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Synthesis and Modular Reactivity of Pyrazole 5-Trifluoroborates: Intermediates for the Preparation of Fully-Functionalized Pyrazoles

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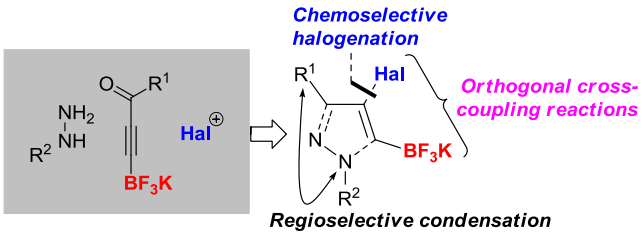
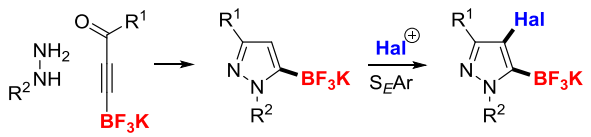


Abstract: The regioselective condensation of hydrazines and ynone trifluoroborates provides access to a range of pyrazole 5-trifluoroborates. The stability of the borate unit allows chemoselective halogenation of the heteroaromatic ring, thereby delivering pyrazole scaffolds that allow orthogonal functionalization at *C*5 and *C*4. The modular reactivity of these intermediates is exemplified by cross-coupling reactions, enabling regiocontrolled synthesis of fully-functionalized pyrazole derivatives.

Introduction

Functionalized pyrazoles represent the core of numerous biologically active molecules and have been heavily targeted by the pharmaceutical and agrochemicals industries.[1] Broadly speaking, pyrazoles are accessed through two strategies comprising condensation or cycloaddition reactions.[2] With respect to the latter approach, alkyne cycloaddition/retro-cycloaddition reactions of sydnones offer a direct means to access highly-substituted analogs.[3] Moreoever, this chemistry is amenable to the synthesis of pyazole boronic acid derivatives by the use of alkynylboronates.[4] In contrast, the direct synthesis of pyrazole boronic acid derivatives by condensation routes has received scant attention. Molander has pioneered the use of stable aryltrifluoroborate salts for heterocycle synthesis *via* cycloaddition and condensation reactions.[5] Moreover, and with specific regard to pyrazoles, we recently introduced ynone trifluoroborates as stable three-carbon atom containing acceptors, and showed how these participate in condensation reactions with hydrazides.[6] We envisaged that this chemistry could deliver a series of pyrazoles that offered the opportunity to carry out late-stage elaboration in a modular fashion. As shown in Figure 1, if we were able to perform a chemoselective halogenation of a pyrazole 5-trifluoroborate (i.e. electrophilic substitution at *C*4 rather than *C*5), then we would have access to a densely-functionalized scaffold with a rich potential for further derivatization. This approach would further avoid the challenge of performing chemistry at *C*3,[7] or the regioselective alkylation of a free pyrazole -*N*H. We report herein the realization of chemoselective chemistries that offer modular derivation strategies for the synthesis of densely-substituted pyrazole products.

Figure 1. Strategy for late-stage diversification of pyrazoles.

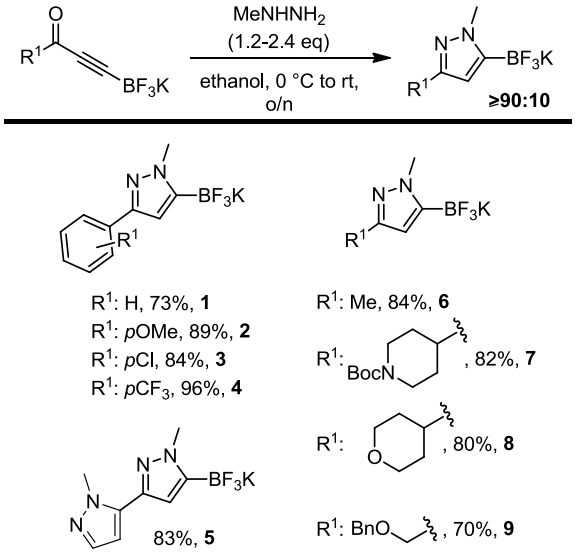


- R^1: incorporate early on, pyrazole *C*3 position difficult to functionalize
- R^2: incorporate early on, avoid regioselective alkylation of free pyrazole NH
- Hal/BF_3K: orthogonally functionalizable groups

Results and Discussion

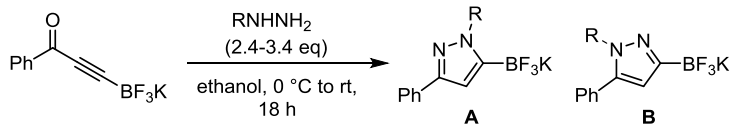
Previous studies on the condensation of hydrazines with ynone trifluoroborates were conducted at, or above, room temperature and offered quite variable regioselectivities (7:1 to >98:2).[6] In preparing a broader range of substrates for the chemoselective functionalization chemistry we decided to re-examine this step. In the event, we found that addition of methylhydrazine at 0 °C and slowly raising the temperature to 20 °C gave consistently higher levels of regiocontrol in the condensation step (Scheme 1). Only in case of Boc-piperidinyl derivative did we observe the minor isomer, and a 90:10 ratio was recorded in this instance. All reactions were high yielding, however, it was essential to ensure complete conversion of the ynone salt as this was difficult to separate from the desired pyrazole product. In this regard, reactions were conveniently monitored by either LC-MS or ^{19}F NMR spectroscopy.

Scheme 1. Synthesis of *N*1,*C*3-substituted pyrazole trifluoroborates.



Having successfully exemplified the introduction of a diverse array of substituents at *C*3, we investigated the reaction of a series of hydrazines in order to vary the substituent at *N*1 (Table 1).

Table 1. Hydrazine scope.



Entry	R	Ratio A:B[a]	Yield[b]
1	H	--	93%, **10**
2	$CH_2C(CH_3)CH_2$	76:24	98%, **11**
3	CH_2CH_2OH	92:8	98%, **12**
4	CH_2CH_2CN	29:71	77%, **13**

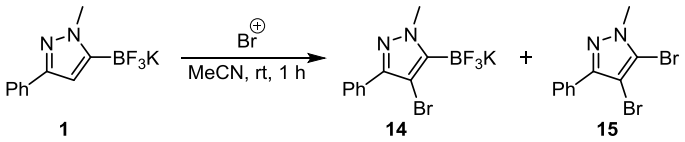
[a] Determined by ^{1}H NMR spectroscopy; [b] Yield of the isolated mixture of isomers.

Hydrazine gave *N*-unsubstituted pyrazole **10** in 93% yield (entry 1), however, methallylhydrazine provided a surprisingly poor level of regiocontrol, generating both **11A/B** in a ~3:1 ratio (entry 2). 2-Hydroxyethylhydrazine proved to be an efficient substrate providing the pyrazole **12** in high yield and regioselectivity (entry 3). Interestingly, and in contrast, condensation of the ynone trifluoroborate with 2-cyanoethylhydrazine (entry 4) led to an inverted ratio of regioisomers, which was not influenced by altering the reaction temperature. Arylhydrazides were not included in this study although our preliminary work has highlighted the propensity for these to generate pyrazoles with type B regiochemistry.[6] The regiochemical assignments were based on a combination of ROESY spectroscopy and NMR correlation, further details are provided in the supporting information.

With a selection of pyrazole trifluoroborate salts in hand, we turned our attention to the functionalization of the remaining position on the pyrazole ring. Pyrazoles are typically reacted at *C*4 *via* the introduction of a halogen. We wanted to assess whether this chemistry was compatible with the

trifluoroborate group as this is known to undergo halodeborylation.[8] Using our model substrate **1**, we first investigated bromination at *C*4 using bromine and K_2CO_3 in acetonitrile (Table 2). Unfortunately, the BF_3K substituent was found to be too reactive resulting in formation of the dibrominated product **15**. Further careful optimization using NBS allowed us to identify a reproducible and selective bromination reaction leading to a 12:1 ratio of **14** over **15**.

Table 2. Optimization of *C*4 bromination.

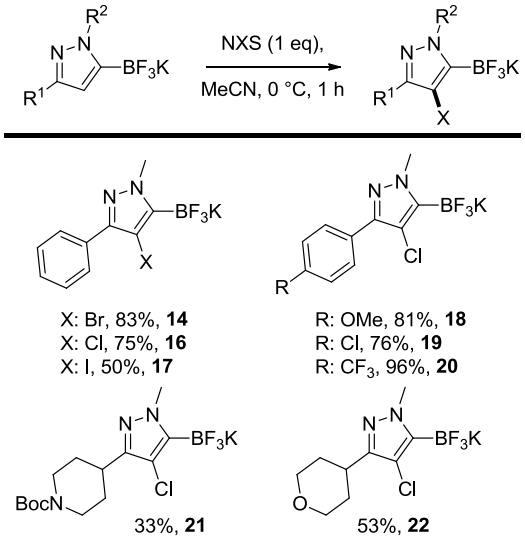


Entry	Brominating agent	Conditions	Ratio **14**:**15**[a]
1	Br_2 (1.1 eq)[b]	K_2CO_3 (2 eq), MeCN	0:1
2	NBS (1 eq)	MeCN	4:1
3	NBS (1 eq)[c]	MeCN[b]	5:1
4	NBS (1 eq)[c,d]	MeCN[b]	12:1

[a] Determined by ^{1}H NMR spectroscopy; [b] 2 Equiv of K_2CO_3 added; [c] Reaction conducted at 0 °C; [d] Introduced as a 0.2 M solution in acetonitrile.

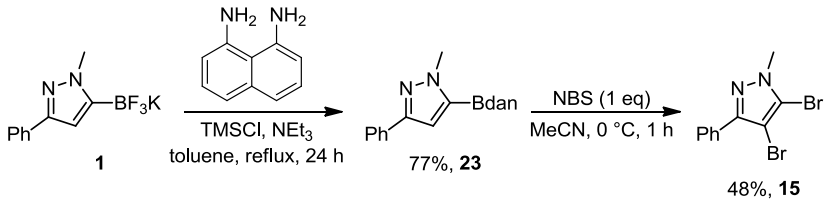
We next investigated the scope of the halogenation reaction (Scheme 2). By analogy to bromination with NBS, chlorination and iodination of trifluoroborate **1** with NCS and NIS led to monohalogenated derivatives **16** and **17** in 75% and 50% yield, respectively. Moreover, chlorination of pyrazoles bearing various substituents at *C*3 under the same reaction conditions yielded the corresponding mono-chlorinated derivatives **18** – **22**.

Scheme 2. *C*4 halogenation of pyrazole 5-trifluoroborates.



In parallel, we investigated the exchange of the BF_3K residue by a Bdan group to develop an alternative class of 4-halogenated 5-boronates. Boronamides are known to be inert to transmetalation[9] and so these offered the prospect of developing a new series of modular intermediates. Pleasingly, employing a similar approach to that described by Churches *et al.*[10], treatment of the pyrazole trifluoroborate **1** with TMSCl, 1,8-diaminonaphthalene and triethylamine yielded the desired 5-Bdan product **23** in 77% yield. Disappointingly however, all attempts to monohalogenate **23** failed and only the dibromide **15** and unreacted starting material **23** were isolated from this reaction (Scheme 3).

Scheme 3. Synthesis and halogenation of 5-Bdan derivatives.

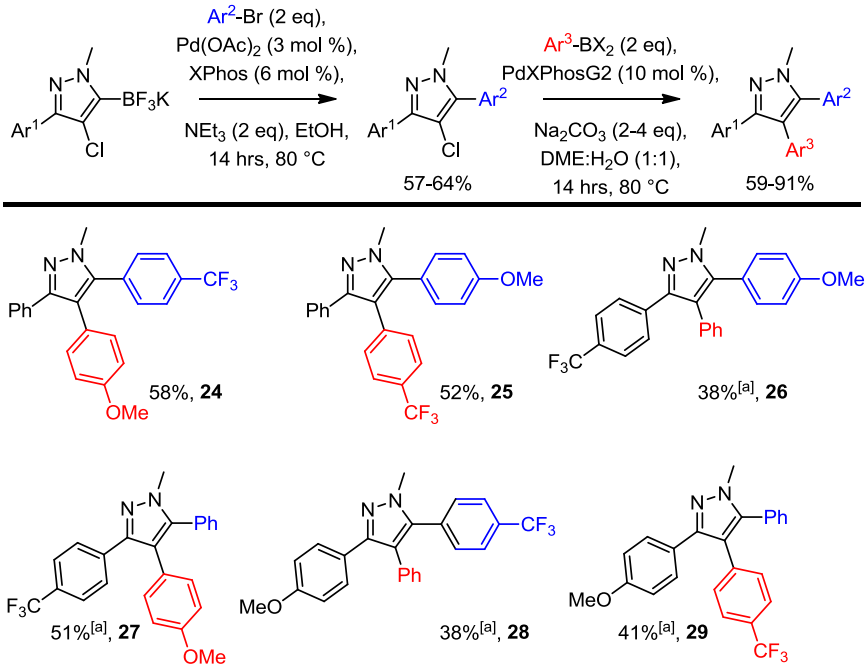


With a series of functionalized pyrazoles in hand, we were in a position to investigate the modular derivatization of these scaffolds. As such, we opted to first use Suzuki-Miyaura coupling as a means of differentiating the borate and halide groups. More specifically, we envisaged that substrates **18**, **20** and **22** would enable us to prepare a small family of polyarylated pyrazoles, whereby all possible isomers could be accessed by sequential coupling reactions. Aryl substituted pyrazoles constitute an important

class of targets and they have been shown to be successful drug candidates.[11] Our results towards this goal are summarized in Scheme 4.

We opted to first carry out the cross-coupling of the trifluoroborate group in each case, as we envisaged that we could tune the catalyst and conditions to favor reaction with a substrate arylbromide, thereby avoiding competitive reaction at the pyrazole chloride in each case. Pleasingly, a combination of $Pd(OAc)_2$, XPhos and NEt_3 in EtOH successfully yielded the corresponding *C*5-arylated products in acceptable yield, leaving the *C*4-Cl substituent intact. Subsequent coupling of the arylchloride moiety with substituted aryl boronic acids proceeded effectively using Buchwald's PdXPhosG2 pre-catalyst and sodium carbonate in a 1:1 mix of DME and water. Ultimately therefore, we were able to access fully-functionalized pyrazoles **24** – **29** with judicious control of the position of the aromatic group, simply by manipulating the order of the coupling sequence.

Scheme 4. Orthogonal cross-coupling at *C*4 and *C*5. Yields shown are over two steps. See Supporting Information for the yields of individual steps.



[a]10 mol % catalyst used in the first step.

Conclusions

In conclusion, we report that pyrazole 5-trifluoroborates offer a platform for the rapid and regiocontrolled synthesis of densely-substituted heterocycles. The trifluoroborates undergo slow halodeborylation in the presence of *N*-halosuccinimides, allowing chemoselective halogenation to take place at the pyrazole *C*4 position. Subsequent orthogonal derivatization of these fully-functionalized pyrazoles by cross-coupling reactions is viable, allowing polysubstituted analogs to be readily accessed with complete regiocontrol. Further studies on the reactivity of 5-BF_3K pyrazoles as well as on the versatility of ynone trifluoroborates as starting materials for the synthesis of alternative heteroaromatics are underway and will be reported in due course.

Experimental Section

The following substrates were prepared according to a previously reported procedures 1-(p-Chlorophenyl)-prop-2-yn-1-ol **3a**,[12] tert-butyl 4-(1-hydroxyprop-2-yn-1-yl)piperidine-1-carboxylate **7a**,[13] 1-benzyloxybut-3-yn-2-ol **9a**,[14] potassium trifluoro(3-oxo-3-phenylprop-1-yn-1-yl)borate **1c**,[6] potassium trifluoro(3-(4-methoxyphenyl)-3-oxoprop-1-yn-1-yl)borate **2c**,[6] potassium trifluoro(3-(4-trifluoromethyl)phenyl)-3-oxoprop-1-yn-1-yl)borate **4c**,[6] potassium trifluoro(3-oxobut-1-yn-1-yl)borate **6c**,[6] potassium trifluoro(1-methyl-3-phenyl-1H-pyrazol-5-yl)borate **1**,[6] potassium trifluoro(3-(4-methoxyphenyl)-1-methyl-1H-pyrazol-5-yl)borate **2**,[6] potassium trifluoro(1-methyl-3-(4-(trifluoromethyl)phenyl)-1H-pyrazol-5-yl)borate **4**[6] a and potassium (1,3-dimethyl-1H-pyrazol-5-yl)trifluoroborate **6**.[6]

General procedure A: Addition of Grignard reagent.[6] To a solution of ethynylmagnesium bromide (0.5 M THF, 1.25 eq) in anhydrous THF (0.5 M) under nitrogen, aldehyde (1 eq) was added dropwise at -78 °C. The mixture was allowed to warm to rt. Upon completion, the reaction was quenched with saturated NH_4Cl, extracted with ethyl acetate and the organic extracts dried over $MgSO_4$. The solvent was removed under vacuum and the residue purified by flash chromatography on silica gel to yield the desired terminal alkynes.

Synthesis of 1-(p-Chlorophenyl)-prop-2-yn-1-ol ***3a***.[12] Following general procedure A, using *p*-chloro-benzaldehyde (1.41 g, 10.0 mmol) and ethynylmagnesium bromide (25.0 mL, 12.5 mmol) in THF (20 mL), the crude product was obtained after 2 h. Chromatographic purification using petrol/EtOAc 80/20 afforded the title compound as a yellow oil (1.58 g, 95% yield). ^{1}H NMR (400 MHz, $CDCl_3$), ppm: 7.46 – 7.41 (m, 2H), 7.36 – 7.30 (m, 2H), 5.39 (dd, *J* = 6.0, 2.0 Hz, 1H), 3.60 (d, *J* = 6.0 Hz, 1H), 2.68 (d, *J* = 2.0 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$), ppm: 138.5, 134.2, 128.8, 128.1, 83.2, 75.2, 63.5.

*Synthesis of 1-(1-methyl-1*H*-pyrazol-5-yl)prop-2-yn-1-ol,* ***5a.*** Following general procedure A, using 1-methyl-1*H*-pyrazole-5-carboxaldehyde (1.0 g, 9.1 mmol) and ethynylmagnesium bromide (23.0 mL, 11.4 mmol) in THF (17 mL), the crude product was obtained after 2 h. The crude material was triturated in dichloromethane by stirring at rt for 30 min and filtering to yield the title compound as a light brown solid (0.98 g, 79% yield). ^{1}H NMR (400 MHz, DMSO-d_6), ppm: 7.29 (d, *J* = 2.0 Hz, 1H), 6.24 (d, *J* = 2.0 Hz, 1H), 5.55 (d, *J* = 2.5 Hz, 1H), 3.82 (s, 3H), 3.56 (d, *J* = 2.5 Hz, 1H), 3.40 (s, 1H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6), ppm: 141.7, 137.0, 104.8, 83.1, 75.6, 54.6, 36.8. M. pt. = 107 °C. FTIR (neat, cm^{-1}), ν_{max}: 3392 (w), 3231 (m), 3120 (m), 3036 (m), 2115 (w), 1420 (s). HRMS calculated for $C_7H_8N_2O$ (ESI^+): 137.0709. Found: 137.0711.

Synthesis of tert-butyl 4-(1-hydroxyprop-2-yn-1-yl)piperidine-1-carboxylate, ***7a.***[13] Following general procedure A, using 4-formylcyclohexanecarboxylic acid *tert*-butyl ester (3.03 g, 14.1 mmol) and ethynylmagnesium bromide (42.0 mL, 21.1 mmol) in THF (28 mL), the crude product was obtained after 2 h. Chromatographic purification using petrol/EtOAc 70/30 afforded the title compound as a yellow oil (2.43 g, 72% yield). ^{1}H NMR (400 MHz, $CDCl_3$), ppm: 4.21 – 4.13 (m, 3H), 2.69 (tt, *J* = 13.0, 3.0 Hz, 2H), 2.49 (d, *J* = 2.0 Hz, 1H), 1.99 (br, 1H), 1.86 – 1.77 (m, 2H), 1.77 – 1.68 (m, 1H), 1.46 (s, 9H), 1.40-1.23 (m, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$), ppm: 154.9, 83.2, 79.5, 74.3, 66.1, 43.6, 42.4, 28.5, 27.7, 27.2.

*Synthesis of 1-tetrahydro-2*H*-pyran-4-yl)prop-2-yn-1-ol,* ***8a.*** Following general procedure A, using 4-formyltetrahydropyran (0.66 g, 5.8 mmol) and ethynylmagnesium bromide (15 mL, 7.2 mmol) in THF

(11 mL), the crude product was obtained after 2 h. Chromatographic purification using petrol/EtOAc 60/40 afforded the title compound as a yellow oil (0.40 g, 49% yield). ^{1}H NMR (400 MHz, $CDCl_3$), ppm: 4.18 (dd, *J* = 6.5, 2.0 Hz, 1H), 4.04-3.94 (m, 3H), 3.42 – 3.35 (m, 2H), 2.50 (d, *J* = 2.0 Hz, 1H), 1.88 – 1.78 (m, 3H), 1.56 – 1.45 (m, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$), ppm: 83.2, 74.2, 67.6, 66.3, 41.4, 28.6, 28.1. FTIR (neat, cm^{-1}), ν_{max}: 3319 (s), 3258 (s), 2954 (m), 2946 (m), 2858 (s), 2109 (s), 1080 (s), 1037 (s), 1023 (s). HRMS calculated for $C_8H_{12}O_2$ (ESI^+): 140.0837. Found: 140.0836.

Synthesis of 1-benzyloxybut-3-yn-2-ol, ***9a.***[14] Following general procedure A, using benzyloxyacetaldehyde (5.0 g, 33 mmol) and ethynylmagnesium bromide (83.0 mL, 41.6 mmol) in THF (61 mL), the crude product was obtained after 2 h. Chromatographic purification using petrol/EtOAc 60/40 afforded the title compound as a yellow oil (5.42 g, 92% yield). ^{1}H NMR (400 MHz, $CDCl_3$), ppm: 7.39 – 7.28 (m, 5H), 4.64 (d, *J* = 12.0 Hz, 1H), 4.60 (d, *J* = 12.0 Hz, 1H), 4.56 (ddd, J = 7.0, 3.5, 2.0 Hz, 1H), 3.66 (dd, *J* = 10.0, 3.5 Hz, 1H), 3.59 (dd, *J* = 10.0, 7.0 Hz, 1H), 2.46 (d, *J* = 2.0 Hz, 1H), 2.39 (s, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$), ppm: 137.5, 128.6, 128.0, 127.9, 81.7, 73.8, 73.5, 73.4, 61.6.

General procedure B: Borylation of terminal alkynes.[6] To a solution of terminal alkyne (1 eq) in anhydrous THF under nitrogen, *n*-BuLi (~2.5 M in hexanes, 2.2 eq) was added dropwise at -78 °C. After stirring the resulting mixture at -78 °C for 1 h, *iso*-propoxy-pinacolborane (3 eq) was added dropwise and the mixture was allowed to warm to -20 °C over 1 h. To this mixture was added slowly a saturated solution of aqueous hydrogen potassium difluoride (12 eq) and the mixture allowed to warm to rt over 1 h. The solvent was then removed under vacuum to yield a solid. The residue was stirred in acetone for 30 min and filtered. The solvent was removed under vacuum and the residue redissolved in minimum of acetone, Et_2O was added and a solid precipitated to yield the desired compound.

Note that for the following trifluoroborate compounds, ^{13}C NMR spectra are missing a signal for the carbon atom directly attached to the boron due to broadening arising from the quadrupolar relaxation effect.

Synthesis of potassium trifluoro(3-hydroxy-3-(4-chlorophenyl)prop-1-yn-1-yl)borate, ***3b.*** Following general procedure B using **3a** (0.99 g, 6.0 mmol), *n*-BuLi (6.8 mL, 13 mmol), B(O^{i}Pr)Pin (3.5 mL, 18 mmol) in THF (25 mL) and KHF_2 (5.43 g, 71.0 mmol) dissolved in water (20 mL) yielded the title compound as a colorless solid (1.13 g, 70% yield). ^{1}H NMR (400 MHz, DMSO-d_6), ppm: 7.46 (d, *J* = 8.5 Hz, 2H), 7.38 (d, *J* = 8.5 Hz, 2H), 5.72 (d, *J* = 5.0 Hz, 1H), 5.18 (d, *J* = 5.0 Hz, 1H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6), ppm: 142.7, 131.4, 128.3, 127.8, 89.9, 62.4. ^{19}F NMR (377 MHz, DMSO-d_6), ppm: -131.6. ^{11}B NMR (128 MHz, DMSO-d_6), ppm: 5.0. M. pt. >290 °C. FTIR (neat, cm^{-1}), ν_{max}: 3537 (w), 2929 (w), 1001 (s), 933 (s). HRMS calculated for $C_9H_6{}^{11}BOF_3{}^{35}Cl$ (ESI^-): 233.0152. Found: 233.0163.

Synthesis of potassium 1-(1-methyl-1H-pyrazol-5-yl)-3-(trifluoroboranyl)prop-2-yn-1-ol, ***5b***.

Following general procedure B using **5a** (0.80 g, 5.8 mmol), *n*-BuLi (5.5 mL, 13 mmol), B(O^{i}Pr)Pin (3.6 mL, 18 mmol) in THF (23 mL) and KHF_2 (5.57 g, 70.1 mmol) dissolved in water (18 mL) yielded the title compound as a brown solid (0.52 g, 37% yield). ^{1}H NMR (400 MHz, DMSO-d_6), ppm: 7.25 (d, *J* = 2.0 Hz, 1H), 6.16 (d, *J* = 2.0 Hz, 1H), 5.78 (s, 1H), 5.33 (s, 1H), 3.82 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6), ppm: 143.7, 137.1, 104.9, 74.0, 55.9, 37.3. ^{19}F NMR (376 MHz, DMSO-d_6), ppm: -131.8. ^{11}B NMR (128 MHz, DMSO-d_6), ppm: 5.2. M. pt. = 111 °C. FTIR (neat, cm^{-1}), ν_{max}: 3598 (m), 3316 (w), 2219 (w), 1645 (w), 1630 (w). HRMS calculated for $C_7H_7{}^{10}BOF_3N_2Na$ (ESI^+): 225.0538. Found: 225.0535.

Synthesis of potassium tert-butyl 4-(1-hydroxy-3-(trifluoroboranyl)prop-2-yn-1-yl)piperidine-1-carboxylate, ***7b***. Following general procedure B using **7a** (2.78 g, 12.0 mmol), *n*-BuLi (12 mL, 26 mmol), B(O^{i}Pr)Pin (7.5 mL, 35 mmol) in THF (48 mL) and KHF_2 (10.93 g, 139.0 mmol) dissolved in water (40 mL) yielded the title compound as a colorless solid (2.91 g, 73% yield). ^{1}H NMR (400 MHz, DMSO-d_6), ppm: 4.89 (d, *J* = 5.0 Hz, 1H), 4.02-3.90 (m, 2H), 3.88 - 3.82 (m, 1H), 2.62 (br, 2H), 1.69 (app. d, *J* = 12.0 Hz, 2H), 1.49 – 1.39 (m, 10H), 1.17-1.03 (m, 2H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6), ppm: 153.9, 78.4, 64.9, 42.4, 28.1, 27.6, 27.4, 24.9. ^{19}F NMR (376 MHz, DMSO-d_6), ppm: -131.3. ^{11}B NMR (128 MHz, DMSO-d_6), ppm: 5.0. M. pt. >290 °C. FTIR (neat, cm^{-1}), ν_{max}: 3402 (br, w),

2975(w), 2931 (w), 2860 (w), 2214 (w), 1690 (m), 1667 (m), 1479 (m), 1425 (m). HRMS calculated for $C_{13}H_{20}{}^{11}BO_3F_3N$ (ESI^-): 306.1494. Found: 306.1504.

Synthesis of potassium 1-(tetrahydro-2H-pyran-4-yl)-3-(trifluoroboranyl)prop-2-yn-1-ol, ***8b***. Following general procedure B using **8a** (0.78 g, 6.0 mmol), *n*-BuLi (5.0 mL, 12 mmol), B(O^iPr)Pin (3.5 mL, 17 mmol) in THF (22 mL) and KHF_2 (5.29 g, 67.0 mmol) dissolved in water (18 mL) yielded the title compound as a colorless solid (0.52 g, 38% yield). ^1H NMR (400 MHz, DMSO-d_6), ppm: 4.86 (d, J = 5.5 Hz, 1H), 3.90 – 3.77 (m, 3H), 3.28 – 3.16 (m, 2H), 1.67 – 1.56 (m, 2H), 1.57 – 1.44 (m, 1H), 1.31 – 1.20 (m, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d_6), ppm: 66.9, 65.3, 41.6, 28.7, 28.3. ^{19}F NMR (376 MHz, DMSO-d_6), ppm: -131.3. ^{11}B NMR (128 MHz, DMSO-d_6), ppm: 5.1. M. pt. > 290 °C. FTIR (neat, cm^{-1}), ν_{max}: 3496 (s), 2957 (m), 2917 (m), 2872 (m), 2854 (m), 1238 (s), 1082 (s), 1024 (s). HRMS calculated for $C_8H_{11}{}^{11}BO_2F_3$ (ESI^-): 207.0810. Found: 207.0817.

Synthesis of potassium 1-(benzyloxy)-4-(trifluoroboranyl)but-3-yn-2-ol, ***9b***. Following general procedure B using **9a** (5.38 g, 31.0 mmol), *n*-BuLi (30 mL, 67 mmol), B(O^iPr)Pin (19 mL, 92 mmol) in THF (125 mL) and KHF_2 (28.61 g, 366.0 mmol) dissolved in water (102 mL) yielded the title compound as a colorless solid (8.12 g, 94% yield). ^1H NMR (400 MHz, DMSO-d_6), ppm: 7.36 – 7.24 (m, 5H), 5.07 (d, J = 6.0 Hz, 1H), 4.52 (s, 2H), 4.26 – 4.19 (m, 1H), 3.43 – 3.33 (m, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d_6), ppm: 139.0, 128.6, 128.0, 127.8, 89.9, 75.4, 72.5, 61.3, 25.5. ^{19}F NMR (376 MHz, DMSO-d_6), ppm: -131.8. ^{11}B NMR (128 MHz, DMSO-d_6*), ppm:* 5.1. M. pt. = 86 °C. FTIR (neat, cm^{-1}), ν_{max}: 3512 (w), 3376 (w), 3034 (w), 2869 (w), 2217 (w), 1097 (s), 1064 (s). HRMS calculated for $C_{11}H_{11}{}^{11}BO_2F_3$ (ESI^-): 243.0810. Found: 243.0819.

General procedure C: Oxidation to ynone trifluoroborates.[6] To a suspension of manganese (IV) oxide (5 eq) in acetone (0.3 M), was added trifluoroborate (1 eq) portionwise at rt. The reaction was followed by ^{19}F NMR spectroscopy. Upon completion, the mixture was filtered through Celite. All volatiles were removed from the filtrate under vacuum. Then the residue was redissolved in minimum of acetone and

upon addition of Et_2O a solid precipitated. The solid was filtered and washed with Et_2O and dried to yield the title compound.

Synthesis of potassium trifluoro(3-oxo-3-(4-chlorophenyl)prop-1-yn-1-yl)borate, ***3c.*** Following general procedure C using **3b** (1.9 g, 7.0 mmol) and manganese (IV) oxide (3.01 g, 34.9 mmol) in acetone (22 mL) yielded the title compound as a pale yellow solid (1.44 g, 76% yield). ^{1}H NMR (500 MHz, DMSO-d_6), ppm: 8.05 (d, *J* = 9.0 Hz, 2H), 7.65 (d, *J* = 9.0 Hz, 2H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6), ppm: 176.9, 138.8, 135.5, 130.7, 129.0, 87.9. ^{19}F NMR (377 MHz, Acetone-d_6), ppm: -136.3. ^{11}B NMR (128 MHz, DMSO-d_6), ppm: -1.8. M. pt. >300 °C. FTIR (neat, cm^{-1}), ν_{max}: 2946 (w), 1661 (s), 1222 (s), 984 (s). HRMS calculated for $C_9H_4{}^{11}BOF_3{}^{35}Cl$ (ESI$^-$): 231.0152. Found: 231.0163.

Synthesis of potassium 1-(1-methyl-1H-pyrazol-5-yl)-3-(trifluoroboranyl)prop-2-yn-1-one, ***5c.*** Following general procedure C using **5b** (0.41 g, 1.7 mmol) and manganese (IV) oxide (0.75 g, 8.5 mmol) in acetone (5.5 mL) yielded the title compound as a light brown solid (0.12 g, 30% yield). ^{1}H NMR (400 MHz, DMSO-d_6), ppm: 7.53 (d, *J* = 2.0 Hz, 1H), 6.95 (d, *J* = 2.0 Hz, 1H), 4.05 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6), ppm: 167.7, 139.6, 137.7, 114.2, 89.0, 39.6. ^{19}F NMR (376 MHz, DMSO-d_6), ppm: -133.3. ^{11}B NMR (128 MHz, DMSO-d_6), ppm: -1.9. M. pt. = 252 °C (deg). FTIR (neat, cm^{-1}), ν_{max}: 3142 (s), 2962 (s), 2191 (m), 3392 (w), 3231 (m), 3120 (m), 3036 (m), 2115 (w), 1420 (s). HRMS calculated for $C_7H_5{}^{11}BOF_3N_2$ (ESI$^-$): 201.0453. Found: 201.0462.

Synthesis of potassium tert-butyl 4-(3-(trifluoroboranyl)propioloyl)piperidine-1-carboxylate, ***7c.*** Following general procedure C using **7b** (0.17 g, 0.50 mmol) and manganese (IV) oxide (0.21 g, 2.5 mmol) in acetone (1.5 mL) yielded the title compound as a colorless solid (0.07 g, 42% yield). ^{1}H NMR (400 MHz, DMSO-d_6), ppm: 3.89 – 3.84 (m, 2H), 2.89 – 2.71 (m, 2H), 2.49 (m 1H), 1.86 – 1.80 (m, 2H), 1.41-1.28 (m, 11H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6), ppm: 190.0, 153.8, 88.9, 78.6, 49.0, 40.1, 28.1, 27.2. ^{19}F NMR (376 MHz, DMSO-d_6), ppm: -133.2. ^{11}B NMR (128 MHz, DMSO-d_6), ppm: -1.9. M. pt. = 169 °C. FTIR (neat, cm^{-1}), ν_{max}: 2932 (w), 2187 (w), 1679 (m), 1658 (m). HRMS calculated for $C_{13}H_{18}{}^{11}BO_3F_3N$ (ESI$^-$): 304.1337. Found: 304.1351.

Synthesis of potassium 1-(tetrahydro-2H-pyran-4-yl)-3-(trifluoroboranyl)prop-2-yn-1-one, ***8c.*** Following general procedure C using **8b** (0.56 g, 2.3 mmol) and manganese (IV) oxide (1.03 g, 11.4 mmol) in acetone (7 mL) yielded the title compound as a colorless solid (0.19 g, 34% yield). ^{1}H NMR (400 MHz, DMSO-d_6), ppm: 3.84 – 3.79 (m, 2H), 3.35 (td, *J* = 11.5, 2.0 z, 2H), 2.58 – 2.50 (m 1H), 1.81 – 1.74 (m, 2H), 1.55 – 1.44 (m, 2H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6), ppm: 190.0, 88.6, 66.1, 48.1, 27.9. ^{19}F NMR (376 MHz, DMSO-d_6), ppm: -133.2. ^{11}B NMR (128 MHz, DMSO-d_6), ppm: -1.9. M. pt. = 158 °C. FTIR (neat, cm^{-1}), ν_{max}: 2960 (w), 2851 (w) 2183 (w), 1649 (m), 1110, (s), 1008 (s). HRMS calculated for $C_8H_9{}^{11}BO_2F_3$ (ESI$^-$): 205.0653. Found: 205.0659.

Synthesis of potassium 1-(benzyloxy)-4-(trifluoroboranyl)but-3-yn-2-one, ***9c.*** Following general procedure C using **9b** (3.30 g, 11.7 mmol) and manganese (IV) oxide (5.12 g, 58.5 mmol) in acetone (35 mL) yielded the title compound as an orange solid (0.37 g, 11% yield). ^{1}H NMR (400 MHz, DMSO-d_6), ppm: 7.37 – 7.26 (m, 5H), 4.52 (s, 2H), 4.23 (s, 2H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6), ppm: 185.4, 137.8, 128.2, 127.8, 127.6, 87.7, 75.8, 72.1. ^{19}F NMR (376 MHz, DMSO-d_6), ppm: -133.5. ^{11}B NMR (128 MHz, DMSO-d_6), ppm: -1.1. M. pt. = 116-117 °C. FTIR (neat, cm^{-1}), ν_{max}: 3032 (w), 2868 (w), 2182 (w), 1676 (s), 1455-1380 (s), 1087 (s). HRMS calculated for $C_{11}H_9{}^{11}BO_2F_3$ (ESI$^-$): 241.0653. Found: 241.0658.

General procedure D: Synthesis of N-methylpyrazoles. To a solution of ynone (1 eq) in ethanol (0.14 M) at 0 °C, *N*-methylhydrazine (1.2 or 2.4 eq) was added dropwise under nitrogen. The flask was covered with foil and left to stir at rt. The reaction was followed by ^{19}F NMR. Upon completion, the mixture was evaporated to dryness. The residue was redissolved in the minimum of acetone and upon addition of Et_2O a solid precipitated. The solid was filtered and washed with Et_2O and dried to yield the title compound.

Synthesis of potassium trifluoro(1-methyl-3-(4-chlorophenyl)-1H-pyrazol-5-yl)borate, ***3***. Following general procedure D using **3c** (0.50 g, 1.9 mmol) and methylhydrazine (0.1 mL, 2 mmol) in ethanol (12 mL) yielded the title compound as a colorless solid (0.47 g, 84% yield, > 98:2). ^{1}H NMR (400 MHz,

DMSO-d_6), ppm: 7.71 (d, *J* = 8.5 Hz, 2H), 7.36 (d, *J* = 8.5 Hz, 2H), 6.31 (s, 1H), 3.78 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d_6), ppm: 146.9, 134.3, 130.9, 128.8, 126.9, 106.1, 38.6. ^{19}F NMR (377 MHz, DMSO-d_6), ppm: -137.1. ^{11}B NMR (128 MHz, DMSO-d_6), ppm: 1.6. M. pt. > 300 °C. FTIR (neat, cm^{-1}), ν_{max}: 2950 (w), 1425 (m), 1191 (m), 1168 (s), 935 (s). HRMS calculated for $C_{10}H_8{}^{11}B^{35}ClF_3N_2$ (ESI^-): 259.0429. Found: 259.0437.

Synthesis of potassium 1,2'-dimethyl-5-(trifluoroboranyl)-1H,2'H-3,3'-bipyrazole, ***5****.* Following general procedure D using **5c** (100 mg, 0.373 mmol) and methylhydrazine (60 µL, 0.9 mmol) in ethanol (3 mL) yielded the title compound as a colorless solid (93 mg, 83% yield, > 90:10). ^1H NMR (400 MHz, DMSO-d_6), ppm: 7.33 (d, *J* = 2.0 Hz, 1H), 6.36 (d, *J* = 2.0 Hz, 1H), 6.18 (s, 1H), 4.01 (s, 3H), 3.80 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d_6), ppm: 139.4, 137.53, 137.47, 108.0, 104.0, 38.3, 38.1. ^{19}F NMR (376 MHz, DMSO-d_6), ppm: -137.2. ^{11}B NMR (128 MHz, DMSO-d_6), ppm: 1.7. M. pt. >300 °C. FTIR (neat, cm^{-1}), ν_{max}: 3152 (s), 3127 (s), 1386 (s). HRMS calculated for $C_8H_9{}^{11}BF_3N_4$ (ESI^-): 229.0878. Found: 229.0888.

Synthesis of potassium tert-butyl 4-(1-methyl-5-(trifluoroboranyl)-1H-pyrazol-3-yl)piperidine-1-carboxylate, ***7.*** Following general procedure D using **7c** (200 mg, 0.539 mmol) and methylhydrazine (55 µL, 1.1 mmol) in ethanol (4 mL) yielded the title compound as a light yellow solid (177 mg, 82% yield, > 90:10). ^1H NMR (400 MHz, DMSO-d_6), ppm: 5.67 (s, 1H), 3.95 – 3.90 (m, 2H), 3.64 (s, 3H), 2.84 – 2.75 (m, 2H), 2.60 (tt, *J* = 11.5, 4.0 Hz, 1H), 1.80 – 1.75 (m, 2H), 1.40 - 1.32 (m, 11H). $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d_6), ppm: 154.0, 152.4, 104.8, 78.4, 37.6, 34.8, 32.0, 28.1, 26.8. ^{19}F NMR (376 MHz, DMSO-d_6), ppm: -136.9. *^{11}B NMR (128 MHz, DMSO-d_6), ppm:* 1.6. M. pt. = 161 °C. FTIR (neat, cm^{-1}), ν_{max}: 2934 (w), 1674 (m), 1425 (m), 1366 (m). HRMS calculated for $C_{14}H_{22}{}^{11}BO_2F_3N_3$ (ESI^-): 332.1763. Found: 332.1779.

Synthesis of potassium 1-methyl-3-(tetrahydro-2H-pyran-4-yl)-5-(trifluoroboranyl)-1H-pyrazole, ***8****.* Following general procedure D using **8c** (204 mg, 0.750 mmol) and methylhydrazine (110 µL, 1.80 mmol) in ethanol (6 mL) yielded the title compound as a light yellow solid (181 mg, 80% yield, >

90:10). ^{1}H NMR (400 MHz, DMSO-d_6), ppm: 5.69 (s, 1H), 3.88 – 3.83 (m, 2H), 3.65 (s, 3H), 3.37 (td, *J* = 11.5, 2.0 Hz, 2H), 2.66 (tt, *J* = 11.5, 4.0 Hz, 1H), 1.75 – 1.69 (m, 2H), 1.55 (qd, *J* = 11.5, 4.0 Hz). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6), ppm: 152.7, 104.8, 67.2, 37.6, 34.0, 33.0. ^{19}F NMR (376 MHz, DMSO-d_6), ppm: -136.9. ^{11}B NMR (128 MHz, DMSO-d_6), ppm: 1.6. M. pt. > 290 °C. FTIR (neat, cm^{-1}), ν_{max}: 2937 (w), 2918 (w), 2850 (w), 1444 (w), 1428 (w), 1168 (m), 1126 (m). HRMS calculated for $C_9H_{13}{}^{11}BOF_3N_2$ (ESI$^-$): 233.1079. Found: 233.1086.

Synthesis of potassium 3-((benzyloxy)methyl)-1-methyl-5-(trifluoroboranyl)-1H-pyrazole, ***9***. Following general procedure D using **9c** (167 mg, 0.596 mmol) and methylhydrazine (80 µL, 1.7 mmol) in ethanol (5 mL) yielded the title compound as an orange oil (110 mg, 70% yield, > 90:10). ^{1}H NMR (400 MHz, DMSO-d_6), ppm: 7.32 – 7.22 (m, 5H), 5.88 (s, 1H), 4.44 (s, 2H), 4.34 (s, 2H), 3.70 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6), ppm: 145.9, 138.8, 128.1, 127.4, 127.2, 107.9, 70.6, 65.6, 37.7. ^{19}F NMR (376 MHz, DMSO-d_6), ppm: -137.0. ^{11}B NMR (128 MHz, DMSO-d_6), ppm: 1.7. FTIR (neat, cm^{-1}), ν_{max}: 3031 (w), 2933 (w), 2865 (w), 1453 (m), 1164 (m), 1148 (m). HRMS calculated for $C_{12}H_{13}{}^{11}BOF_3N_2$ (ESI$^-$): 269.1079. Found: 269.1086.

General procedure E: Synthesis of N-alkylpyrazoles. To a solution of ynone (1 eq) in ethanol (0.14 M) at 0 °C, *N*-alkylhydrazine (2.4 eq) was added dropwise under nitrogen. The mixture was left to stir at 0 °C for 4-6 h and left to warm to rt overnight. The reaction was followed by ^{19}F NMR spectroscopy. Upon completion, the mixture was evaporated to dryness. The residue was redissolved in the minimum of acetone and upon addition of Et_2O a solid precipitated. The solid was filtered and washed with Et_2O and dried to yield the title compound.

Synthesis of potassium 1-(2-methylallyl)-3-phenyl-5-(trifluoroboranyl)-1H-pyrazole, ***11A*** *and Potassium 1-(2-methylallyl)-5-phenyl-3-(trifluoroboranyl)-1H-pyrazole,* ***11B.*** Following general procedure E using **1c** (200 mg, 0.847 mmol) and (2-methyl-2-propenyl)hydrazine (182 mg, 2.03 mmol) in ethanol (6 mL) yielded the title compound as a mixture of the 2 regioisomers A/B in a 76:24 ratio (254 mg, 98% yield). ^{1}H NMR (400 MHz, DMSO-d_6), ppm: 7.69 (d, *J* = 7.0 Hz, 1.5H), 7.44 – 7.34 (m,

1.25H), 7.32 (t, *J* = 7.0Hz, 1.5H), 7.18 (t, *J* = 7.0 Hz, 0.75H), 6.30 (s, 0.75H), 6.10 (s, 0.25H), 4.76 (s, 1.5H), 4.67 (s, 2H), 4.58 (s, 0.5H), 1.58 (s, 2.25H), 1.56 (s, 0.75H). $^{13}C\{^{1}H\}$ NMR (101 MHz, DMSO-d_6), ppm: 148.8, 143.5, 143.2, 141.8, 135.5, 132.6, 129.0, 128.8, 128.3, 127.8, 126.7, 125.3, 111.6, 111.4, 110.0, 105.7, 56.5, 54.7, 20.4, 20.3. ^{19}F NMR (376 MHz, DMSO-d_6), ppm: -136.2. ^{11}B NMR (128 MHz, DMSO-d_6), ppm: 1.7. FTIR (neat, cm^{-1}), ν_{max}: 2973 (w), 1640 (w), 1604 (w), 1458 (m), 1190 (m), 1136 (s). HRMS calculated for $C_{13}H_{13}{}^{11}BF_3N_2$ (ESI^-): 265.1129. Found: 265.1142.

Synthesis of potassium 2-(3-phenyl-5-(trifluoroboranyl)-1H-pyrazol-1-yl)ethan-1-ol, ***12A*** *and Potassium 2-(5-phenyl-3-(trifluoroboranyl)-1H-pyrazol-1-yl)ethan-1-ol,* ***12B.*** Following general procedure E using **1c** (200 mg, 0.847 mmol) and 2-hydroxyethylhydrazine (186 mg, 2.03 mmol) in ethanol (6 mL) yielded the title compound as a mixture of the 2 regioisomers A/B in a 92:8 ratio (244 mg, 98% yield). Upon trituration in acetone, isomer B remained insoluble and it was filtered off. Isomer A was precipitated by addition of ether. Isomer **12A** was isolated as an orange oil (151 mg, 61% yield). ^{1}H NMR (400 MHz, DMSO-d_6), ppm: 7.69 (d, *J* = 8.0 Hz, 2H), 7.32 (t, *J* = 8.0 Hz, 2H), 7.19 (t, *J* = 8.0 Hz, 1H), 6.29 (s, 1H), 4.67 (t, *J* = 6.0 Hz, 1H), 4.17 (t, *J* = 7.0 Hz, 2H), 3.73 – 3.69 (m, 2H). $^{13}C\{^{1}H\}$ NMR (101 MHz, DMSO-d_6), ppm: 147.9, 134.9, 128.3, 126.2, 124.8, 105.4, 61.1, 52.6. ^{19}F NMR (376 MHz, DMSO-d_6), ppm: -136.7. ^{11}B NMR (128 MHz, DMSO-d_6), ppm: 2.2. FTIR (neat, cm^{-1}), ν_{max}: 3364 (br. w), 2947 (w), 1604 (w), 1430 (m), 1189 (s), 1139 (s). HRMS calculated for $C_{11}H_{11}{}^{11}BOF_3N_2$ (ESI^-): 255.0922. Found: 255.0928. Isomer **12B** was isolated as a colorless solid (8 mg, 3% yield). ^{1}H NMR (400 MHz, DMSO-d_6), ppm: 7.48 – 7.41 (m, 4H), 7.38 – 7.33 (m, 1H), 6.03 (s, 1H), 4.96 (t, *J* = 5.0 Hz, 1H), 4.02 (t, *J* = 6.0 Hz, 2H), 3.76 – 3.72 (m, 2H). $^{13}C\{^{1}H\}$ NMR (101 MHz, DMSO-d_6), ppm: 141.5, 132.0, 128.5, 128.5, 127.3, 109.2, 60.6, 50.3. ^{19}F NMR (376 MHz, DMSO-d_6), ppm: -136.3. ^{11}B NMR (128 MHz, DMSO-d_6), ppm: 2.2. M. pt. = 222-223 °C. FTIR (neat, cm^{-1}), ν_{max}: 3193 (br. w), 2930 (w), 2920 (w), 1460 (m), 1429 (m), 1407 (m), 1140 (s). HRMS calculated for $C_{11}H_{11}{}^{11}BOF_3N_2$ (ESI^-): 255.0922. Found: 255.0933.

Synthesis of potassium 3-(5-phenyl-3-(trifluoroboranyl)-1H-pyrazol-1-yl)propanenitrile, ***13B.*** Following general procedure E using **1c** (203 mg, 0.860 mmol) and 2-hydroxyethylhydrazine (126 mg,

2.06 mmol) in ethanol (6 mL) yielded the title compound as a mixture of the 2 regioisomers A/B in a 29:71 ratio (218 mg, 84% yield). Trituration in acetone and filtration provided a pure sample of **13B** as a colorless solid. ^{1}H NMR (400 MHz, DMSO-d_6), ppm: 7.49-7.38 (m, 5H), 6.06 (s, 1H), 4.20 (t, J = 6.5 Hz, 2H), 3.03 (t, J = 6.5 Hz, 2H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6), ppm: 141.7, 131.5, 128.6, 128.5, 127.7, 118.9, 109.8, 43.7, 18.4. ^{19}F NMR (376 MHz, DMSO-d_6), ppm: -136.4. ^{11}B NMR (128 MHz, DMSO-d_6), ppm: 2.3. M. pt. = 199 °C. FTIR (neat, cm^{-1}), ν_{max}: 3059 (w), 2977 (w), 2247 (w), 1486 (m), 1134 (s). HRMS calculated for $C_{12}H_{10}{}^{11}BF_3N_3$ (ESI⁻): 264.0925. Found: 264.0951.

*Naphthalen(1-methyl-3-phenyl-1H-pyrazol-5-yl)boronamide, **23**.* To a solution of pyrazole **1** (103 mg, 0.436 mmol) and 1,8-diaminonaphthalene (68 mg, 0.48 mmol) in toluene (10 mL) under nitrogen, NEt_3 (0.1 mL, 0.8 mmol) was added. After 5 min, TMS-Cl (0.20 mL, 1.2 mmol) was added dropwise then the mixture was heated at reflux overnight. The solvent was removed under vacuum and the crude was purified by flash chromatography on silica gel (petrol / CH_2Cl_2, gradient from 100/0 to 0/100) to yield the title compound as a pink oil (100 mg, 77% yield). ^{1}H NMR (400 MHz, DMSO-d_6), ppm: 8.24 (s, 2H), 7.23 (d, J = 7.5 Hz, 2H), 4.42 (t, J = 7.5 Hz, 2H), 7.29 (t, J = 7.5 Hz, 1H), 7.13 -7.08 (m, 2H), 7.06 (s, 1H), 6.95 (dd, J = 8.0, 1.0 Hz, 2H), 6.57 (dd, J = 7.5, 1.0 Hz, 2H), 4.07 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6), ppm: 149.1, 141.8, 135.9, 133.4, 128.7, 127.6, 127.2, 125.0, 119.8, 116.8, 110.1, 105.9, 39.6. ^{11}B NMR (128 MHz, DMSO-d_6), ppm: 27.3. FTIR (neat, cm^{-1}), ν_{max}: 3403 (w), 3280 (br), 3049 (w), 1596 (s), 1398 (s), 764 (s). HRMS calculated for $C_{20}H_{18}{}^{11}BN_4$ (ESI⁺): 325.1619. Found: 325.1639.

General procedure F: Halogenation of pyrazoles. A solution of halogenating agent (1 eq) in MeCN (0.2 M) was added to the pyrazole (1 eq) and the mixture stirred for 1 h at rt. The solvent was removed *in vacuo* and a small amount of CH_2Cl_2 was added. EtOAc was added dropwise to the suspension with stirring until all material was solubilized. The solution was transferred to a larger vessel before CH_2Cl_2 was added leading to the precipitation of a solid. The solid was isolated by filtration and washed with CH_2Cl_2.

Synthesis of potassium trifluoro(1-methyl-3-phenyl-4-bromo-1H-pyrazol-5-yl)borate, ***14****.* Following general procedure F using **1** (0.1 g, 0.4 mmol), *N*-bromosuccinimide (0.07 g, 0.4 mmol) in acetonitrile (3 mL) yielded the title compound as a colorless solid (0.11 g, 83% yield). ^{1}H NMR (400 MHz, DMSO-d_6), ppm: 7.76 (d, *J* = 7.0 Hz, 2H), 7.39 (t, *J* = 7.0 Hz, 2H), 7.30 (t, *J* = 7.0 Hz, 1H), 3.82 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6), ppm: 145.9, 134.0, 128.5, 127.8, 127.4, 94.2, 30.0. ^{19}F NMR (377 MHz, DMSO-d_6), ppm: -135.4. ^{11}B NMR (128 MHz, DMSO-d_6), ppm: 0.9. M. pt. 221-222 °C. FTIR (neat, cm^{-1}), ν_{max}: 2901 (w), 2845 (w), 1440 (m), 1426 (m), 1182 (s), 1144 (m), 986 (s), 936 (s). HRMS calculated for $C_{10}H_8{}^{11}B^{79}BrF_3N_2$ (ESI$^-$): 302.9921. Found: 302.9935.

Synthesis of potassium trifluoro(1-methyl-3-phenyl-4-chloro-1H-pyrazol-5-yl)borate, ***16.*** Following general procedure F using **1** (0.1 g, 0.4 mmol), *N*-chlorosuccinimide (0.05 g, 0.4 mmol) in acetonitrile (3 mL) yielded the title compound as a colorless solid (0.09 g, 75% yield). ^{1}H NMR (400 MHz, DMSO-d_6), ppm: 7.78 (d, *J* = 7.5 Hz, 2H), 7.39 (t, *J* = 7.5 Hz, 2H), 7.28 (t, *J* = 7.5 Hz, 1H), 3.79 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6), ppm: 144.1, 133.6, 128.6, 127.4, 127.3, 109.1, 40.6. ^{19}F NMR (377 MHz, DMSO-d_6), ppm: -135.7. ^{11}B NMR (128 MHz, DMSO-d_6), ppm: 1.3. FTIR (neat, cm^{-1}), ν_{max}: 2950 (w), 2875 (w), 1430 (w), 1197 (m), 1144 (m), 1005 (s), 966 (s), 924 (s). HRMS calculated for $C_{10}H_8{}^{10}B^{35}ClF_3N_2$ (ESI$^-$): 258.0463. Found: 258.0471.

Synthesis of potassium trifluoro(1-methyl-3-phenyl-4-iodo-1H-pyrazol-5-yl)borate, ***17****.* Following general procedure F using **1** (0.1 g, 0.4 mmol), *N*-iodosuccinimide (0.09 g, 0.4 mmol) in acetonitrile (3 mL) yielded the title compound as a colorless solid (0.06 g, 50% yield). ^{1}H NMR (400 MHz, DMSO-d_6), ppm: 7.69 (d, *J* = 7.0 Hz, 2H), 7.39 (t, *J* = 7.0 Hz, 2H), 7.30 (t, *J* = 7.0 Hz, 1H), 3.85 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6), ppm: 149.6, 134.9, 128.6, 128.3, 127.4, 60.9, 40.6. ^{19}F NMR (377 MHz, DMSO-d_6), ppm: -134.9. ^{11}B NMR (128 MHz, DMSO-d_6), ppm: 1.2. FTIR (neat, cm^{-1}), ν_{max}: 2957 (w), 1436 (m), 1424 (m), 1171, (m) 1140 (m), 1028 (m), 974 (s), 935 (s). HRMS calculated for $C_{10}H_8{}^{11}BF_3IN_2$ (ESI$^-$): 349.9819. Found: 349.9822.

Synthesis of potassium 5-(1-methyl-3-(4-methoxyphenyl)-4-chloropyrazole) trifluoroborate, ***18.*** Following general procedure F using **2c** (500 mg, 1.70 mmol) and *N*-chlorosuccinimide (227 mg, 1.70 mmol) in MeCN (8.5 mL), **18** was isolated as a colorless solid (450 mg, 81%). ^{1}H NMR (400 MHz, DMSO-d_6), ppm: 7.69 (d, *J* = 9.0 Hz, 2H), 6.95 (d, *J* = 9.0 Hz, 2H), 3.77 (s, 3H), 3.76 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6), ppm: 158.3, 143.5, 128.1, 125.7, 113.6, 108.2, 55.1, 29.5. ^{19}F NMR (377 MHz, DMSO-d_6), ppm: -135.8. ^{11}B NMR (128 MHz, DMSO-d_6), ppm: 1.40. FTIR (neat, cm^{-1}), ν_{max}: 2947 (w), 1614 (w), 1533 (m), 1438 (m), 1245 (m), 1177 (s), 1026 (s), 996 (s), 938 (s). HRMS (ESI^-) calculated for $C_{11}H_{10}{}^{11}B\ N_2OF_3{}^{35}Cl$: 289.0527. Found: 289.0513.

Synthesis of potassium 5-(1-methyl-3-(4-chlorophenyl)-4-chloropyrazole) trifluoroborate, ***19****.* Following general procedure F using **3c** (250 mg, 0.837 mmol) and *N*-chlorosuccinimide (112 mg, 0.837 mmol) in MeCN (4 mL), **19** was isolated as a colorless solid (212 mg, 76%). ^{1}H NMR (400 MHz, DMSO-d_6), ppm: 7.81 (d, *J* = 8.5 Hz, 2H), 7.44 (d, *J* = 8.5 Hz, 2H), 3.79 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6), ppm: 142.4, 132.0, 131.5, 128.4, 128.2, 108.7, 29.5. ^{19}F NMR (377 MHz, DMSO-d_6), ppm: -135.9. ^{11}B NMR (128 MHz, DMSO-d_6), ppm: 1.28. FTIR (neat, cm^{-1}), ν_{max}: 2948 (w), 1611 (m), 1439 (m), 1321 (m), 1246 (m), 1109 (s), 1070 (s), 1007 (s), 836 (s). HRMS (ESI^+) calculated for $C_{10}H_8{}^{11}B\ N_2F_3{}^{35}Cl_2K$: 322.9747. Found: 322.9732.

Synthesis of potassium 5-(1-methyl-3-(4-trifluoromethylphenyl)-4-chloropyrazole) trifluoroborate, ***20****.* Following general procedure F using **4c** (500 mg, 1.51 mmol) and *N*-chlorosuccinimide (201 mg, 1.51 mmol) in MeCN (7.6 mL), **20** was isolated as a colorless solid (529 mg, 96%). ^{1}H NMR (400 MHz, DMSO-d_6), ppm: 8.03 (d, *J* = 8.0 Hz, 2H), 7.75 (d, *J* = 8.0 Hz, 2H), 3.82 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6), ppm: 142.1, 137.1, 127.98, 127.09 (q, *J* = 32 Hz), 125.2 (d, *J* = 4 Hz), 124.5 (q, *J* = 272 Hz) 109.3, 29.5. ^{19}F NMR (377 MHz, DMSO-d_6), ppm: -60.9, -136.0. ^{11}B NMR (128 MHz, DMSO-d_6), ppm: 1.15. FTIR (neat, cm^{-1}), ν_{max}: 1620 (m), 1325 (s), 1200 (m), 1108 (s), 1067 (s), 965 (s), 846 (s). HRMS (ESI^-) calculated for $C_{11}H_7{}^{11}B\ N_2F_6{}^{35}Cl$: 327.0295. Found: 327.0283.

Synthesis of potassium tert-butyl 4-(4-chloro-1-methyl-5-(trifluoroboranyl)-1H-pyrazol-3-yl)piperidine-1-carboxylate, ***21.*** Following general procedure F using **7** (102 mg, 0.274 mmol), *N*-chlorosuccinimide (37 mg, 0.27 mmol) in acetonitrile (2.1 mL) and heated at 45 °C yielded the title compound as a colorless solid (36 mg, 33% yield). ^{1}H NMR (400 MHz, DMSO-d_6), ppm: 3.99 – 3.94 (m, 2H), 3.66 (s, 3H), 2.89 – 2.75 (m, 2H), 2.71 (tt, *J* = 11.5, 4.0, 1H), 1.73 – 1.68 (m, 2H), 1.57 – 1.43 (m, 2H), 1.40 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6), ppm: 153.9, 148.2, 108.3, 78.4, 43.3, 32.9, 30.6, 28.1. ^{19}F NMR (376 MHz, DMSO-d_6), ppm: -135.8. ^{11}B NMR (128 MHz, DMSO-d_6), ppm: 0.8. FTIR (neat, cm^{-1}), ν_{max}: 2977 (w), 2950 (w), 2860 (w), 1664 (s), 1429 (s),1162 (s), 971 (s), 956 (s). HRMS calculated for $C_{14}H_{21}{}^{11}B^{35}ClO_2F_3N_3$ (ESI^-): 366.1373. Found: 366.1389.

Synthesis of potassium 4-chloro-1-methyl-3-(tetrahydro-2H-pyran-4-yl)-5-(trifluoroboranyl)-1H-pyrazole, ***22.*** Following general procedure F using **8** (100 mg, 0.367 mmol), *N*-chlorosuccinimide (50 mg, 0.37 mmol) in acetonitrile (3 mL) heated at 45 °C yielded the title compound as a colorless solid (60 mg, 53% yield). ^{1}H NMR (400 MHz, DMSO-d_6), ppm: 3.90 – 3.86 (m, 2H), 3.67 (s, 3H), 3.42 – 3.34 (m, 2H), 2.82 – 2.71 (m, 1H), 1.75 – 1.62 (m, 4H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6), ppm: 148.9, 108.8, 67.7, 32.0, 28.6, 26.5.^{19}F NMR (376 MHz, DMSO-d_6), ppm: -135.8. ^{11}B NMR (128 MHz, DMSO-d_6), ppm: 0.8. FTIR (neat, cm^{-1}), ν_{max}: 2958 (w), 2919 (m), 2855 (w), 1238 (m), 1060 (s), 953 (s), 930 (s). HRMS calculated for $C_9H_{12}{}^{11}B^{35}ClOF_3N_2$ (ESI^-): 267.0689. Found: 267.0680.

General Procedure G: Suzuki-Miyaura of pyrazole trifluoroborates. A flask was charged with trifluoroborate (1 eq), aryl bromide (2 eq), palladium acetate (0.03 – 0.1 eq), XPhos (0.06 – 0.2 eq), triethylamine (2 eq) and thoroughly degassed EtOH (0.1 M) and the reaction heated at reflux for 14 h. The mixture was allowed to cool to ambient temperature, poured into aqueous $NaHCO_3$, extracted with EtOAc, dried over $MgSO_4$ and volatiles removed *in vacuo*. The crude residue was purified by flash silica chromatography (gradient 100% petroleum ether – 40% ethyl acetate in petroleum ether) affording the target pyrazoles.

Synthesis of 1-Methyl-3-phenyl-4-chloro-5-(4-methoxyphenyl)pyrazole, ***24a***. Following general procedure G using **16** (50 mg, 0.17 mmol) 4-bromoanisole (62 mg, 0.34 mmol), palladium acetate (1 mg, 0.005 mmol), XPhos (5 mg, 0.01 mmol) and NEt_3 (34 mg, 0.34 mmol) in EtOH (1.5 mL), **24a** was isolated as a colorless solid (32 mg, 64%). ^{1}H NMR (400 MHz, $CDCl_3$), ppm: 7.97-7.92 (m, 2H), 7.49-7.33 (m, 5H), 7.05 (d, *J* = 9.0 Hz, 2H), 3.88 (s, 3H), 3.84 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$), ppm: 160.4, 146.5, 141.2, 132.1, 131.2, 128.5, 128.1, 127.5, 120.5, 114.4, 106.5, 55.5, 38.3. FTIR (neat, cm^{-1}), ν_{max}: 2948 (w), 1609 (m), 1485 (m), 1443 (m), 1358 (w), 1293 (m), 1247 (s), 1181 (s), 1015 (s), 1007 (s), 851 (s). HRMS (ESI^+) calculated for $C_{17}H_{15}N_2O^{35}Cl$: 299.0946. Found: 299.0950.

Synthesis of 1-Methyl-3-phenyl-4-chloro-5-(4-trifluoromethylphenyl)pyrazole, ***25a***. Following general procedure G using **16** (50 mg, 0.17 mmol) 4-bromotrifluoromethylbenzene (75 mg, 0.34 mmol), palladium acetate (1 mg, 0.005 mmol), XPhos (5 mg, 0.01 mmol) and NEt_3 (34 mg, 0.34 mmol) in EtOH (1.5 mL), **25a** was isolated as a colorless solid (36 mg, 64%). ^{1}H NMR (400 MHz, $CDCl_3$), ppm: 7.98-7.90 (m, 2H), 7.81 (d, *J* = 8.0 Hz, 2H), 7.62 (d, *J* = 8.0 Hz, 2H), 7.46 (t, *J* = 7.5 Hz, 2H), 7.42-7.36 (m, 1H), 3.88 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$), ppm: 146.9, 139.8, 131.7, 131.4 (q, *J* = 33.0 Hz), 130.3, 128.6, 128.4, 128.0, 127.5, 126.0 (q, *J* = 3.5 Hz), 124.0 (q, *J* = 272.5 Hz), 107.2, 38.5. ^{19}F NMR (377 MHz, $CDCl_3$), ppm: -62.8. FTIR (neat, cm^{-1}), ν_{max}: 1621 (w), 1445 (m), 1322 (s), 1155 (m), 1120 (s), 1108 (s), 1068 (s), 1009 (m), 845 (s). HRMS (ESI^+) calculated for $C_{17}H_{13}N_2F_3{}^{35}Cl$: 337.0719. Found: 337.0709.

Synthesis of 1-Methyl-3-(4-trifluoromethylphenyl)-4-chloro-5-(4-methoxyphenyl)-pyrazole, ***26a.*** Following general procedure G using **20** (50 mg, 0.14 mmol) 4-bromoanisole (51 mg, 0.27 mmol), palladium acetate (3 mg, 0.01 mmol), XPhos (13 mg, 0.027 mmol) and NEt_3 (28 mg, 0.27 mmol) in EtOH (1.4 mL), **26a** was isolated as a colorless solid (32 mg, 64%). ^{1}H NMR (400 MHz, $CDCl_3$), ppm: 8.09 (d, *J* = 8.0 Hz, 2H), 7.70 (d, *J* = 8.0 Hz, 2H), 7.39 (d, *J* = 9.0 Hz, 2H), 7.06 (d, *J* = 9.0 Hz, 2H), 3.89 (s, 3H), 3.85 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$), ppm: 158.5, 147.0, 142.7, 137.4, 131.6, 130.3, 129.1 (q, *J* = 32.0 Hz), 128.7, 128.2, 125.3 (q, *J* = 3.5 Hz), 124.5 (q, *J* = 272.0 Hz), 114.0, 55.2, 37.7. ^{19}F NMR (377 MHz, $CDCl_3$), ppm: -62.5. FTIR (neat, cm^{-1}), ν_{max}: 2966 (w), 1611 (m), 1492 (m),

1321 (s), 1161 (m), 1107 (s), 1065 (s), 1017 (m), 848 (s). HRMS (ESI^+) calculated for $C_{18}H_{15}N_2OF_3{}^{35}Cl$: 367.0825. Found: 367.0810.

Synthesis of 1-Methyl-3-(4-trifluoromethylphenyl)-4-chloro-5-phenylpyrazole, ***27a***. Following general procedure G using **20** (50 mg, 0.14 mmol) bromobenzene (43 mg, 0.27 mmol), palladium acetate (3 mg, 0.01 mmol), XPhos (13 mg, 0.027 mmol) and NEt_3 (28 mg, 0.27 mmol) in EtOH (1.4 mL), **27a** was isolated as a colorless solid (29 mg, 64%). ^1H NMR (400 MHz, $CDCl_3$), ppm: 8.09 (d, J = 8.0 Hz, 2H), 7.70 (d, J = 8.0 Hz, 2H), 7.58-7.45 (m, 5H), 3.87 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$), ppm: 145.1, 141.7, 135.6, 130.0 (q, J = 32.0 Hz), 129.9, 129.6, 129.0, 128.0, 127.6, 125.5 (q, J = 3.5 Hz), 124.4 (q, J = 272.0 Hz), 107.1, 38.5. ^{19}F NMR (377 MHz, $CDCl_3$), ppm: -62.5. FTIR: ν_{max} 2929 (w), 1619 (w), 1323 (s), 1158 (m), 1112 (s), 1066 (s), 1013 (m), 850 (s). HRMS (ESI^+) calculated for $C_{17}H_{13}N_2F_3{}^{35}Cl$: 337.0719. Found: 337.0735.

Synthesis of 1-Methyl-3-(4-methoxyphenyl)-4-chloro-5-(4-trifluoromethylphenyl)-pyrazole, ***28a***. Following general procedure G using **18** (50 mg, 0.15 mmol) 4-bromotrifluoromethylbenzene (68 mg, 0.30 mmol), palladium acetate (3 mg, 0.02 mmol), XPhos (14 mg, 0.03 mmol) and NEt_3 (31 mg, 0.30 mmol) in EtOH (1.5 mL), **28a** was isolated as a colorless solid (32 mg, 57%). ^1H NMR (400 MHz, $CDCl_3$), ppm: 7.87 (d, J = 9.0 Hz, 2H), 7.80 (d, J = 8.0 Hz, 2H), 7.61 (d, J = 8.0 Hz, 2H), 6.99 (d, J = 9.0 Hz, 2H), 3.86 (s, 3H,), 3.86 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$), ppm: 159.8, 146.8, 139.7, 132.0, 131.4 (q, J = 33.0 Hz), 130.3, 128.8, 125.9 (q, J = 3.5 Hz), 124.3, 124.0 (q, J = 272.5 Hz), 114.1, 106.8, 55.4, 38.4. ^{19}F NMR (377 MHz, $CDCl_3$), ppm: -62.8. FTIR (neat, cm^{-1}), ν_{max}: 2943 (w), 1611 (m), 1531 (m), 1439 (m), 1321 (s), 1246 (m), 1167 (s), 1123 (s), 1109 (s), 1071 (m), 1031 (m), 1012 (m), 836 (s). HRMS (ESI^+) calculated for $C_{18}H_{14}N_2OF_3{}^{35}Cl$: 367.0820. Found: 367.0822.*Synthesis of 1-Methyl-3-(4-methoxyphenyl)-4-chloro-5-phenylpyrazole,* ***29a***. Following general procedure G using **18** (50 mg, 0.15 mmol), bromobenzene (48 mg, 0.30 mmol), palladium acetate (3 mg, 0.02 mmol), XPhos (14 mg, 0.029 mmol) and NEt_3 (31 mg, 0.30 mmol) in EtOH (1.5 mL), **29a** was isolated as a colorless solid (29 mg, 64%). ^1H NMR (400 MHz, $CDCl_3$), ppm: 7.88 (d, J = 9.0 Hz, 2H), 7.58-7.44 (m, 5H), 6.99 (d, J = 9.0 Hz, 2H), 3.86 (s, 3H), 3.84 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$), ppm: 159.7,

146.5, 141.2, 129.9, 129.4, 128.9, 128.8, 128.4, 124.7, 114.0, 106.3, 55.4, 38.3. FTIR (neat, cm^{-1}), ν_{max}: 2947 (w), 1612 (m), 1579 (m), 1529 (m), 1482 (m), 1451 (m), 1438 (m), 1300 (m), 1246 (s), 1182 (s), 1171 (s), 1031 (s), 1010 (s). HRMS (ESI^+) calculated for $C_{17}H_{15}N_2O^{35}Cl$: 299.0946. Found: 299.0948.

General Procedure H: Suzuki-Miyaura of 4-chloropyrazoles. A flask was charged with chloropyrazole (1 eq), aryl boronic acid (2 eq), XPhosPdG2 (0.1 eq), sodium carbonate (3 eq), degassed 1,2-dimethoxyethane:water (1/1, 0.1 M) and the reaction heated at 80 °C for 14 h. The mixture was allowed to cool to ambient temperature, poured into aqueous $NaHCO_3$, extracted with EtOAc, dried over $MgSO_4$ and volatiles removed *in vacuo*. The crude residue was purified by flash silica chromatography (gradient 100% petroleum ether – 40% ethyl acetate in petroleum ether) affording the target pyrazoles.

Synthesis of 1-Methyl-3-phenyl-4-(4-methoxyphenyl)-5-(4-trifluoromethylphenyl)pyrazole, ***24****.* Following general procedure H using **24a** (50 mg, 0.15 mmol) 4-methoxyphenylboronic acid (45 mg, 0.30 mmol), XPhosPdG2 (12 mg, 0.015 mmol), Na_2CO_3 (47 mg, 0.44 mmol) in 1,2-DME:H_2O (1:1, 1.5 mL), **24** was isolated as a colorless solid (55 mg, 91%). ^1H NMR (400 MHz, $CDCl_3$), ppm: 7.63 (d, *J* = 8.0 Hz, 2H), 7.50-7.45 (m, 2H), 7.37 (d, *J* = 8.0 Hz, 2H), 7.31-7.25 (m, 3H), 6.95 (d, *J* = 8.5 Hz, 2H), 6.75 (d, *J* = 8.5 Hz, 2H), 3.89 (s, 3H), 3.77 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$), ppm: 159.9, 147.0, 142.6, 137.3, 131.5, 130.5, 129.2 (q, *J* = 32.0 Hz), 128.5, 128.2, 126.8, 125.1 (q, *J* = 3.5 Hz), 124.3 (q, *J* = 272.0 Hz), 122.0, 119.6, 114.2, 103.5, 55.4, 37.6. ^{19}F NMR (377 MHz, $CDCl_3$), ppm*:* -62.7. FTIR (neat, cm^{-1}), ν_{max}: 2941 (w), 1619 (m), 1525 (m), 1437 (m), 1326 (s), 1244 (s), 1162 (m), 1115 (s), 1069 (s), 1031 (m). HRMS (ESI^+) calculated for $C_{24}H_{19}N_2OF_3$: 409.1522. Found: 409.1524.

Synthesis of 1-Methyl-3-phenyl-4-(4-trifluoromethylphenyl)-5-(4-methoxyphenyl)pyrazole, ***25****.* Following general procedure H using **25a** (50 mg, 0.17 mmol) 4-trifluoromethylphenylboronic acid (62 mg, 0.34 mmol), XPhosPdG2 (13 mg, 0.017 mmol), Na_2CO_3 (53 mg, 0.50 mmol) in 1,2-DME / H_2O (1:1, 1.7 mL), **25** was isolated as a colorless solid (56 mg, 82%). ^1H NMR (400 MHz, $CDCl_3$), ppm: 7.45-7.38 (m, 4H), 7.34-7.27 (m, 3H), 7.18-7.11 (m, 4H), 6.92 (d, *J* = 9.0 Hz, 2H), 3.86 (s, 3H), 3.84 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$), ppm: 160.1, 148.8, 142.6, 137.6, 133.3, 131.5, 130.5, 128.5,

128.4, 127.8, 125.2 (q, J = 4.0 Hz), 124.4 (q, J = 272.0 Hz), 121.9, 117.7, 114.4, 55.4, 37.4 (one sp^2 carbon not observed). ^{19}F NMR (377 MHz, $CDCl_3$), ppm: -62.3; FTIR (neat, cm^{-1}), ν_{max}: 2939 (w), 1611 (m), 1446 (m), 1330 (s), 1253 (s), 1156 (m), 1102 (s), 1064 (s), 906 (m). HRMS (ESI^+) calculated for $C_{24}H_{19}N_2OF_3$: 409.1522. Found: 409.1530.

Synthesis of 1-Methyl-3-(4-trifluoromethylphenyl)-4-phenyl-5-(4-methoxyphenyl)pyrazole, ***26***. Following general procedure H using **26a** (50 mg, 0.14 mmol) phenylboronic acid (33 mg, 0.27 mmol), XPhosPdG2 (11 mg, 0.014 mmol), Na_2CO_3 (43 mg, 0.41 mmol) in 1,2-DME:H_2O (1:1, 1.4 mL), **26** was isolated as a colorless solid (33 mg, 59%). ^1H NMR (400 MHz, $CDCl_3$), ppm: 7.58 (d, J = 8.0 Hz, 2H), 7.51 (d, J = 8.0 Hz, 2H), 7.23-7.19 (m, 3H), 7.16 (d, J = 8.5 Hz, 2H), 7.08-7.02 (m, 2H), 6.89 (d, J = 8.5 Hz, 2H), 3.87 (s, 3H), 3.82 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$), ppm: 159.9, 147.0, 142.6, 137.3, 133.3, 131.5, 130.5, 129.2 (q, J = 32.0 Hz), 128.5, 128.2, 125.7, 125.3 (q, J = 3.5 Hz), 124.5 (q, J = 272.0 Hz), 122.0, 119.6, 114.2, 55.4, 37.6. ^{19}F NMR (377 MHz, $CDCl_3$), ppm: -62.4. FTIR (neat, cm^{-1}), ν_{max}: 2961 (w), 1617 (m), 1322 (s), 1249 (m), 1165 (s), 1105 (s), 1065 (s), 841 (s). HRMS (ESI^+) calculated for $C_{24}H_{19}N_2OF_3$: 409.1522. Found: 409.1526.

Synthesis of 1-Methyl-3-(4-trifluoromethylphenyl)-4-(4-methoxyphenyl)-5-phenylpyrazole, ***27***. Following general procedure H using **27a** (50 mg, 0.15 mmol) 4-methoxyphenylboronic acid (45 mg, 0.30 mmol), XPhosPdG2 (12 mg, 0.015 mmol), Na_2CO_3 (47 mg, 0.44 mmol) in 1,2-DME:H_2O (1:1, 1.5 mL), **27** was isolated as a colorless oil (49 mg, 81%). ^1H NMR (400 MHz, $CDCl_3$), ppm: 7.60 (d, J = 8.0 Hz, 2H), 7.52 (d, J = 8.0 Hz, 2H), 7.40-7.35 (m, 3H), 7.28-7.20 (m, 2H), 6.96 (d, J = 8.5 Hz, 2H), 6.75 (d, J = 8.5 Hz, 2H), 3.88 (s, 3H), 3.77 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$), ppm: 160.5, 145.0, 141.6, 135.7, 131.2, 130.2, 129.9 (q, J = 32.5 Hz), 127.5, 127.4, 125.7, 125.5 (q, J = 3.5 Hz), 124.4 (q, J = 272.0 Hz), 120.1, 114.5, 107.0, 55.5, 38.4 (one sp^2 carbon not observed). ^{19}F NMR (377 MHz, $CDCl_3$), ppm: -62.4. FTIR (neat, cm^{-1}), ν_{max}: 2941 (w), 1616 (m), 1513 (m), 1325 (s), 1240 (m), 1161 (m), 1107 (s), 1066 (s), 1015 (m). HRMS (ESI^+) calculated for $C_{24}H_{19}N_2OF_3$: 409.1522. Found: 409.1526.

Synthesis of 1-Methyl-3-(4-methoxyphenyl)-4-phenyl-5-(4-trifluoromethylphenyl)pyrazole, ***28****.* Following general procedure H using **28a** (50 mg, 0.14 mmol) phenylboronic acid (33 mg, 0.27 mmol), XPhosPdG2 (11 mg, 0.014 mmol), Na_2CO_3 (43 mg, 0.41 mmol) in 1,2-DME:H_2O (1:1, 1.4 mL), **28** was isolated as a colorless oil (37 mg, 67%). ^{1}H NMR (400 MHz, $CDCl_3$), ppm: 7.62 (d, *J* = 8.0 Hz, 2H), 7.44-7.34 (m, 4H), 7.22-7.16 (m, 3H), 7.07-7.01 (m, 2H), 6.81 (d, *J* = 9.0 Hz, 2H), 3.88 (s, 3H), 3.79 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$), ppm: 159.2, 148.6, 140.8, 134.0, 133.2, 130.6, 130.6 (q, *J* = 33.0 Hz), 130.5, 129.4, 128.5, 126.8, 125.8, 125.6 (q, *J* = 3.5 Hz), 124.0 (q, *J* = 272.0 Hz), 119.5, 113.8, 55.3, 37.6. ^{19}F NMR (377 MHz, $CDCl_3$), ppm: -62.7. FTIR (neat, cm^{-1}), ν_{max}: 2940 (w), 1612 (m), 1530 (m), 1434 (m), 1324 (s), 1248 (s), 1164 (s), 1115 (s), 1071 (s), 1020 (s), 840 (s). HRMS (ESI^+) calculated for $C_{24}H_{19}N_2OF_3$: 409.1522. Found: 409.1528.

Syntheis of 1-Methyl-3-(4-methoxyphenyl)-4-(4-trifluoromethylphenyl)-5-phenylpyrazole, ***29****.* Following general procedure H using **29a** (53 mg, 0.18 mmol) 4-trifluoromethylphenylboronic acid (67 mg, 0.35 mmol), XPhosPdG2 (14 mg, 0.018 mmol), Na_2CO_3 (56 mg, 0.53 mmol) in 1,2-DME:H_2O (1:1, 1.8 mL), **29** was isolated as a colorless solid (46 mg, 64%). ^{1}H NMR (400 MHz, $CDCl_3$), ppm: 7.43-7.38 (m, 5H), 7.35 (d, *J* = 9.0 Hz, 2H), 7.24-7.20 (m, 2H), 7.12 (d, *J* = 8.0 Hz, 2H), 6.84 (d, *J* = 9.0 Hz, 2H), 3.85 (s, 3H), 3.81 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$), ppm: 159.4, 148.7, 142.6, 137.6, 130.5, 130.3, 129.9, 129.6, 129.0, 128.9, 128.3 (q, *J* = 32.0 Hz), 125.7, 125.2 (q, *J* = 4.0 Hz), 124.4 (q, *J* = 272.0 Hz), 117.5, 114.0, 55.3, 37.4. *^{19}F NMR (377 MHz, $CDCl_3$), ppm:* -62.4. FTIR (neat, cm^{-1}), ν_{max}: 2932 (w), 1616 (m), 1526 (m), 1434 (m), 1331 (s), 1247 (s), 1158 (m), 1115 (s), 1065 (s), 839 (s). HRMS (ESI^+) calculated for $C_{24}H_{19}N_2OF_3$: 409.1522. Found: 409.1521.

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Supporting Information Available: ^{1}H, ^{13}C, ^{19}F and ^{11}B NMR spectra for selected compounds and structure elucidation analyses performed on selected compounds. This material is available free of charge at http://pubs.acs.org

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