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 C5 and C4. 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.\(^3\) Moreover, 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 C4 rather than C5), 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 C3,\(^7\) or the regioselective alkylation of a free pyrazole -NH. 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 C3 position difficult to functionalize
-\( R^2\): incorporate early on, avoid regioselective alkylation of free pyrazole NH
-\( \text{Hal}/\text{BF}_3\text{K}\): 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). 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 N1,C3-substituted pyrazole trifluoroborates.
Having successfully exemplified the introduction of a diverse array of substituents at C3, we investigated the reaction of a series of hydrazines in order to vary the substituent at N1 (Table 1).

Table I. Hydrazine scope.

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Ratio A:B[a]</th>
<th>Yield[b]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H</td>
<td>--</td>
<td>93%, 10</td>
</tr>
<tr>
<td>2</td>
<td>CH₂C(CH₃)CH₂</td>
<td>76:24</td>
<td>98%, 11</td>
</tr>
<tr>
<td>3</td>
<td>CH₃CH₂OH</td>
<td>92:8</td>
<td>98%, 12</td>
</tr>
<tr>
<td>4</td>
<td>CH₂CH₂CN</td>
<td>29:71</td>
<td>77%, 13</td>
</tr>
</tbody>
</table>

[a] Determined by ¹H 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. 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 C4 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. Using our model substrate 1, we first investigated bromination at C4 using bromine and K₂CO₃ in acetonitrile (Table 2). Unfortunately, the BF₃K 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 C4 bromination.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Brominating agent</th>
<th>Conditions</th>
<th>Ratio 14:15[a]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Br₂ (1.1 eq)[b]</td>
<td>K₂CO₃ (2 eq), MeCN</td>
<td>0:1</td>
</tr>
<tr>
<td>2</td>
<td>NBS (1 eq)</td>
<td>MeCN</td>
<td>4:1</td>
</tr>
<tr>
<td>3</td>
<td>NBS (1 eq)[c]</td>
<td>MeCN[b]</td>
<td>5:1</td>
</tr>
<tr>
<td>4</td>
<td>NBS (1 eq)[c,d]</td>
<td>MeCN[b]</td>
<td>12:1</td>
</tr>
</tbody>
</table>

[a] Determined by ¹H NMR spectroscopy; [b] 2 Equiv of K₂CO₃ 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 C3 under the same reaction conditions yielded the corresponding monochlorinated derivatives 18 – 22.
In parallel, we investigated the exchange of the BF$_3$K 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 2. C4 halogenation of pyrazole 5-trifluoroborates.**

In parallel, we investigated the exchange of the BF$_3$K 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.\textsuperscript{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 C5-arylated products in acceptable yield, leaving the C4-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 C4 and C5. 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 C4 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$_3$K 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, tert-butyl 4-(1-hydroxyprop-2-yn-1-yl)piperidine-1-carboxylate 7a, 1-benzyloxybut-3-yn-2-ol 9a, potassium trifluoro(3-oxo-3-phenylprop-1-yn-1-yl)borate 1c, potassium trifluoro(3-(4-methoxyphenyl)-3-oxoprop-1-yn-1-yl)borate 2c, potassium trifluoro(3-(4-trifluoromethyl)phenyl)-3-oxoprop-1-yn-1-yl)borate 4c, potassium trifluoro(3-oxobut-1-yn-1-yl)borate 6c, potassium trifluoro(1-methyl-3-phenyl-1H-pyrazol-5-yl)borate 1, potassium trifluoro(3-(4-methoxyphenyl)-1-methyl-1H-pyrazol-5-yl)borate 2, potassium trifluoro(1-methyl-3-(4(trifluoromethyl)phenyl)-1H-pyrazol-5-yl)borate 4, and potassium (1,3-dimethyl-1H-pyrazol-5-yl)trifluoroborate 6.

General procedure A: Addition of Grignard reagent. 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$_4$Cl, 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. Following general procedure A, using p-chlorobenzaldehyde (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, 75.2, 63.5.

Synthesis of 1-(1-methyl-1H-pyrazol-5-yl)prop-2-yn-1-ol, 5a. Following general procedure A, using 1-methyl-1H-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$^{-1}$), $\nu_{\text{max}}$: 3392 (w), 3231 (m), 3120 (m), 3036 (m), 2115 (w), 1420 (s). HRMS calculated for C$_7$H$_8$N$_2$O (ESI$^+$): 137.0709. Found: 137.0711.

Synthesis of tert-butyl 4-(1-hydroxyprop-2-yn-1-yl)piperidine-1-carboxylate, 7a. 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-2H-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$^{-1}$), $\nu_{\text{max}}$: 3319 (s), 3258 (s), 2954 (m), 2946 (m), 2858 (s), 2109 (s), 1080 (s), 1037 (s), 1023 (s). HRMS calculated for C$_8$H$_{12}$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$_2$O 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(OiPr)Pin (3.5 mL, 18 mmol) in THF (25 mL) and KHF₂ (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-d₆), 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-d₆), ppm: 142.7, 131.4, 128.3, 127.8, 89.9, 62.4. \(^{19}\)F NMR (377 MHz, DMSO-d₆), ppm: -131.6. \(^{11}\)B NMR (128 MHz, DMSO-d₆), ppm: 5.0. M. pt. >290 °C. FTIR (neat, cm⁻¹), \(\nu_{\text{max}}\): 3537 (w), 2929 (w), 1001 (s), 933 (s). HRMS calculated for C₉H₆BF₃Cl: 233.0152. Found: 233.0163.

Synthesis of potassium 1-(1-methyl-1H-pyrazol-5-yl)-3-(trifluoroboranyl)prop-2-yn-1-yl, 5b. Following general procedure B using 5a (0.80 g, 5.8 mmol), n-BuLi (5.5 mL, 13 mmol), B(OiPr)Pin (3.6 mL, 18 mmol) in THF (23 mL) and KHF₂ (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-d₆), 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-d₆), ppm: 143.7, 137.1, 104.9, 74.0, 55.9, 37.3. \(^{19}\)F NMR (376 MHz, DMSO-d₆), ppm: -131.8. \(^{11}\)B NMR (128 MHz, DMSO-d₆), ppm: 5.2. M. pt. = 111 °C. FTIR (neat, cm⁻¹), \(\nu_{\text{max}}\): 3598 (m), 3316 (w), 2219 (w), 1645 (w), 1630 (w). HRMS calculated for C₇H₇BOF₃N₂Na (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(OiPr)Pin (7.5 mL, 35 mmol) in THF (48 mL) and KHF₂ (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-d₆), 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-d₆), ppm: 153.9, 78.4, 64.9, 42.4, 28.1, 27.6, 27.4, 24.9. \(^{19}\)F NMR (376 MHz, DMSO-d₆), ppm: -131.3. \(^{11}\)B NMR (128 MHz, DMSO-d₆), ppm: 5.0. M. pt. >290 °C. FTIR (neat, cm⁻¹), \(\nu_{\text{max}}\): 3402 (br, w),
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(OMe)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). $^1$H 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{$^1$H} 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$^{-1}$), $\tilde{\nu}$max: 3496 (s), 2957 (m), 2917 (m), 2872 (m), 2854 (m), 1238 (s), 1082 (s), 1024 (s). HRMS calculated for C$_{13}$H$_{20}$BO$_2$F$_3$N (ESI$^-$): 306.1494. Found: 306.1504.

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(OMe)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). $^1$H 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{$^1$H} 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$^{-1}$), $\tilde{\nu}$max: 3512 (w), 3376 (w), 3034 (w), 2869 (w), 2217 (w), 1097 (s), 1064 (s). HRMS calculated for C$_{11}$H$_{11}$BO$_2$F$_3$ (ESI$^-$): 243.0810. Found: 243.0819.

General procedure C: Oxidation to ynone trifluoroborates. 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 Et₂O a solid precipitated. The solid was filtered and washed with Et₂O 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). ¹H NMR (500 MHz, DMSO-d₆), ppm: 8.05 (d, J = 9.0 Hz, 2H), 7.65 (d, J = 9.0 Hz, 2H). ¹³C{¹H} NMR (126 MHz, DMSO-d₆), ppm: 176.9, 138.8, 135.5, 130.7, 129.0, 87.9. ¹⁹F NMR (377 MHz, Acetone-d₆), ppm: -136.3. ¹¹B NMR (128 MHz, DMSO-d₆), ppm: -1.8. M. pt. >300 °C. FTIR (neat, cm⁻¹), v_max: 2946 (w), 1661 (s), 1222 (s), 984 (s). HRMS calculated for C₉H₄¹¹BOF₃Cl (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). ¹H NMR (400 MHz, DMSO-d₆), ppm: 7.53 (d, J = 2.0 Hz, 1H), 6.95 (d, J = 2.0 Hz, 1H), 4.05 (s, 3H). ¹³C{¹H} NMR (126 MHz, DMSO-d₆), ppm: 167.7, 139.6, 137.7, 114.2, 89.0, 39.6. ¹⁹F NMR (376 MHz, DMSO-d₆), ppm: -133.3. ¹¹B NMR (128 MHz, DMSO-d₆), ppm: -1.9. M. pt. = 252 °C (deg). FTIR (neat, cm⁻¹), v_max: 3142 (s), 2962 (s), 2191 (m), 3392 (w), 3231 (m), 3120 (m), 3036 (m), 2115 (w), 1420 (s). HRMS calculated for C₇H₅¹¹BOF₃N₂ (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). ¹H NMR (400 MHz, DMSO-d₆), 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). ¹³C{¹H} NMR (126 MHz, DMSO-d₆), ppm: 190.0, 153.8, 88.9, 78.6, 49.0, 40.1, 28.1, 27.2. ¹⁹F NMR (376 MHz, DMSO-d₆), ppm: -133.2. ¹¹B NMR (128 MHz, DMSO-d₆), ppm: -1.9. M. pt. = 169 °C. FTIR (neat, cm⁻¹), v_max: 2932 (w), 2187 (w), 1679 (m), 1658 (m). HRMS calculated for C₁₃H₁₈¹¹BO₂F₃N (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$^{-1}$), $\nu_{max}$: 2960 (w), 2851 (w) 2183 (w), 1649 (m), 1110, (s), 1008 (s). HRMS calculated for C$_{8}$H$_{9}$11BO$_2$F$_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$^{-1}$), $\nu_{max}$: 3032 (w), 2868 (w), 2182 (w), 1676 (s), 1455-1380 (s), 1087 (s). HRMS calculated for C$_{11}$H$_9$11BO$_2$F$_3$ (ESI): 241.0653. Found: 241.0658.

General procedure D: Synthesis of N-methylpyrazoles. To a solution of ynene (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 redisolved in the minimum of acetone and upon addition of Et$_2$O a solid precipitated. The solid was filtered and washed with Et$_2$O 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{$^1$H} 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$^{-1}$), $\tilde{\nu}_{\text{max}}$: 2950 (w), 1425 (m), 1191 (m), 1168 (s), 935 (s). HRMS calculated for C$_{10}$H$_8$B$_3$ClF$_3$N$_2$ (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). $^1$H 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{$^1$H} 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$^{-1}$), $\tilde{\nu}_{\text{max}}$: 3152 (s), 3127 (s), 1386 (s). HRMS calculated for C$_8$H$_9$BF$_3$N$_4$ (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). $^1$H 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{$^1$H} 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$^{-1}$), $\tilde{\nu}_{\text{max}}$: 2934 (w), 1674 (m), 1425 (m), 1366 (m). HRMS calculated for C$_{14}$H$_{22}$BO$_2$F$_3$N$_3$ (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$^{-1}$), $\nu_{\text{max}}$: 2937 (w), 2918 (w), 2850 (w), 1444 (w), 1428 (w), 1168 (m), 1126 (m). HRMS calculated for C$_9$H$_{13}$BOF$_3$N$_2$ (ESI$^-$): 233.1079. Found: 233.1086.

**Synthesis of potassium 3-((benzoyloxy)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$^{-1}$), $\nu_{\text{max}}$: 3031 (w), 2933 (w), 2865 (w), 1453 (m), 1164 (m), 1148 (m). HRMS calculated for C$_{12}$H$_{13}$BOF$_3$N$_2$ (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$_2$O a solid precipitated. The solid was filtered and washed with Et$_2$O 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{\textsuperscript{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, 110.7, 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$^{-1}$), $\nu$ max: 2973 (w), 1640 (w), 1604 (w), 1458 (m), 
nm 1190 (m), 1136 (s). HRMS calculated for C$_{11}$H$_{11}$BF$_3$N$_2$ (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{\textsuperscript{1}H} 
NMR (101 MHz, DMSO-d$_6$), ppm: 147.9, 134.9, 128.3, 126.2, 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$^{-1}$), $\nu$ max: 3364 (br. w), 
2947 (w), 1604 (w), 1458 (m), 1190 (m), 1136 (s). HRMS calculated for C$_{11}$H$_{11}$BF$_3$N$_2$ (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{\textsuperscript{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$^{-1}$), $\nu$ max: 3193 (br. w), 
2930 (w), 2920 (w), 1460 (m), 1429 (m), 1407 (m), 1140 (s). HRMS calculated for C$_{11}$H$_{11}$BF$_3$N$_2$ 

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$^{-1}$), $\nu_{max}$: 3059 (w), 2977 (w), 2247 (w), 1486 (m), 1134 (s). HRMS calculated for C$_{12}$H$_{10}$BF$_3$N$_3$ (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$_2$Cl$_2$, 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$^{-1}$), $\nu_{max}$: 3403 (w), 3280 (br), 3049 (w), 1596 (s), 1398 (s), 764 (s). HRMS calculated for C$_{20}$H$_{18}$B$_4$N$_4$ (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$_2$Cl$_2$ 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$_2$Cl$_2$ was added leading to the precipitation of a solid. The solid was isolated by filtration and washed with CH$_2$Cl$_2$. 
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$^{-1}$), $\tilde{\nu}_{\text{max}}$: 2901 (w), 2845 (w), 1440 (m), 1426 (m), 1182 (s), 1144 (m), 986 (s), 936 (s). HRMS calculated for C$_{10}$H$_8$B$_7$9BrF$_3$N$_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$^{-1}$), $\tilde{\nu}_{\text{max}}$: 2950 (w), 2875 (w), 1430 (w), 1197 (m), 1144 (m), 1005 (s), 966 (s), 924 (s). HRMS calculated for C$_{10}$H$_8$B$_{35}$ClF$_3$N$_2$ (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$^{-1}$), $\tilde{\nu}_{\text{max}}$: 2957 (w), 1436 (m), 1424 (m), 1171, (m) 1140 (m), 1028 (m), 974 (s), 935 (s). HRMS calculated for C$_{10}$H$_8$BF$_3$IN$_2$ (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$^{-1}$), $\nu_{\text{max}}$: 2947 (w), 1614 (m), 1438 (m), 1245 (m), 1177 (s), 1026 (s), 996 (s), 938 (s). HRMS (ESI$^-$) calculated for C$_{11}$H$_{10}$B$_2$OF$_3$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$^{-1}$), $\nu_{\text{max}}$: 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$_8$B$_2$F$_3$Cl$_2$K: 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 = 272 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$^{-1}$), $\nu_{\text{max}}$: 1620 (m), 1325 (s), 1200 (m), 1108 (s), 1067 (s), 965 (s), 846 (s). HRMS (ESI$^+$) calculated for C$_{11}$H$_7$B$_2$F$_6$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$^{-1}$), $\nu_{\text{max}}$: 2977 (w), 2950 (w), 2860 (w), 1664 (s), 1429 (s), 1162 (s), 971 (s), 956 (s). HRMS calculated for C$_{14}$H$_{21}$B$_{35}$ClO$_2$F$_3$N$_3$ (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$^{-1}$), $\nu_{\text{max}}$: 2958 (w), 2950 (w), 2855 (w), 1238 (m), 1060 (s), 953 (s), 930 (s). HRMS calculated for C$_9$H$_{12}$B$_{35}$ClOF$_3$N$_2$ (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($^1$H) 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$^{-1}$), $\tilde{\nu}_{max}$: 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$_2$O$_3$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($^1$H) 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$^{-1}$), $\tilde{\nu}_{max}$: 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$_{13}$F$_3$N$_2$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($^1$H) 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$^{-1}$), $\tilde{\nu}_{max}$: 2966 (w), 1611 (m), 1492 (m),
1321 (s), 1161 (m), 1065 (s), 1017 (m), 848 (s). HRMS (ESI+) calculated for C_{18}H_{15}N_{2}OF_{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%). $^1$H NMR (400 MHz, CDCl$_3$), ppm: 8.09 (d, J = 8.0 Hz, 2H), 7.70 (d, J = 8.0 Hz, 2H), 7.58-7.45 (m, 5H), 3.87 (s, 3H); $^{13}$C($^1$H) 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 (neat, cm$^{-1}$), $\tilde{\nu}_{\text{max}}$: 2939 (w), 1619 (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_{17}H_{13}N_{2}OF_{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%). $^1$H 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($^1$H) 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$^{-1}$), $\tilde{\nu}_{\text{max}}$: 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_{2}OF_{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%). $^1$H 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($^1$H) 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$^{-1}$), $\nu_{max}$: 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$_2$O$_3$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 $^\circ$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$_2$CO$_3$ (47 mg, 0.44 mmol) in 1,2-DME:H$_2$O (1:1, 1.5 mL), 24 was isolated as a colorless solid (55 mg, 91%). $^1$H 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{$_1^H$} 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$^{-1}$), $\nu_{max}$: 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$_2$OF$_3$: 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$_2$CO$_3$ (53 mg, 0.50 mmol) in 1,2-DME / H$_2$O (1:1, 1.7 mL), 25 was isolated as a colorless solid (56 mg, 82%). $^1$H 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{$_1^H$} 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 sp² carbon not observed). ¹⁹F NMR (377 MHz, CDCl₃), ppm: -62.3; FTIR (neat, cm⁻¹), νmax: 2939 (w), 1611 (m), 1446 (m), 1330 (s), 1253 (s), 1102 (s), 1064 (s), 906 (m). HRMS (ESI⁺) calculated for C₂₄H₁₉N₂OF₃: 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), Na₂CO₃ (43 mg, 0.41 mmol) in 1,2-DME:H₂O (1:1, 1.4 mL), 26 was isolated as a colorless solid (33 mg, 59%). ¹H NMR (400 MHz, CDCl₃), 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). ¹³C{¹H} NMR (101 MHz, CDCl₃), 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. ¹⁹F NMR (377 MHz, CDCl₃), ppm: -62.4. FTIR (neat, cm⁻¹), νmax: 2961 (w), 1617 (m), 1322 (s), 1249 (m), 1165 (s), 1105 (s), 1065 (s), 841 (s). HRMS (ESI⁺) calculated for C₂₄H₁₉N₂OF₃: 409.1522. Found: 409.1530.

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), Na₂CO₃ (47 mg, 0.44 mmol) in 1,2-DME:H₂O (1:1, 1.5 mL), 27 was isolated as a colorless oil (49 mg, 81%). ¹H NMR (400 MHz, CDCl₃), 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). ¹³C{¹H} NMR (101 MHz, CDCl₃), ppm: 160.5, 145.0, 141.6, 135.7, 131.2, 130.2, 129.9 (q, J = 32.5 Hz), 127.6, 127.4, 125.7, 125.5 (q, J = 3.5 Hz), 124.4 (q, J = 272.0 Hz), 121.0, 114.5, 107.0, 55.5, 38.4 (one sp² carbon not observed). ¹⁹F NMR (377 MHz, CDCl₃), ppm: -62.4. FTIR (neat, cm⁻¹), νmax: 2941 (w), 1616 (m), 1513 (m), 1325 (s), 1240 (m), 1161 (m), 1107 (s), 1066 (s), 1015 (m). HRMS (ESI⁺) calculated for C₂₄H₁₉N₂OF₃: 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), Na₂CO₃ (43 mg, 0.41 mmol) in 1,2-DME:H₂O (1:1, 1.4 mL), 28 was isolated as a colorless oil (37 mg, 67%). ¹H NMR (400 MHz, CDCl₃), ppm: 7.62 (d, J = 8.0 Hz, 2H), 7.44-7.34 (m, 4H), 7.07-7.01 (m, 2H), 6.81 (d, J = 9.0 Hz, 2H), 3.88 (s, 3H), 3.79 (s, 3H). ¹³C{¹H} NMR (101 MHz, CDCl₃), 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. ¹⁹F NMR (377 MHz, CDCl₃), ppm: -62.7. FTIR (neat, cm⁻¹), v_max: 2940 (w), 1612 (m), 1530 (m), 1434 (m), 1248 (s), 1164 (s), 1115 (s), 1071 (s), 1020 (s), 840 (s). HRMS (ESI⁺) calculated for C₂₄H₁₉N₂O₃F: 409.1522. Found: 409.1528.

Synthesis 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), Na₂CO₃ (56 mg, 0.53 mmol) in 1,2-DME:H₂O (1:1, 1.8 mL), 29 was isolated as a colorless solid (46 mg, 64%). ¹H NMR (400 MHz, CDCl₃), 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). ¹³C{¹H} NMR (101 MHz, CDCl₃), 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. ¹⁹F NMR (377 MHz, CDCl₃), ppm: -62.4. FTIR (neat, cm⁻¹), v_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 C₂₄H₁₉N₂O₃F: 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

References


