46*, 4247.
90. (a) Duursma, A.; Boiteau, J.-G.; Lefort, L.; Boogers, J. A. F.; de Vries, J. G.; Minnaard, A. J.; Feringa, B. L. *J. Org. Chem.* **2004**, *69*, 8045; (b) Duursma, A.; Lefort, L.; Boogers, J. A. F.; de Vries, A. H. M.; de Vries, J. G.; Minnaard, A. J.; Feringa, B. L. *Org. Biomol. Chem.* **2004**, *2*, 1682.
91. Moss, R. J.; Wadsworth, K. J.; Chapman, C. J.; Frost, C. G. *Chem. Commun.* **2004**, 1984.
92. Abbiati, G.; Arcadi, A.; Marinelli, F.; Rossi, E.; Verdecchia, M. *Synlett* **2006**, 3218.
93. Navarre, L.; Darses, S.; Genêt, J.-P. *Eur. J. Org. Chem.* **2004**, *1*, 69.
94. Navarre, L.; Darses, S.; Genêt, J.-P. *Angew. Chem., Int. Ed.* **2004**, *43*, 719.
95. Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207.
96. Batey, R. A.; Thadani, A. N.; Smil, D. V.; Lough, A. J. *Synthesis* **2000**, 990.
97. Thadani, A. N.; Batey, R. A. *Org. Lett.* **2002**, *4*, 3827.
98. Thadani, A. N.; Batey, R. A. *Tetrahedron Lett.* **2003**, *44*, 8051.
99. Pucheault, M.; Michaut, V.; Darses, S.; Genêt, J.-P. *Tetrahedron Lett.* **2004**, *45*, 4729.
100. Li, S.-W.; Batey, R. A. *Chem. Commun.* **2004**, 1382.
101. (a) Solin, N.; Wallner, O. A.; Szabó, J. K. *Org. Lett.* **2005**, *7*, 689; (b) Wallner, O. A.; Szabó, J. K. *Chem.—Eur. J.* **2006**, *12*, 6976.
102. Petasis, N. A.; Akritopoulo, I. *Tetrahedron Lett.* **1993**, *34*, 583.
103. Schlienger, N.; Ryce, M. R.; Hansen, T. K. *Tetrahedron Lett.* **2000**, *41*, 1303.
104. Kabalka, G. W.; Venkataiah, B.; Dong, G. *Tetrahedron Lett.* **2004**, *45*, 729.
105. Tremblay-Morin, J.-P.; Raeppel, S.; Gaudette, F. *Tetrahedron Lett.* **2004**, *45*, 3471.
106. Billard, T.; Langois, B. R. *J. Org. Chem.* **2002**, *67*, 997.
107. Kabalka, G. W.; Mereddy, A. R. *Tetrahedron Lett.* **2004**, *45*, 343.
108. Kabalka, G. W.; Mereddy, A. R. *Tetrahedron Lett.* **2004**, *45*, 1417.
109. Kabalka, G. W.; Mereddy, A. R. *Organometallics* **2004**, *23*, 4519.
110. Kabalka, G. W.; Mereddy, A. R. *Nucl. Med. Biol.* **2004**, *31*, 935.
111. Kabalka, G. W.; Mereddy, A. R. *J. Label Compd. Radiopharm.* **2005**, *48*, 359.
112. Kabalka, G. W.; Mereddy, A. R.; Green, J. F. *J. Label Compd. Radiopharm.* **2006**, *49*, 11.
113. Molander, G. A.; Dehmel, F. *J. Am. Chem. Soc.* **2004**, *126*, 10313.
114. Skaff, O.; Jolliffe, K. A.; Hutton, C. A. *J. Org. Chem.* **2005**, *70*, 7353.
115. Lautens, M.; Maddess, M. L. *Org. Lett.* **2004**, *6*, 1883.
116. Lautens, M.; Ouellet, S. G.; Raeppel, S. *Angew. Chem., Int. Ed.* **2000**, *39*, 4079.
117. Che, C.; Zhang, Z. *Synth. Commun.* **2004**, *34*, 4499.
118. Doubský, J.; Streinz, L.; Lesetický, L.; Koutek, B. *Synlett* **2003**, 937.
119. Doubský, J.; Streinz, L.; Saman, D.; Zedníd, J.; Koutek, B. *Org. Lett.* **2004**, *6*, 4909.
120. Matteson, D. S.; Kim, G. Y. *Org. Lett.* **2002**, *4*, 2153.
121. Quach, T. D.; Batey, R. A. *Org. Lett.* **2003**, *5*, 4397.
122. Quach, T. D.; Batey, R. A. *Org. Lett.* **2003**, *5*, 1381.
123. Wang, L.; Wang, M.; Huang, F. *Synlett* **2005**, 2007.

Biographical sketch

Professor Hélio A. Stefani received his M.S. and Ph.D. degrees from the University of São Paulo in 1988 and 1991, working under the supervision of Professor João V. Comasseto in the field of organic selenium and tellurium chemistry. In 1993 he accepted a faculty position at the Faculty of Pharmaceutical Sciences at the same university where he is currently Associated Professor. He spent a year (2001) at University of Pennsylvania—Philadelphia—PA, United States, working with Professor Gary A. Molander. His interests in chemistry include development of synthetic methodology of selenium, tellurium, and boron compounds, natural products total synthesis and heterocyclic chemistry.



Rodrigo Cella was born in 1981 in Santo Angêlo, Brazil, and spent his childhood in Giruá, Brazil. He received a Diploma in industrial chemistry (2002) and his M.S. (2004) from the Federal University of Santa Maria. Currently, he is a Ph.D. student at University of São Paulo under the supervision of Professor Hélio A. Stefani. His current research interest includes asymmetric synthesis, sonochemistry, and organometallic chemistry.

Adriano S. Vieira was born in 1979 in Júlio de Castilhos—RS, Brazil. He received his under graduate education in industrial chemistry at Federal University of Santa Maria—RS (Brazil, 2001) and his M.S. and Ph.D. degrees in organic chemistry from the same University in 2002 and 2006, working under the guidance of Professor C. C. Silveira in the field of organochalcogen chemistry. He immediately started the postdoctoral fellow in the laboratory of Professor Hélio A. Stefani at the University of São Paulo (Brazil). His research interests are focused in the area of organometallic chemistry and heterocyclic natural product synthesis.