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Authors: Oleksandr V. Hryshchuk, Anatolii O. Varenyk, Yevhen Yurov, Yuliya Kuchkovska, Andriy V. Tymtsunik, and Oleksandr O Grygorenko

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gem-Difluorocyclopropanation of Alkenyl Trifluoroborates with the CF_3SiMe_3–NaI System

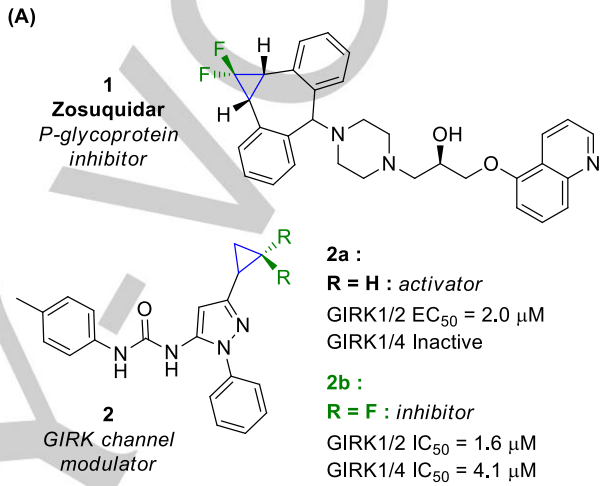
Oleksandr V. Hryshchuk,[a,b] Anatolii O. Varenyk,[a] Yevhen Yurov,[a,b] Yuliya O. Kuchkovska,[a,b] Dr. Andriy V. Tymtsunik,[a,c] and Dr. Oleksandr O. Grygorenko*[a,b]

Abstract: Difluorocyclopropanation of alkenyl trifluoroborates using $TMSCF_3$–NaI system was reported for the first time. The developed method allowed preparation of monocyclic, spiro- and fused-bicyclic *gem*-difluorocyclopropanes bearing additional functional groups. The preparation of potassium (2,2-difluorocyclopropyl)trifluoroborates was achieved in up to 90% yield on a multigram scale.

Introduction

In light of exceptionally high importance of fluorinated substituents and cyclopropane ring for drug discovery,[1–7] their combination in *gem*-difluorocyclopropane is expected to provide an advanced motif for optimization of therapeutic properties. One of the notable *gem*-difluorocyclopropane derivative is Zosuquidar (**1**),[8] which was investigated for treatment of acute myeloid leukemia and reached the phase III of clinical trials (Figure 1, **A**). G protein-coupled inwardly rectifying potassium (GIRK) channel inhibitor **2b** is also worth mentioning as an example of extraordinary ability of fluorinated cyclopropane moiety to act as a 'molecular switch'.[9] In particular, the substitution of cyclopropyl group at the pyrazole ring of **2a** to its *gem*-difluorinated counterpart resulted in alteration of **2** mode of action from activator to inhibitor.

Since functionalized *gem*-difluorocyclopropane-derived compounds present pharmaceutically valuable building blocks, most of the literature discussing these derivatives was mainly focused on carbonyl-, amino- and ether substituted derivatives (Figure 1, **B**).[10] However, several classes of heterosubstituted cyclopropanes were only scarcely studied, despite their potential to expand the scope of reactions used for introduction of *gem*-difluorocyclopropane moiety to the biologically active molecules. Among them, boron-substituted *gem*-difluorocyclopropanes are of special interest due to numerous possibilities of their further modifications.[11–14]



(B)

Number of papers / patents reporting synthesis and reactions of difluorocyclopropanes (referenced by *Reaxys* database)

FG	COR	NR_2	OR	SiR_3	SR	BR_2
# of papers	95	31	74	20	8	3
# of patents	364	92	32	2	7	3

Figure 1. Examples of biologically active *gem*-difluorocyclopropanes (**A**); number of publications reporting synthesis and reactions of functionalized gem-difluorocyclopropanes referenced by *Reaxys* database (**B**).[10]

To date, preparation of *gem*-difluorocyclopropyl boronates was reported only in a few works, and was mostly aimed at non-functionalized derivatives **3** and **4** (Scheme 1).[15–17] Importantly, the previous methods used XCF_2CO_2Na (X = Cl, Br) and required heating up to 180 °C. Because application of these reaction conditions to functionalized substrates is limited by their thermal stability and their susceptibility to side reactions at elevated temperatures, a selection of a $TMSCF_3$–NaI system as a difluorocarbene equivalent[18] was envisaged. The usage of $TMSCF_3$, which is also referred as Ruppert–Prakash reagent, for *gem*-difluoromethylation reaction was first developed by Hu, Prakash and co-workers,[19] and was further adapted for preparation of *gem*-difluorocyclopropanes bearing diverse functional groups.[20–24] Nonetheless, the addition of difluoro-

[a] O. V. Hryshchuk, A. O. Varenyk, Y. Yurov, Y. O. Kuchkovska, Dr. A. V. Tymtsunik, Dr. O. O. Grygorenko
Enamine Ltd. (www.enamine.net)
Chervonotkatska Street 78, Kyiv 02094, Ukraine
[b] O. V. Hryshchuk, Y. Yurov, Y. O. Kuchkovska, Dr. O. O. Grygorenko
Taras Shevchenko National University of Kyiv
Volodymyrska Street 60, Kyiv 01601, Ukraine
E-mail: gregor@univ.kiev.ua
URL: https://orcid.org/0000-0002-6036-5859
[c] Dr. A. V. Tymtsunik
Faculty of Chemical Technology
National Technical University of Ukraine "Igor Sikorsky Kyiv Polytechnic Institute"
Prospect Peremogy 37, Kyiv 03056, Ukraine

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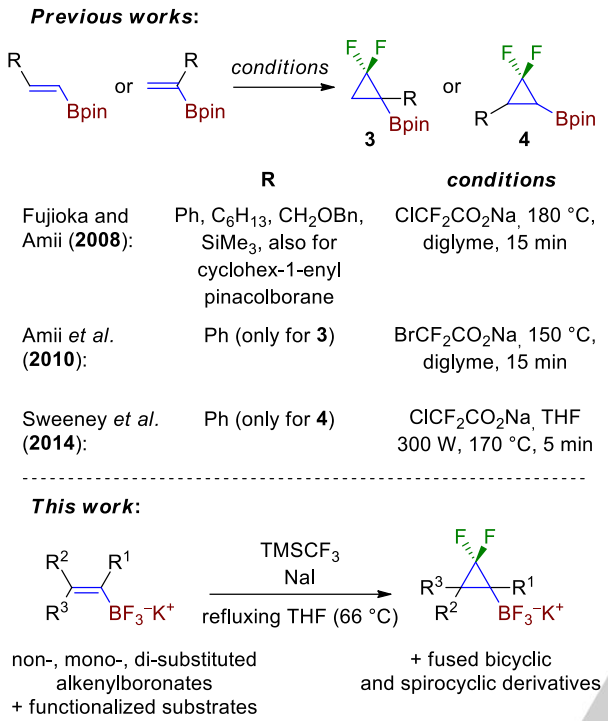
carbene equivalent derived from $TMSCF_3$ to alkenylboronic derivatives was unknown until the present study.



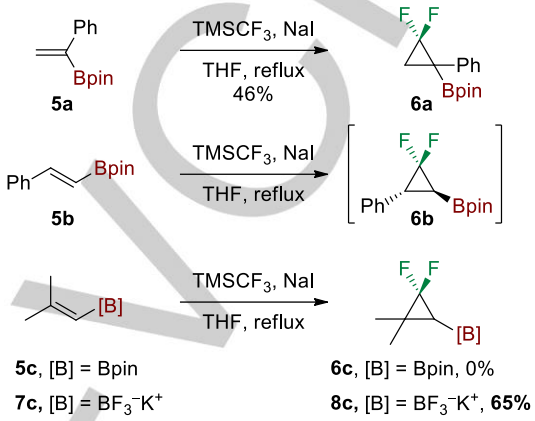
Scheme 1. Difluorocyclopropanation of alkenylboronic derivatives.

In this work, application of $TMSCF_3$–NaI system in refluxing THF (66 °C) for the synthesis of *gem*-difluorocyclopropyl boronic derivatives and its effectiveness for multigram scale synthesis is reported (Scheme 1). It is shown that alkenyl trifluoroborates are optimal substrates for the preparation of aliphatic derivatives which facilitate isolation of the target products. The studied reaction scope included substrates bearing secondary *N*-Boc protected amine, ester, ether, phenyl and cyclopropyl moieties and provided products with spiro- and fused-bicyclic molecular topologies.

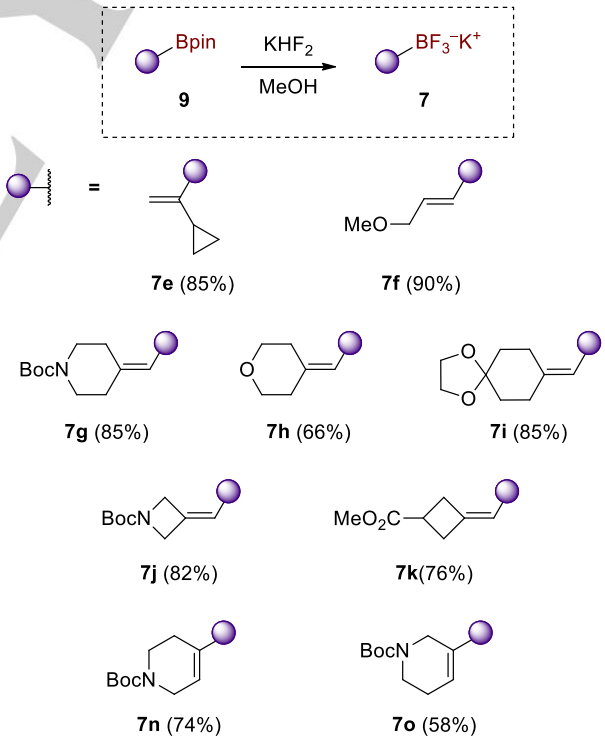
Results and Discussion

Our study commenced with testing $TMSCF_3$–NaI system in reaction with substrate **5a** (Scheme 2), for which the difluorocyclopropanation using XCF_2CO_2Na (X = Cl, Br) at 180 °C and 150 °C, respectively, was previously reported (Scheme 1).[15–17] As a result, compound **6a** was synthesized in 46% yield by this method. However, its isomer **6b** was obtained only as a crude mixture (*ca.* 0.8 g of mixture containing 35% by moles of **6b** from 1.0 g of **5b**) the further purification of which was unsuccessful. Although formation of **6c** was indicated by ^1H and ^{19}F NMR spectra of a crude product obtained after the reaction of **5c**, its isolation in pure form was not achieved, presumably due to its instability on silica gel.

In order to address the problematic isolation of difluorocyclopropyl boronates, the substitution of Bpin moiety to potassium trifluoroborate salt was envisaged to enhance stability of the final products and facilitate their purification by simple recrystallization. As a result, when the same difluorocyclopropanation protocol was applied to the substrate **7c**, the target compound **8c** was isolated in 65% yield (Scheme 2).



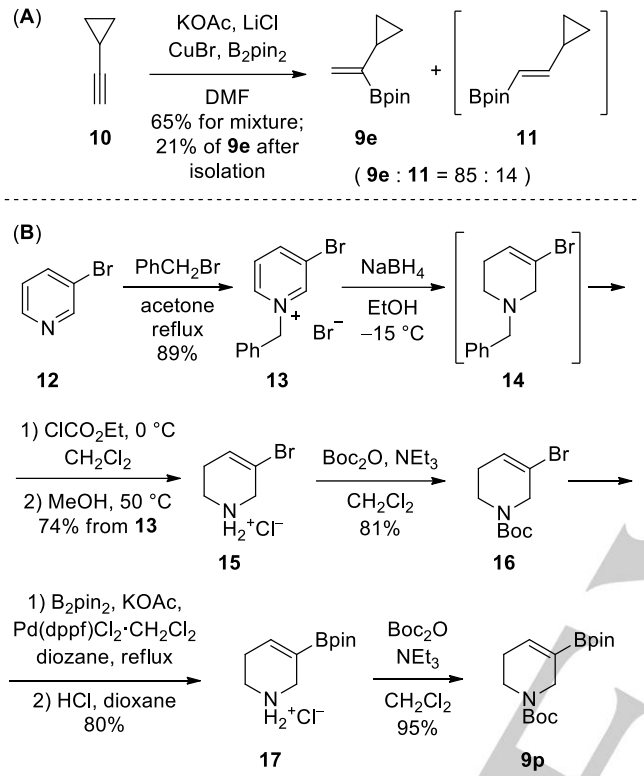
Scheme 2. Attempted difluorocyclopropanation of alkenyl boronic derivatives using the $TMSCF_3$–NaI system.



Scheme 3. Preparation of trifluoroborate salts **7** from pinacolboronates **9**.

The following evaluation of the difluorocyclopropanation reaction efficiency with the $TMSCF_3$–NaI system was carried out

with three types of trifluoroborate substrates – acyclic, exocyclic and endocyclic alkenes **7**. For our study, trifluoroborates **7a–d** and **7m** were accessed from commercial sources, whereas substrares **7e–k** and **7n,o** were obtained from the corresponding pinacolboronates **9**[25–27] by treatment with KHF_2 in MeOH (Scheme 3). Of them, compounds **9f–l** and **9n** were prepared according to the previously reported procedures.[25,27,28]



Scheme 4. . Synthesis of pinacolboronates **9e** (**A**) and **9p** (**B**).

Cyclopropyl-substituted derivative **9e** was synthesized by Cu-catalyzed hydroboration of alkyne **10** (Scheme 4, **A**). Although the total yield of the mixture of **9e** and **11** was 65%, separation of major isomer **9e** allowed its isolation in only 21% yield.

For the preparation of pinacolboronate **9p**, a multistep reaction sequence was developed (Scheme 4, **B**). In particular, pyridine **12** was first benzylated to give **13**, and then reduced with $NaBH_4$ into intermediate **14**. *N*-Bn protecting group of **14** was exchanged to *N*-Boc group in **16** in three steps through amine hydrochloride intermediate **15**. In order to simplify purification of the pinacolboronate product after borylation of **16**, it was converted into a salt form to yield **17**, which was treated with Boc_2O to provide pure pinacolboronate **9p**.

First, the $TMSCF_3$–NaI system in refluxing THF was used for the synthesis of **8a** from potassium (*E*)-trifluoro(styryl)borate (**7a**) (Table 1, Entry 1), which allowed increasing the reaction yield up to 67% (as compared to the reported 50% yield for the corresponding pinacolboronate[15]). Besides, the developed protocol allowed scaling up the reaction from milligram quantities (as reported in the cited work) up to *ca.* 10 g of the final product **8a**. Next, potassium trifluoro(vinyl)borate (**7b**) and its methyl-substituted derivatives **7c,d** were tested under the same reaction conditions and provided corresponding *gem*-difluoro-cyclopropanes **8b–d** in 60–80% yield (Entries 2–4). Substitution of the methyl group in **7d** with the cyclopropyl moiety in **7e** allowed retaining high reaction yield (79% for **8e,** Entry 5). Similarly, introduction of CH_2OMe substituent to the *C*-2 atom of **7f** was found to be well-tolerated by the developed method and provided **8f** with 78% yield (Entry 6). The reactions of (*E*)-alkenes **7a** and **7f** additionally demonstrated the stereospecificity of the addition of difluorocarbene to alkenyl trifluoroborates. The *trans* configuration of products **8a** and **8f** was confirmed by ^1H–^1H and ^1H–^{19}F NOESY experiments (Figure 2).

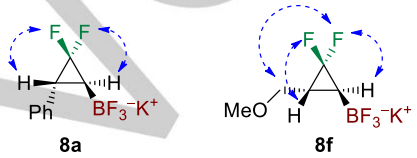


Figure 2. Important ^1H–^{19}F NOESY correlations for **8a** and **8f**.

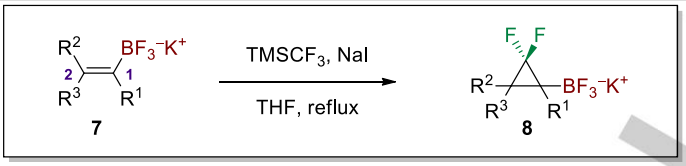
Next, the preparation of spirocyclic compounds **8g–l** was attempted from alkenes **7g–l** under the same reaction conditions (Table 1, Entries 7–12). Alkenyl trifluoroborate substrates bearing endocyclic *N*-Boc amine group, ketal and carboxylic acid ester moieties were well-suited for the developed method and provided bicyclic products **8g–k** in 70–90% yield. Notably, six-membered (hetero)cycloalkenyl derivatives **7g–i** provided slightly better yields than their four-membered counterparts **7j,k** (85–90% versus 70–75%). In contrast to alkenes **7g–k**, *gem*-difluorocyclopropanation of oxetane derivative **7l** led to the formation of a complex mixture of products which could result from oxetane ring-opening.

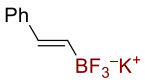
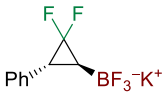
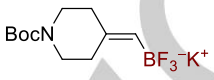
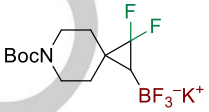
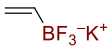
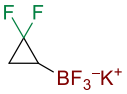
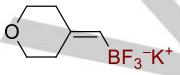
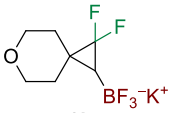
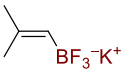
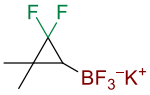
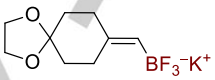
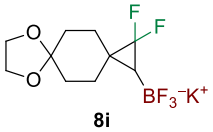
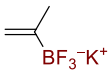
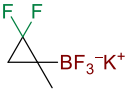
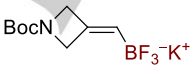
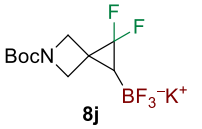
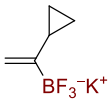
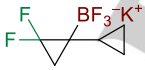
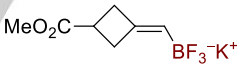
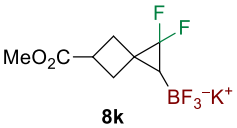
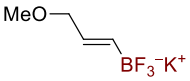
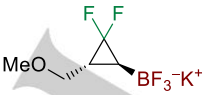
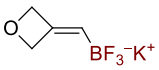
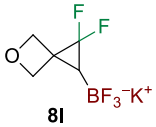
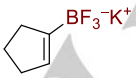
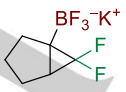
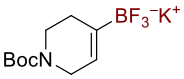
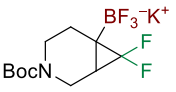
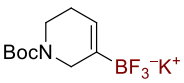
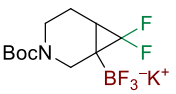
Finally, the developed method was shown to be efficient for the preparation of fused *gem*-difluorocyclopropanes with the trifluoroborate functionality at the tertiary *C*-atom. Although the reaction of non-functionalized cyclopentene derivative **7m** allowed obtaining of **7m** in moderate 65% yield, the preparation of Boc-protected piperidine-fused analogues from **7n** and **7o** was more successful. As a result, two isomeric *gem*-difluoro-cyclopropanated products **8n** and **8o** were isolated in 84% and 70% yield, respectively. Moreover, the high reaction yield was retained when the target compound **8n** was prepared in up to 50 g quantitiy in a single run.

Conclusions

A method for the preparation of *gem*-difluorocyclopropyl trifluoroborate derivatives based on difluorocyclopropanation of alkene moiety was developed and applied on up to 50 g scale. Using the $TMSCF_3$–NaI system as the difluorocarbene equivalent allowed performing the reaction at moderate temperature (65 °C) and increasing the scope of functional groups that

Table 1. Synthesis of *gem*-difluorocyclopropanes **8** from alkenyl trifluoroborates **7**.



Entry	Alkene 7	Product 8	Yield, %	Entry	Alkene 7	Product 8	Yield, %
1	 **7a**	 **8a**	67%[a]	7	 **7g**	 **8g**	90%
2	 **7b**	 **8b**	60%	8	 **7h**	 **8h**	82%
3	 **7c**	 **8c**	65%	9	 **7i**	 **8i**	85%
4	 **7d**	 **8d**	80%	10	 **7j**	 **8j**	75%
5	 **7e**	 **8e**	79%	11	 **7k**	 **8k**	70%
6	 **7f**	 **8f**	78%[a]	12	 **7l**	 **8l**	0%
13	 **7m**	 **8m**	65%	14	 **7n**	 **8n**	84%
				15	 **7o**	 **8o**	70%

[a] Relative configuration is shown.

tolerate the reaction conditions Application of alkenyl trifluoroborates instead of pinacolboronates was found to facilitate the purification of the target products and increase their yield up to 90%. The developed synthesis of *gem*-difluorocyclopropyl trifluoroborates is amenable for structurally diverse fluorinated derivatives including monocyclic, fused bicyclic, spirocyclic and bifunctionalized compounds – promising organoboron reagents for synthetic and medicinal chemistry.

Experimental Section

General. The solvents were purified according to the standard procedures.[29] Melting points were measured on MPA100 OptiMelt automated melting point system. Analytical TLC was performed using Polychrom SI F254 plates. Column chromatography was performed using Kieselgel Merck 60 (230–400 mesh) as the stationary phase. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker 170 Avance 500 spectrometer (at 499.9 MHz for Protons and 124.9 MHz for Carbon-13) and Varian Unity Plus 400 spectrometer (at 400.4 MHz for protons and 100.7 MHz for Carbon-13). Chemical shifts are reported in ppm with solvent residual signal used as an internal standard (^{1}H, ^{13}C); and $CFCl_3$ (^{19}F) or $BF_3{\cdot}Et_2O$ (^{11}B) – as external standards. Elemental analyses were performed at the Laboratory of Organic Analysis, Department of Chemistry, Taras Shevchenko National University of Kyiv. Mass spectra were recorded on an Agilent 1100 LCMSD SL instrument (chemical ionization (APCI), electrospray ionization (ESI)) and Agilent 5890 Series II 5972 GCMS instrument (electron impact ionization (EI)).

General procedure for synthesis of compounds 7. KHF_2 (31.2 g, 400 mmol) was added to a solution of pinacolboronate **9** (100 mmol) in MeOH (1 L) and the reaction mixture was stirred overnight. The resulting solution was concentrated under vacuum, dissolved in a minimal amount of acetone (*ca.* 50 mL) and poured into ten-fold excess of Et_2O (*ca.* 500 mL). The obtained precipitate was filtered to give the target product **7.**

Potassium (1-cyclopropylvinyl)trifluoroborate (7e). Yield 8.39 g (85%) from 11.0 g of **9**. White solid, mp 197–199 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 4.71 (d, J = 5.2 Hz, 1H), 4.63 (s, 1H), 1.30 – 1.16 (m, 1H), 0.52 – 0.40 (m, 2H), 0.40 – 0.30 (m, 2H) ppm. ^{13}C NMR (151 MHz, DMSO-d_6) δ 159.9 (br s), 109.9, 16.8, 6.5 ppm. ^{19}F NMR (376 MHz, DMSO-d_6) δ –139.6 – –140.2 (m) ppm. MS(EI) m/z = 116 $[M – K – F]^+$. Anal. Calcd. for $C_5H_7BF_3K$: C 34.51; H 4.05. Found: C 34.55; H 3.67.

Potassium (*E*)-trifluoro(3-methoxyprop-1-en-1-yl)borate (7f). Yield 4.05 g (90%) from 5.00 g of **9f**. White solid, mp 157–160 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 5.62 – 5.37 (m, 2H), 3.71 (d, J = 4.9 Hz, 2H), 3.14 (s, 3H) ppm. ^{13}C NMR (151 MHz, DMSO-d_6) δ 141.6 (br s), 130.2, 75.8, 56.6 ppm. ^{19}F NMR (376 MHz, DMSO-d_6) δ –138.0 – –139.0 (m) ppm. MS(APCI) m/z = 213 $[C_8H_{15}B_2O_5]^-$. Anal. Calcd. for $C_4H_7BF_3KO$: C 26.99; H 3.96. Found: C 26.89; H 3.74.

Potassium ((1-(*tert*-butoxycarbonyl)piperidin-4-ylidene)methyl)trifluoroborate (7g). Yield 3.99 g (85%) from 5.00 g of **9g**. White solid, mp > 215 °C (dec). ^{1}H NMR (400 MHz, DMSO-d_6) δ 4.94 (q, J = 5.1 Hz, 1H), 3.26 (t, J = 5.8 Hz, 2H), 3.21 (t, J = 5.8 Hz, 2H), 2.22 (t, J = 5.8 Hz, 2H), 1.94 (t, J = 5.8 Hz, 2H), 1.39 (s, 9H) ppm. ^{13}C NMR (151 MHz, DMSO-d_6) δ 153.9, 139.0, 133.2 (br s), 78.2, 45.6 (2C), 38.3, 31.1, 28.1 ppm. ^{19}F NMR (376 MHz, DMSO-d_6) δ –132.4 ppm. MS(APCI) m/z = 186 $[M – K – CH_2C(CH_3)_2 – 2F + 2OH + H]^+$, 264 $[M – K – 2F + 2OH + Na]^+$. Anal. Calcd. for $C_{11}H_{18}BF_3KNO_2$: C 43.58; H 5.98; N 4.62. Found: C 43.28; H 5.70; N 4.31.

Potassium ((dihydro-*2H*-pyran-4(3*H*)-ylidene)methyl)trifluoroborate (7h). Yield 1.20 g (66%) from 2.00 g of **9h**. White solid, mp 218–220 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 4.90 (q, J = 5.2 Hz, 1H), 3.52 (t, J = 5.4 Hz, 2H), 3.47 (t, J = 5.4 Hz, 2H), 2.29 (t, J = 5.4 Hz, 2H), 2.01 (t, J = 5.4 Hz, 2H) ppm. ^{13}C NMR (151 MHz, DMSO-d_6) δ 138.8, 131.3 (br s), 69.2, 68.8, 39.5, 32.8 ppm. ^{19}F NMR (376 MHz, DMSO-d_6) δ –131.9 – –132.8 (m) ppm. ^{11}B NMR (160 MHz, DMSO-d_6) δ 3.4 – 1.0 (m) ppm. MS(APCI) m/z = 161 $[M – K – 2F + 2OH]^-$. Anal. Calcd. for $C_6H_9BF_3KO$: C 35.32; H 4.45. Found: C 35.02; H 4.82.

Potassium (1,4-dioxaspiro[4.5]decan-8-ylidenemethyl)trifluoroborate (7i). Yield 1.58 g (85%) from 2.00 g of **7i**. White solid, mp 209–211 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 4.89 – 4.81 (m, 1H), 3.88 – 3.80 (m, 4H), 2.27 (t, J = 6.3 Hz, 2H), 2.03 (t, J = 6.3 Hz, 2H), 1.52 (t, J = 6.3 Hz, 2H), 1.47 (t, J = 6.3 Hz, 2H) ppm. ^{13}C NMR (151 MHz, DMSO-d_6) δ 141.3, 131.6 (br s), 108.4, 63.5, 36.4, 36.2, 35.9, 27.7 ppm. ^{19}F NMR (376 MHz, DMSO-d_6) δ –132.2 – –132.9 (m) ppm. Anal. Calcd. for $C_9H_{13}BF_3KO_2$: C 41.56; H 5.04. Found: C 41.39; H 4.83.

Potassium ((1-(*tert*-butoxycarbonyl)azetidin-3-ylidene)methyl)trifluoroborate (7j). Yield 2.29 g (82%) from 3.00 g of **9j**. Beige solid, mp 180–182 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 5.13 – 5.05 (m, 1H), 4.29 (s, 2H), 4.24 (s, 2H), 1.37 (s, 9H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6) δ 155.9, 131.2, 129.5 (br s), 78.1, 59.3 (2C), 28.1 ppm. ^{19}F NMR (376 MHz, DMSO-d_6) δ –135.9 – –136.6 (m) ppm. MS(APCI) m/z = 157 $[M – K – CH_2C(CH_3)_2 – 3F + 2OH]^+$. Anal. Calcd. for $C_9H_{14}BF_3KNO_2$: C 39.29; H 5.13; N 5.09. Found: C 39.52; H 5.04; N 4.89.

Potassium trifluoro((3-(methoxycarbonyl)cyclobutylidene)methyl)borate (7k). Yield 7.70 g (76%) from 11.0 g of **9k**.The compound was obtained with *ca.* 90% purity. White solid, mp 98–101 °C. ^{1}H NMR (400 MHz, D_2O) δ 5.18 – 5.11 (m, 1H), 3.73 (s, 3H), 3.22 (quint, J = 8.1 Hz, 1H), 3.08 – 2.96 (m, 2H), 2.96 – 2.90 (m, 2H) ppm. ^{1}H NMR (400 MHz, DMSO-d_6) δ 4.89 (s, 1H), 3.59 (s, 3H), 3.00 (quint, J = 8.2 Hz, 1H), 2.90 – 2.75 (m, 2H), 2.74 – 2.65 (m, 2H) ppm. ^{13}C NMR (151 MHz, D_2O) δ 179.1, 146.8, 122.3 (br s), 52.3, 36.7, 35.8, 33.2 ppm. ^{19}F NMR (376 MHz, DMSO-d_6) δ –134.1 – –135.3 (m) ppm. MS(APCI) m/z = 95 $[M – K – BF_3 – OCH_3 + H]^+$, 127 $[M – K – BF_3 + 2H]^+$.

Potassium (1-(*tert*-butoxycarbonyl)-1,2,3,6-tetrahydropyridin-4-yl)trifluoroborate (7n). Yield 63.1 g (75%) from 90.0 g of **9n**. For characterization data and spectra see ref.[30]

Potassium (1-(*tert*-butoxycarbonyl)-1,2,5,6-tetrahydropyridin-3-yl)trifluoroborate (7o). Yield 38.0 g (58%) from 70.0 g of **9o**. The compound was obtained with *ca.* 90% purity as *ca.* 1:1 mixture of rotamers. ^{1}H NMR (400 MHz, DMSO-d_6) δ 5.54 (s, 1H), 3.70 (s, 2H), 3.30 – 3.20 (m, 2H), 1.90 (s, 2H), 1.39 (s, 9H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6) δ 154.4, 142.9, 120.2, 77.8, 45.8, 45.3 and 40.9, 28.3, 25.2 ppm. ^{19}F NMR (376 MHz, DMSO-d_6) δ -142.7 ppm. MS(APCI) = 250 $[M – K]^+$.

General procedure for the preparation of compounds 8. Alkenyl trifluoroborates **7** and NaI were dried under vacuum at 80 °C prior usage in the difluorocyclopropanation reaction. A mixture of **7** (100 mmol) and NaI (6.00 g, 40.0 mmol) in THF (2 L) was heated to reflux and then $TMSCF_3$ (71.1 g, 500 mmol) was slowly added dropwise (CAUTION: the reaction is exothermic). After stirring for 30 min at reflux, the reaction mixture was allowed to cool down to rt, and NaI was filtered off. The filtrate was concentrated under vacuum, dissolved in a minimal amount of acetone (*ca.* 80 mL) and poured into ten-fold excess of Et_2O (*ca.* 800 mL). The obtained precipitate was filtered to give the target product **8.**

Potassium (*trans*-2,2-difluoro-3-phenylcyclopropyl)trifluoroborate (8a). Yield 12.4 g (67%) from 15.0 g of **7a**. White solid, mp 176–178 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.26 (t, J = 7.4 Hz, 2H), 7.19 – 7.08 (m, 3H), 2.35 (t, J = 10.2 Hz, 1H), 0.88 – 0.66 (m, 1H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6) δ 137.4, 128.0, 127.3, 125.7, 118.0 (dd, J = 291.1, 282.2 Hz), 29.1 (t, J = 10.8 Hz), 23.0 (br s) ppm. ^{19}F NMR (376 MHz, DMSO-d_6) δ –126.9 (d, J = 140.3 Hz, 1F), –133.3 (d, J = 140.3 Hz, 1F), –138.0 – –139.8 (m, 3F) ppm. MS(APCI) m/z = 221 $[M–K]^–$. Anal. Calcd. for $C_9H_7BF_5K$: C 41.57; H 2.71. Found: C 41.90; H 2.96.

Potassium (2,2-difluorocyclopropyl)trifluoroborate (8b). Yield 16.5 g (60%) from 20.0 g of **7b**. White solid, mp 193–195 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 0.89 (t, J = 11.1 Hz, 1H), 0.79 (s, 1H), 0.29 (s, 1H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6) δ 119.1 (t, J = 277.4 Hz), 15.6 (br s), 12.2 ppm. ^{19}F NMR (376 MHz, DMSO-d_6) δ –121.6 (d, J = 142.2 Hz, 1F), –135.1 (d, J = 142.2 Hz, 1F), –138.9 (q, J = 47.8 Hz, 3F) ppm. MS(APCI) m/z = 145 $[M–K]^–$. Anal. Calcd. for $C_3H_3BF_5K$: C 19.59; H 1.64. Found: C 19.20; H 1.93.

Potassium (2,2-difluoro-3,3-dimethylcyclopropyl)trifluoroborate (8c). Yield 4.25 g (65%) from 5.00 g of **7c**. White solid, mp >185 °C (dec). ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.05 (s, 6H), –0.00 – –0.18 (m, 1H) ppm. ^{13}C NMR (151 MHz, DMSO-d_6) δ 122.4 (t, J = 289.2 Hz), 26.1 (br s), 22.5 (d, J = 6.0 Hz), 21.4 (t, J = 9.4 Hz), 15.8 (d, J = 6.0 Hz) ppm. ^{19}F NMR (376 MHz, DMSO-d_6) δ –129.3 (d, J = 137.2 Hz, 1F), –132.8 (q, J = 48.8 Hz, 3F), –140.6 (d, J = 137.2 Hz, 1F) ppm. MS(APCI) = 171 $[M – K – F + OH]^–$. Anal. Calcd. for $C_5H_7BF_5K$: C 28.33; H 3.33. Found: C 28.53; H 3.68.

Potassium (2,2-difluoro-1-methylcyclopropyl)trifluoroborate (8d). Yield 8.29 g (80%) from 7.75 g of **7d**. White solid, mp 178–180 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.03 – 0.95 (m, 1H), 0.90 (s, 3H), 0.38 (dd, J = 13.4, 5.1 Hz, 1H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6) δ 120.8 (dd, J = 288.4, 278.0 Hz), 19.0, 18.4 (br s), 15.9 – 15.6 (m) ppm. ^{19}F NMR (376 MHz, DMSO-d_6) δ –129.4 (d, J = 142.5 Hz, 1F), –135.3 (d, J = 142.5 Hz, 1F), –144.1 (q, J = 49.5 Hz, 3F) ppm. MS(APCI) m/z = 159 $[M–K]^–$. Anal. Calcd. for $C_4H_5BF_5K$: C 24.27; H 2.55. Found: C 24.65; H 2.59.

Potassium (6-(*tert*-butoxycarbonyl)-2,2-difluoro-6-azaspiro[2.5]-octan-1-yl)trifluoroborate (8g). Yield 2.10 g (90%) from 2.00 g of **7g**. White solid, mp 178–180 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.40 – 3.13 (m, 4H), 1.67 – 1.56 (m, 1H), 1.54 – 1.41 (m, 2H), 1.39 (s, 9H), 1.31 – 1.24 (m, 1H), 0.09 – 0.00 (m, 1H) ppm. ^{13}C NMR (151 MHz, DMSO-d_6) δ 154.0, 121.6 (t, J = 288.1 Hz), 78.4, 43.8, 42.9, 31.9, 28.1, 26.8 (t, J = 9.5 Hz), 25.8 (br s), 25.4 ppm. ^{19}F NMR (376 MHz, DMSO-d_6) δ –130.0 (d, J = 140.5 Hz, 1F), –132.3 – –133.0 (m, 3F), –140.5 (d, J = 140.5 Hz, 1F) ppm. MS(APCI) m/z = 218 $[M – K – OC(CH_3)_3 – 3F + 2OH]^+$, 236 $[M – K – CH_2C(CH_3)_2 – 3F + 2OH + H]^+$. Anal. Calcd. for $C_{12}H_{18}BF_5KNO_2$: C 40.81; H 5.14; N 3.97. Found: C 40.64; H 5.18; N 4.17.

Potassium (2,2-difluoro-6-oxaspiro[2.5]octan-1-yl)trifluoroborate (8h). Yield 1.23 g (82%) from 1.20 g of **7h**. Beige solid, mp 166–169 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.67 (ddd, J = 10.8, 6.9, 3.6 Hz, 1H), 3.58 (ddd, J = 10.8, 6.9, 3.6 Hz, 1H), 3.49 (ddd, J = 10.8, 6.9, 3.6 Hz, 1H), 3.42 (ddd, J = 10.8, 6.9, 3.6 Hz, 1H), 1.72 – 1.61 (m, 1H), 1.61 – 1.53 (m, 1H), 1.53 – 1.42 (m, 1H), 1.42 – 1.28 (m, 1H), 0.10 – –0.03 (m, 1H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6) δ 121.6 (t, J = 288.7 Hz), 66.9, 66.7, 32.8, 26.6, 26.1 (t, J = 9.8 Hz), 25.6 (br s) ppm. ^{19}F NMR (376 MHz, DMSO-d_6) δ –130.2 (d, J = 140.7 Hz, 1F), –132.1 – –133.1 (m, 3F), –140.8 (d, J = 140.7 Hz, 1F) ppm. MS(APCI) m/z = 365 $[C_{14}H_{19}B_2F_4O_5]^–$. Anal. Calcd. for $C_7H_9BF_5KO$: C 33.09; H 3.57. Found: C 33.42; H 3.65.

Potassium (2,2-difluoro-7,10-dioxadispiro[2.2.4^6.2^3]dodecan-1-yl)-trifluoroborate (8i). Yield 1.01 g (85%) from 1.00 g of **7i**. White solid, mp 189–191 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.84 (s, 4H), 1.77 – 1.63 (m, 2H), 1.61 – 1.47 (m, 4H), 1.43 – 1.35 (m, 2H), –0.04 (d, J = 22.3 Hz, 1H) ppm. ^{13}C NMR (151 MHz, DMSO-d_6) δ 122.3 (t, J = 288.3 Hz), 108.4, 63.6, 63.5, 33.9, 33.6, 29.9 (d, J = 4.6 Hz), 27.4 (t, J = 9.4 Hz), 25.7 (br s), 22.6 ppm. ^{19}F NMR (376 MHz, DMSO-d_6) δ –130.2 (d, J = 140.5 Hz, 1F), –132.4 – –133.6 (m, 3F), –140.8 (d, J = 140.5 Hz, 1F) ppm. ^{11}B NMR (160 MHz, DMSO-d_6) δ 3.9 – 0.5 (m) ppm. MS(APCI) m/z = $[M – K – 3F + H_2O + HCO_2H]^–$. Anal. Calcd. for $C_{10}H_{13}BF_5KO_2$: C 38.73; H 4.23. Found: C 38.42; H 3.86.

Potassium (5-(*tert*-butoxycarbonyl)-2,2-difluoro-5-azaspiro[2.3]-hexan-1-yl)trifluoroborate (8j). Yield 0.886 g (75%) from 1.00 g of **7j**. Beige solid, mp 180–182 °C. The compound was obtained as *ca*. 1:1 mixture of rotamers. ^{1}H NMR (400 MHz, DMSO-d_6) δ 4.01 – 3.79 (m, 2H), 3.79 – 3.62 (m, 2H), 1.38 (s, 9H), 0.49 – 0.28 (m, 1H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6) δ 155.5, 116.5 (dd, J = 288.5, 281.7 Hz), 78.6, 53.5 and 52.5, 52.4 and 51.3, 28.0, 23.2 (t, J = 10.9 Hz), 21.2 (br s) ppm. ^{19}F NMR (376 MHz, DMSO-d_6) δ –129.2 (d, J = 145.7 Hz, 1F), –134.7 – –136.1 (m, 3F), –142.8 (d, J = 145.7 Hz, 1F) ppm. MS(APCI) m/z = 286 $[M–K]^–$. Anal. Calcd. for $C_{10}H_{14}BF_5KNO_2$: C 36.94; H 4.34; N 4.31. Found: C 37.28; H 4.01; N 4.42.

Potassium (2,2-difluoro-5-(methoxycarbonyl)spiro[2.3]hexan-1-yl)tri-fluoroborate (8k). Yield 2.13 g (70%) from 2.50 g of **7k**. White solid, mp 100–102 °C. The compound was obtained as *ca*. 40:60 mixture of diastereomers. ^{1}H NMR (400 MHz, D_2O) δ 3.74 (s, 1.8H), 3.72 (s, 1.2H), 3.35 – 3.18 (m, 1H), 2.59 – 2.46 (m, 1H), 2.44 – 2.28 (m, 3H), 0.53 – 0.39 (m, 1H) ppm. ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.61 (s, 1.8H), 3.60 (s, 1.2H), 3.15 – 3.05 (m, 1H), 2.45 – 2.10 (m, 4H), 0.26 – –0.01 (m, 1H) ppm. ^{13}C NMR (126 MHz, D_2O) δ 179.0 and 178.3, 118.4 (t, J = 285.7 Hz) and 117.7 (t, J = 284.8 Hz), 52.4, 33.4 and 33.0, 28.7 and 28.5, 27.0 and 26.4, 25.8, 21.2 (br s) ppm. ^{19}F NMR (376 MHz, DMSO-d_6) δ –128.7 (d, J = 141.8 Hz, 1F), –134.1 – –134.4 (m, 1.2F) and –134.4 – –134.8 (m, 1.8F), –141.7 (d, J = 141.8 Hz, 0.4F) and –142.0 (d, J = 141.8 Hz, 0.6F) ppm. MS(APCI) m/z = 421 $[C_{16}H_{19}B_2F_4O_7]^–$. Anal. Calcd. for $C_8H_9BF_5KO_2$: C 34.07; H 3.22. Found: C 33.95; H 3.41.

Potassium (6,6-difluorobicyclo[3.1.0]hexan-1-yl)trifluoroborate (8m). Yield 4.18 g (65%) from 5.00 g of **7m**. White solid, mp 126–128 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.92 – 1.69 (m, 3H), 1.66 – 1.49 (m, 2H), 1.46 – 1.25 (m, 2H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6) δ 122.6 (dd, J = 295.5, 282.2 Hz), 31.4 (br s), 29.3 (t, J = 10.3 Hz), 29.2, 26.6, 25.2 (d, J = 6.5 Hz) ppm. ^{19}F NMR (376 MHz, DMSO-d_6) δ –123.2 (d, J = 146.8 Hz, 1F), –139.6 – –140.3 (m, 4F) ppm. MS(APCI) m/z = 118 $[M – K – BF_3 + H]^+$. Anal. Calcd. for $C_6H_7BF_5K$: C 32.17; H 3.15. Found: C 32.35; H 2.91.

Potassium (3-(*tert*-butoxycarbonyl)-7,7-difluoro-3-azabicyclo[4.1.0]-heptan-6-yl)trifluoroborate (8n). Yield 54.2 g (84%) from 55.0 g of **7n**. Beige solid, mp 194–196 °C. The compound was obtained as *ca*. 7:3 mixture of rotamers. ^{1}H NMR (400 MHz, DMSO-d_6_d_6) δ 3.62 (d, J = 14.4 Hz, 0.3H), 3.46 – 3.34 (m, 1H), 3.31 – 3.16 (m, 1H), 2.79 – 2.62 (m, 0.7H), 1.72 (d, J = 13.1 Hz, 1H), 1.55 – 1.16 (m, 3H), 1.36 (s, 9H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6) δ 153.9, 119.4 (dd, J = 291.9, 279.6 Hz), 78.0, 36.5, 35.2, 28.1, 19.2 (d, J = 28.2 Hz), 17.5 (d, J = 45.5 Hz) ppm (the signal of *C* near the boron atom was not registered due to its low intensity). ^{19}F NMR (376 MHz, DMSO-d_6) δ –128.9 (d, J = 144.6 Hz, 0.5F) and –129.2 (d, J = 144.6 Hz, 0.5F), –143.1 (d, J = 144.6 Hz, 0.5F) and –143.3 (d, J = 144.6 Hz, 0.5F), –144.1 – –145.1 (m, 3F) ppm. MS(APCI) m/z = 300 $[M–K]^–$. Anal. Calcd. for $C_{11}H_{16}BF_5KNO_2$: C 38.96; H 4.76; N 4.13. Found: C 38.56; H 4.82; N 4.04.

Potassium (3-(*tert*-butoxycarbonyl)-7,7-difluoro-3-azabicyclo[4.1.0]-heptan-1-yl)trifluoroborate (8o). Yield 30.4 g (70%) from 37.0 g of **7o**. White solid, mp 185–187 °C. The compound was obtained as *ca*. 1:1 mixture of rotamers. ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.91 – 3.10 (m, 4H), 2.50 – 2.31 (m, 1H), 1.82 – 1.44 (m, 3H), 1.36 (s, 9H) ppm. ^{13}C NMR (101 MHz, DMSO-d_6) δ 147.4, 110.5 (t, *J* = 285.3 Hz), 71.0, 32.3 and 31.6, 31.3 and 30.5, 19.3, 9.8 (t, *J* = 9.9 Hz), 8.0 and 7.6 ppm (the signal of *C* near the boron atom was not registered due to its low intensity). ^{19}F NMR (376 MHz, DMSO-d_6) δ –128.3 (d, *J* = 146.8 Hz, 0.5F) and –128.5 (d, *J* = 146.8 Hz, 0.5F), –143.3 – –143.8 (m, 3F), –144.1 (d, *J* = 146.8 Hz, 0.5F) and –144.5 (d, *J* = 146.8 Hz, 0.5F) ppm. MS(APCI) *m/z* = 300 [M–K]$^-$. Anal. Calcd. for $C_{11}H_{16}BF_5KNO_2$: C 38.96; H 4.76; N 4.13. Found: C 39.35; H 4.97; N 4.36.

Potassium (2,2-difluoro-[1,1'-bi(cyclopropan)]-1-yl)trifluoroborate (8e). Alkenyl trifluoroborates **7e** and NaI were dried under vacuum at 80 °C prior usage in the difluorocyclopropanation reaction. Next, **7e** (1.00g, 5.75 mmol) in THF (115 mL) was heated to reflux and then $TMSCF_3$ (1.64 g, 11.5 mmol) was added dropwise. After stirring at reflux for additional 10 min, NaI (0.0862 g, 0.575 mmol) was added, followed by a slow dropwise addition of $TMSCF_3$ (8.18 g, 57.5 mmol) (CAUTION: the reaction is exothermic). After stirring for 30 min at reflux, the reaction mixture was allowed to cool down to r.t. and NaI was filtered off. The filtrate was concentrated under vacuum, dissolved in a minimal amount of acetone (*ca.* 25 mL) and poured into ten-fold excess of Et_2O (*ca.* 250 mL). The obtained precipitate was filtered to give the title product. Yield 1.02 g (79%). White solid, mp >290 °C (dec). ^{1}H NMR (400 MHz, DMSO-d_6) δ 0.86 – 0.78 (m, 1H), 0.69 (dt, *J* = 13.2, 6.5 Hz, 1H), 0.33 (dd, *J* = 13.8, 4.9 Hz, 1H), 0.29 – 0.20 (m, 1H), 0.20 – 0.11 (m, 1H), 0.11 – 0.01 (m, 2H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6) δ 119.9 (t, *J* = 293.1 Hz), 14.7, 9.8, 3.0, 1.3 ppm (the signal of *C* near the boron atom was not registered due to its low intensity). ^{19}F NMR (376 MHz, DMSO-d_6) δ –126.4 (d, *J* = 143.4 Hz, 1F), –133.8 (d, *J* = 143.4 Hz, 1F), –141.4 (q, *J* = 72.2 Hz, 3F) ppm. ^{11}B NMR (160 MHz, DMSO-d_6) δ 2.4 (q, *J* = 51.4 Hz) ppm. MS(APCI) *m/z* = 161 [M – K – 3F + 2OH – H]$^+$. Anal. Calcd. for $C_6H_7BF_5K$: C 32.17; H 3.15. Found: C 32.32; H 3.54.

Potassium (*trans*-2,2-difluoro-3-(methoxymethyl)cyclopropyl)tri-fluoroborate (8f). The compound was obtained by the same procedure described for **8e** using **7f** (1.00 g, 5.62 mmol), first portion of $TMSCF_3$ (1.59 g, 11.2 mmol), second portion of $TMSCF_3$ (15.9 g, 112 mmol), and NaI (0.084 g, 0.562 mmol). After filtering off the NaI and concentration of the filtrate under vacuum, the obtained residue was triturated in EtOAc – CH_2Cl_2 (1:1) mixture to give the pure title product. Yield 0.999 g (78%). White solid, mp 141–143 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.44 (dt, *J* = 10.4, 5.0 Hz, 1H), 3.19 (s, 3H), 3.17 – 3.09 (m, 1H), 1.41 – 1.28 (m, 1H), 0.16 – 0.00 (m, 1H) ppm. ^{13}C NMR (101 MHz, DMSO-d_6) δ 119.7 (t, *J* = 281.4 Hz), 70.7 (dd, *J* = 4.9, 1.6 Hz), 57.4, 23.4 (td, *J* = 10.6, 2.4 Hz), 19.5 (br s) ppm. ^{19}F NMR (376 MHz, DMSO-d_6) δ –131.0 (d, *J* = 145.0 Hz, 1F), –133.1 (d, *J* = 145.0 Hz, 1F), –137.9 – –138.8 (m, 3F) ppm. MS(APCI) *m/z* = 189 [M – K]$^-$. Anal. Calcd. for $C_5H_7BF_5KO$: C 26.34; H 3.09. Found: C 26.35; H 3.11.

2-(2,2-Difluoro-1-phenylcyclopropyl)-4,4,5,5-tetramethyl-1,3,2-dioxa-borolane (6a).[15] A mixture of **5a** (10.0 g, 43.5 mmol) and NaI (2.61 g, 17.4 mmol) in THF (200 mL) was heated to reflux and then $TMSCF_3$ (12.4 g, 87.0 mmol) was slowly added dropwise (CAUTION: the reaction is exothermic). After stirring for 30 min at reflux, the reaction mixture was allowed to cool down to rt, and NaI was filtered off. The filtrate was concentrated under vacuum. The residue was recrystallized from pentane to obtain the title product. Yield 5.60 g (46%)**.** White solid, mp 97–99 °C (lit. 97–99 °C).[15] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.20 (m, 5H), 2.09 – 2.01 (m, 1H), 1.69 (ddd, *J* = 12.1, 6.7, 2.6 Hz, 1H), 1.22 (s, 6H), 1.18 (s, 6H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.3, 129.3, 128.4, 126.7, 114.3 (t, *J* = 284.5 Hz), 84.6, 24.8, 24.5, 20.6 (t, *J* = 10.1 Hz) ppm (the signal of *C* near the boron atom was not registered due to its low intensity). ^{19}F NMR (376 MHz, $CDCl_3$) δ –125.7 (d, *J* = 145.4 Hz), –132.6 (d, *J* = 145.4 Hz) ppm. MS(EI) *m/z* = 280 [M]$^+$, 265 [M – CH_3]$^+$, 153 [M – $B(OC(CH_3)_2]$. Anal. Calcd. for $C_{15}H_{19}BF_2O_2$: C 64.32; H 6.84. Found: C 64.55; H 6.67.

2-(1-Cyclopropylvinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (9e).[31] A mixture of ethynylcyclopropane (40.0 g, 605 mmol), KOAc (52.3 g, 533 mmol), LiCl (14.4, 339 mmol), CuBr (76.5 g, 533 mmol) and B_2pin_2 (135 g, 533 mmol) in DMF (1.2 L) was stirred at 25 °C overnight. The resulting solution was extracted with hexane (2×1.2 L), and the combined hexane layers were concentrated under vacuum. The residue containing two isomeric products was the subjected to column chromatography (gradient hexane – $CHCl_3$ as eluent) to give the title product. Yield 21.7 g (21%). Colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.61 (s, 1H), 5.46 (s, 1H), 1.54 – 1.43 (m, 1H), 1.24 (s, 12H), 0.68 – 0.61 (m, 2H), 0.58 – 0.52 (m, 2H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.7 (br s), 125.3, 83.3, 24.8, 15.5, 7.6 ppm. MS(EI) *m/z* = 194 [M]$^+$. Anal. Calcd. for $C_{11}H_{19}BO_2$: C 68.08; H 9.87. Found: C 68.44; H 10.21.

1-Benzyl-3-bromopyridin-1-ium bromide (13). To a pre-heated to 45 °C solution of 3-bromopyridine (**12**) (143 g, 905 mmol) in acetone (2 L), BnBr (155 g, 905 mmol) was added dropwise, and the resulting mixture was stirred under reflux for 2 days. Then, the reaction mixture was allowed to cool to rt and the precipitate was filtered. The obtained solids were washed with acetone (2×200 mL) and dried to give the title product. Yield 265 g (89%). For characterization data and spectra see ref.[32]

5-Bromo-1,2,3,6-tetrahydropyridine hydrochloride (15). To a pre-cooled to –15 °C solution of **13** (170 g, 517 mmol) in EtOH (1.7 L), $NaBH_4$ (29.3 g, 775 mmol) was added portionwise while the temperature was maintained below –10 °C. The reaction was stirred for additional 30 min at the same temperature and then concentrated under vacuum. H_2O (400 mL) was added to a residue, and the solution was extracted with *t*-BuOMe (3×400 mL). The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The obtained crude product **14** (120 g) was used in the next step without additional purification. To a solution of **14** (120 g) in CH_2Cl_2 (700 mL), $ClCO_2Et$ (77 mL, 809 mmol) was added dropwise at 0 °C. The reaction mixture was stirred for additional 30 min and then concentrated under vacuum to the half of its initial volume. The resulting solution was added dropwise to a pre-heated to 50 °C MeOH (1 L) and the mixture was stirred until the gas evolution ceased (about 2 h). Then, the mixture was concentrated *in vacuo* and the residue was triturated with warm CH_3CN (400 mL). The solids were filtered, washed with CH_3CN (3×50 mL), Et_2O (100 mL) and dried to give the title product. Yield 76.0 g (74%). White solid, mp 220–222 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.73 (s, 2H), 6.33 (tt, *J* = 4.0, 1.8 Hz, 1H), 3.80 – 3.75 (m, 2H), 3.16 (t, *J* = 6.0 Hz, 2H), 2.40 – 2.33 (m, 2H) ppm. ^{13}C NMR (101 MHz, DMSO-d_6) δ 127.8, 112.2, 46.0, 38.6, 23.5 ppm. MS(APCI) *m/z* = 162/164 [M – Cl]$^+$. Anal. Calcd. for C_5H_9BrClN: C 30.26; H 4.57; N 7.06; Cl 17.86; Br 40.26. Found: C 30.58; H 4.87; N 6.81; Cl 17.89; Br 40.24.

***tert*-Butyl 3-bromo-5,6-dihydropyridine-1(2*H*)-carboxylate (16).** Et_3N (58 mL, 416 mmol) was added dropwise to a solution of **15** (75 g, 378 mmol) and Boc_2O (95.5 mL, 416 mmol) in CH_2Cl_2 (1 L) at rt. The reaction mixture was stirred for 12 h and then treated with H_2O (500 mL). The organic phase was separated, washed with brine (400 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Yield 80.2 g (81%). Yellow liquid. The compound was obtained as *ca*. 1:1 mixture of rotamers. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.14 (s, 1H), 4.06 (s, 2H), 3.50 (t, *J* = 5.8 Hz, 2H), 2.20 (s, 2H), 1.47 (s, 9H) ppm. ^{13}C NMR (126 MHz,

$CDCl_3$) δ 154.3, 127.5 and 127.1, 118.3 and 117.5, 80.3, 50.1 and 49.6, 40.3 and 38.8, 28.5, 27.4 ppm. MS(APCI) *m/z* = 162/164 [M – $CH_2C(CH_3)_2$ – CO_2 + H]$^+$. Anal. Calcd. for $C_{10}H_{16}BrNO_2$: C 45.82; H 6.15; N 5.34; Br 30.48. Found: C 46.09; H 6.09; N 5.36; Br 30.38.

5-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-1,2,3,6-tetrahydropyridine hydrochloride (17). To a solution of **16** (100 g, 382 mmol) in dry dioxane (2 L), B_2pin_2 (193 g, 764 mmol) and KOAc (130 g, 1.34 mol) were added. The reaction vessel was filled with Ar, Pd(dppf)Cl_2·CH_2Cl_2 (9.36 g, 11.5 mmol) was added and the reaction mixture was refluxed for 12 h. The resulting mixture was allowed to warm to rt and concentrated under reduced pressure. H_2O (500 mL) was added to the residue, and the mixture was extracted with EtOAc (1.5 L). The organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. A solution of 4 M HCl in dioxane (1 L) was added to the residue and the reaction mixture was stirred for 12 h. The formed precipitate was filtered, washed with Et_2O (200 mL) and dried to give the title compound. Yield 75.0 g (80%). White solid, mp 190–192 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.41 (s, 2H), 6.58 – 6.53 (m, 1H), 3.53 – 3.45 (m, 2H), 3.14 – 3.04 (m, 2H), 2.41 – 2.29 (m, 2H), 1.21 (s, 12H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6) δ 140.1, 122.9, 83.6, 66.3, 41.9, 24.5, 22.5 ppm. MS(EI) *m/z* = 209 [M – HCl]$^+$, 194 [M – HCl – CH_3]$^+$. Anal. Calcd. for $C_{11}H_{21}BClNO_2$: C 53.81; H 8.62; N 5.70; Cl 14.44. Found: C 53.55; H 8.71; N 5.85; Cl 14.33.

***tert*-Butyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,6-dihydropyridine-1(2*H*)-carboxylate (9p).** The compound was obtained by the same procedure described for **16**. Yield 89.8 g (95%) from **17** (75.0 g, 306 mmol). White solid, mp 103–105 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.62 (s, 1H), 4.01 – 3.92 (m, 2H), 3.44 (t, *J* = 5.6 Hz, 2H), 2.23 – 2.12 (m, 2H), 1.46 (s, 9H), 1.24 (s, 12H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.1, 140.3, 127.7 (br s), 83.5, 79.5, 44.6, 39.8, 28.7, 26.6, 24.9 ppm. MS(EI) *m/z* = 294 [M – CH_3]$^+$, 252 [M – $C(CH_3)$]$^+$, 208 [M – $C(CH_3)_3$ – CO_2]$^+$. Anal. Calcd. for $C_{16}H_{28}BNO_4$: C 62.15; H 9.13; N 4.53. Found: C 62.23; H 9.26; N 4.67.

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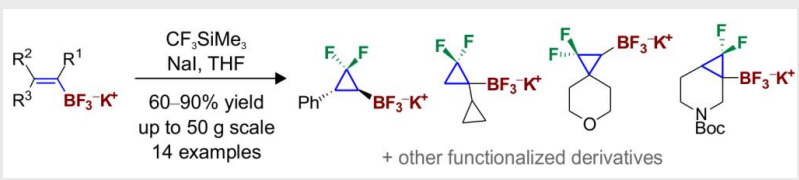

Difluorocyclopropanation of alkenyl trifluoroborates using the $TMSCF_3$–NaI system was achieved in up to 90% yield on a multigram scale. The developed method allowed preparation of monocyclic, spiro- and fused-bicyclic *gem*-difluorocyclopropanes bearing additional functional groups.

Twitter accounts:
@DrGregor2 (O.O.G.)
@EnamineLtd (Enamine Ltd.)
@KyivUniversity (Taras Shevchenko National University of Kyiv)

***gem*-Difluorocyclopropanes**

*Oleksandr V. Hryshchuk, Anatolii O. Varenyk, Yevhen Yurov, Yuliya O. Kuchkovska, Dr. Andriy V. Tymtsunik, Dr. Oleksandr O. Grygorenko**

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gem-Difluorocyclopropanation of Alkenyl Trifluoroborates with the CF_3SiMe_3–NaI System