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A One-Pot Suzuki-Hydrogenolysis Protocol for the Modular Synthesis of 2,5-Diaryl Tetrazoles

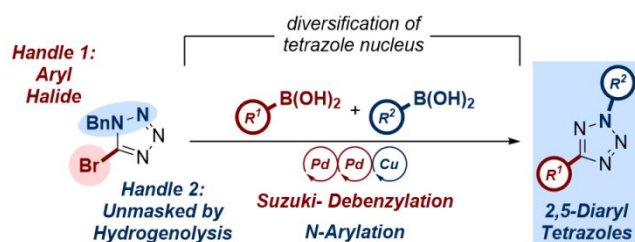
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Abstract



2,5-Diaryl tetrazoles are a diverse range of compounds of considerable interest within the field of photochemistry as a valuable precursor of the nitrile imine 1,3-dipole. Current literature approaches towards this heterocycle remain unsuitable for the practical synthesis of a library of these derivatives. Herein, we disclose the development of a modular approach towards 2,5-diaryl tetrazoles compatible with an array-type protocol, facilitated by a tandem Suzuki-hydrogenolysis approach.

Introduction

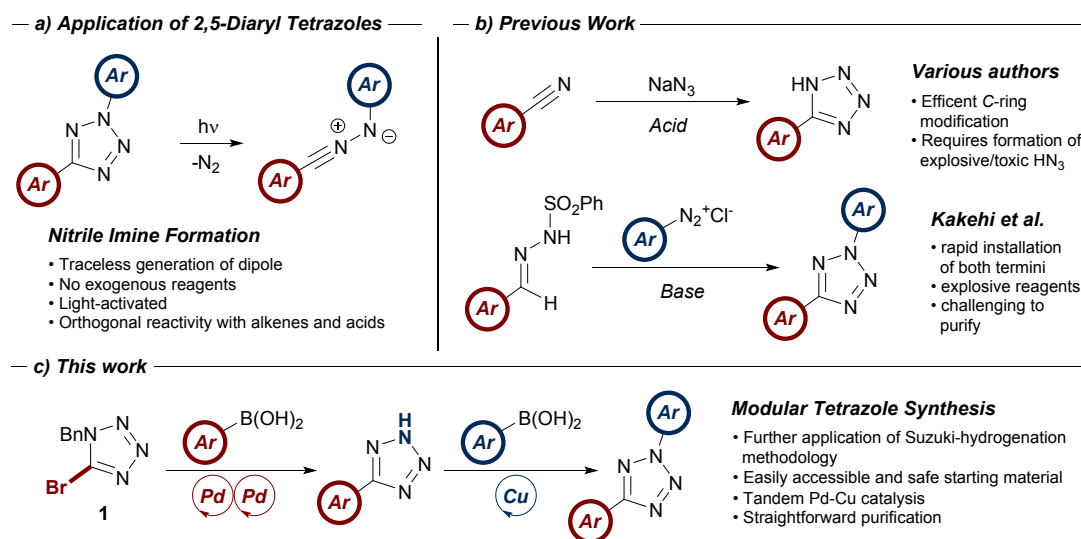
The recent resurgence of photochemistry as a unique and powerful method of forging and manipulating C-C bonds has stimulated the development and adaption of numerous synthetic protocols.¹ One such transformation is the photolysis of the 2,5-diaryl tetrazole moiety to yield the versatile nitrile imine 1,3-dipole (*Scheme 1a*).²⁻⁴ Owing to its facile reactivity with a number of functional groups including, alkenes^{4b,5} and carboxylic acids,⁶ the nitrile imine has recently found widespread application in fields where an orthogonal reactivity profile (click chemistry⁷) is desirable, such as materials chemistry and chemical biology.⁸⁻⁹

Due to the traceless reaction profile and inherent simplicity of photolyzing tetrazole systems, this protocol has become the most common method of nitrile imine generation. However, synthetic approaches towards 2,5-tetrazoles are limited relative to the requirement for structural diversity from the corresponding dipole precursors. In our laboratories, we were interested in the synthesis of a small library of 2,5-diaryl tetrazoles,¹⁰ and were surprised to find that the majority of recent reports on the preparation of these compounds rely on a cycloaddition-mediated approach reported by Kakehi (*Scheme 1b*) over 40 years ago.¹¹ While this robust synthesis is compatible with a range of substrates, it also typically employs hazardous reagents, and often laborious purification protocols. An alternative approach was introduced by Liu in 2015, however this route is somewhat limited by the commercial availability of the requisite aryl amidines.¹² The continuing limitation in the synthesis of these heterocycles appears to be simultaneous modification of both the *N* and *C*-aryl rings of the tetrazole. Multiple procedures for the diversification of 5-aryl tetrazoles with a palette of *N*-aryl groups have been developed,¹³ however, modification of the *C*-aryl ring itself is primarily restricted to classical syntheses *via* cycloaddition between the relevant benzonitrile and hydrazoic acid (*Scheme 1b*).¹⁴ This approach again requires use of toxic and explosive reagents. More recently, Kamenecka disclosed a route towards 2-aryl-5-bromotetrazoles, however this also requires the use of hazardous reagents, and subsequent derivatization to furnish *C*-aryl functionalized systems was not conducted.¹⁵

While the existing approaches are well-suited to the focused synthesis of specific 2,5-diaryl tetrazole species, we found most methods incompatible with an array-type approach towards a library of such compounds. We envisioned that a

common intermediate containing the pre-formed tetrazole nucleus encoded with chemoselective functional handles would allow for simple, rapid modification of both the 2- and 5-positions of the heterocyclic ring system.

The use of 1-benzyl-5-bromotetrazole (**1**) as a starting material fulfilled all of the requirements discussed above for a facile and robust synthesis of tetrazole systems ready for further functionalization (Scheme 1c). Given our laboratory's previous efforts in the development of a tandem Suzuki-hydrogenation protocol in the synthesis of sp^3 -rich pharmaceutical building-blocks,¹⁶ we reasoned that the treatment of **1** to similar conditions would facilitate modification of the 5-position, while simultaneously unmasking the 2-position for derivatization using existing literature methodology.^{13c} Furthermore, **1** itself could be easily accessed on scale by alkylation and bromination of 1H-tetrazole, a commodity precursor, obviating the need for the hazardous synthesis of the heterocyclic constituent.



Scheme 1: a) The application of 2,5-tetrazoles as a nitrile imine source; b) Previous efforts towards the synthesis of functionalized tetrazoles; c) This work: the modular synthesis of 2,5-diaryl tetrazoles via a two-step tandem Pd and Cu catalysis approach.

Results and Discussion

The current study commenced with the investigation of the initial Suzuki coupling between **1** and aryl boronic acids. An initial literature search identified conditions reported by Yi in the coupling of similar substrates, using $\text{Pd}(\text{PPh}_3)_4$ as a catalyst.¹⁷ As the presence of the triphenylphosphine ligand has previously been shown to be detrimental in one-pot Suzuki-hydrogenation methodology,¹⁶ we sought to identify a suitable replacement Pd complex. Our optimization campaign began with the screening of six palladium precatalysts in combination with a number of different solvents and bases (Figure 1). XPhos Pd G3 was quickly identified as a potential alternative catalyst. When employed in conjunction with toluene, these reaction conditions afforded a substantially greater conversion than all other combinations examined.

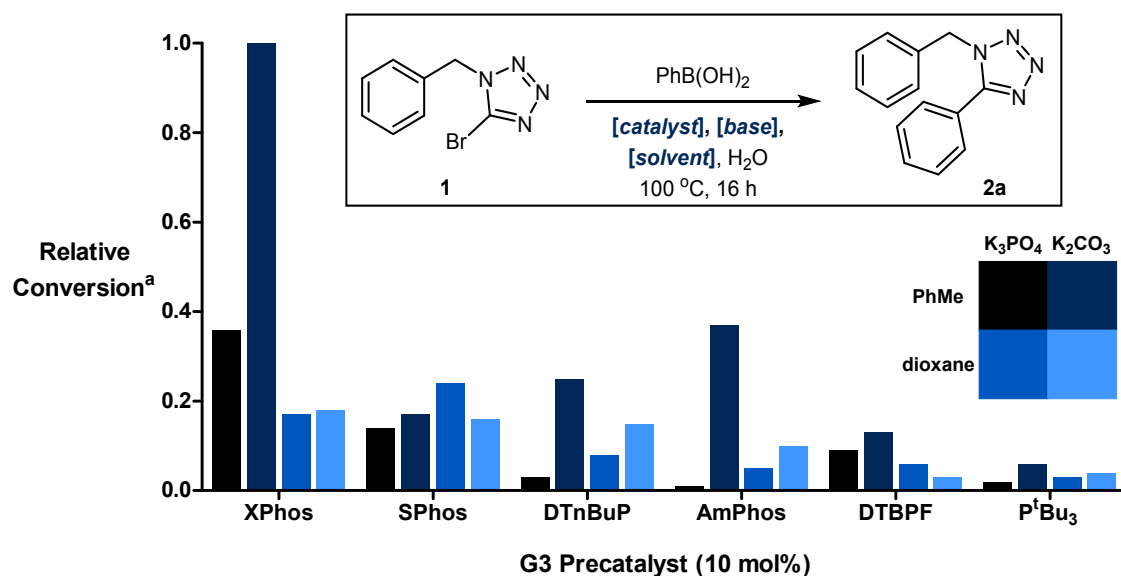
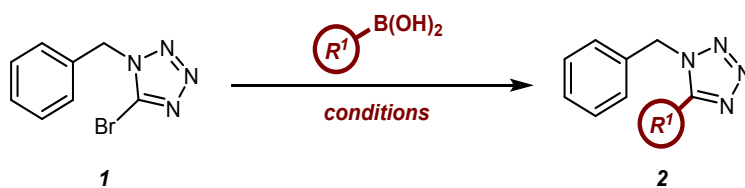


Figure 1: Initial catalyst screening identified XPhos Pd G3 as a suitable candidate for further study. ^aConversion was determined by HPLC with reference to an internal standard. All reactions were performed on a 2.5 μmol scale using 1.5 equiv. PhB(OH)₂, 2 equiv. of base and a 4:1 solvent:H₂O ratio (0.8 M).

Gratifyingly, a direct comparison between the previously reported conditions and this emerging approach furnished nearly identical yields (Table 1, entries 1 and 2). Furthermore, this was accomplished over a much shorter time frame of 3 hours, however the catalyst loading remained higher. Both electron-donating and mildly electron-deficient boronic acids were shown to be compatible substrates (Table 1, entries 3 and 4), however 4-cyanophenylboronic acid proved recalcitrant to product formation (Table 1, entry 5). In an effort to determine the compatibility of strongly electron-deficient boron species within the reaction manifold, a second screening effort was conducted, using an array of relevant variables selected based on the results of the initial screen (Figure 2). These results suggested that while the nitrile derivative remained intolerant to the reaction conditions, the improved performance of 4-(trifluoromethyl)-phenylboronic acid indicated that this issue was substrate-specific, rather than a consequence of electronic factors. Throughout this additional screen, XPhos was again shown to represent the most favorable precatalyst, while cesium was identified as the carbonate counterion.

Table 1: A direct comparison between established literature precedent and the newly identified reaction conditions.



Entry	R ¹	Conditions	Isolated Yield (%)
1 ^a	Ph	Pd(PPh ₃) ₄ (3 mol%), Na ₂ CO ₃ , PhMe, EtOH, H ₂ O, 110 °C, 16 h ¹⁷	75
2 ^b	Ph	XPhos Pd G3 (10 mol%), K ₂ CO ₃ , PhMe, H ₂ O, 100 °C, 3 h	76
3 ^b	4-(MeO)PhB(OH) ₂	as above	72
4 ^b	4-(F)PhB(OH) ₂	as above	60
5 ^b	4-(NC)PhB(OH) ₂	as above	trace

^aPerformed on a 1 mmol scale using 1.3 equiv. PhB(OH)₂, 2 equiv. Na₂CO₃ and 50 equiv. H₂O at a concentration of 0.1 M.

^bPerformed on a 0.25 mmol scale using 1.5 equiv. PhB(OH)₂, 2 equiv. K₂CO₃ and 100 equiv. H₂O at a concentration of 0.1 M.

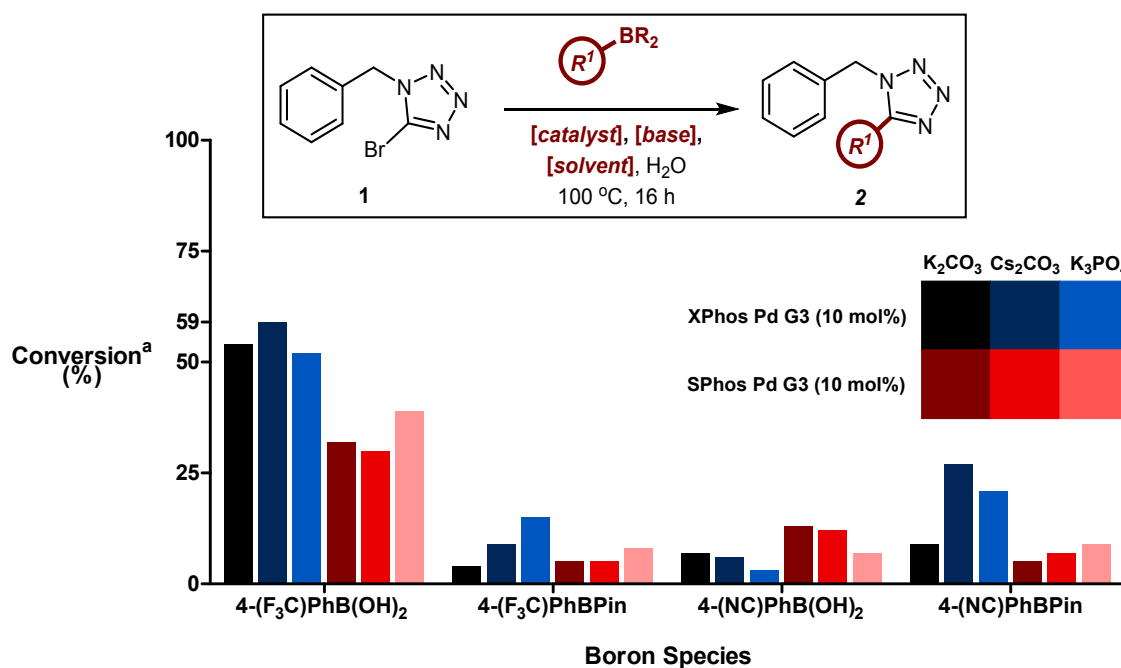
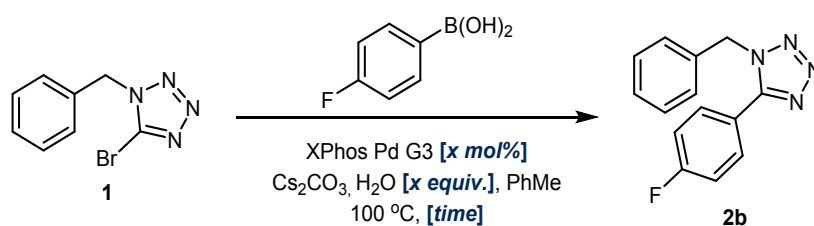


Figure 2: An additional screen of electron-deficient boron species indicated that some substrates were compatible with the conditions, while Cs₂CO₃ represented a minor improvement over K₂CO₃. ^aConversion was determined by LCMS with reference to caffeine as an internal standard. All reactions were performed on a 50 μmol scale using 1.5 equiv. PhB(OH)₂, 2 equiv. of base and 50 equiv. H₂O at a concentration of 0.1 M.

With optimal discrete variables in hand, we turned our attention to the catalyst loading. Preliminary efforts proved frustrating, with a significant decrease in yield observed upon reduction of catalyst loading (Table 2, entries 1 – 3). However, a concurrent Design of Experiments study^{18,19} highlighted an unanticipated correlation between the water stoichiometry of the reaction, relative to the overall concentration, and the observed conversion (Figure 3, see Supporting Information for full details). Exploiting this finding successfully furnished the optimized reaction conditions for the Suzuki component of the proposed process, with a catalyst loading of 3 mol% (Table 2, entries 4–9).

Table 2: Minimization of catalyst loading through manipulation of water stoichiometry^a



Entry	Catalyst Loading (mol%)	H ₂ O Stoichiometry (equiv.)	Time (h)	Conversion (%) ^b
1	10	10	16	52
2	5	10	16	47
3	2.5	10	16	14
4	10	100	4	70
5	5	100	4	71
6	4	100	4	70
7	3	100	4	71
8	2	100	4	66
9	1	100	4	38

^aReactions performed on a 50 μmol scale using 1.3 equiv. PhB(OH)₂ and 1.5 equiv. Cs₂CO₃ at a concentration of 0.1 M. ^bConversion was determined by LCMS with reference to caffeine as an internal standard.

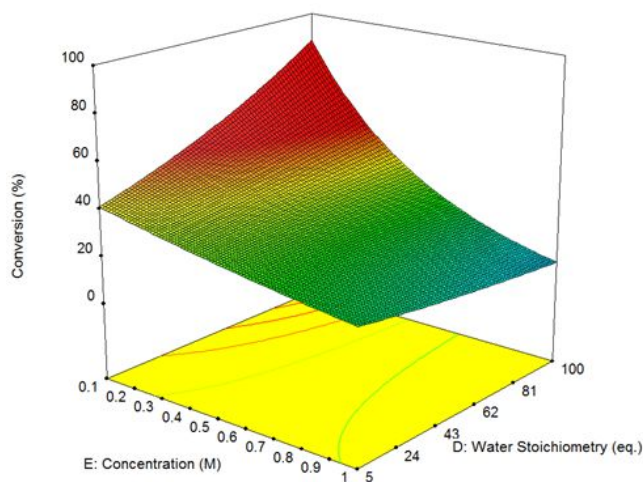


Figure 3: A response surface from the Design of Experiments study that revealed the importance of water stoichiometry to conversion, through a secondary correlation with overall reaction concentration. See the Supporting Information for full details.

Studies into the subsequent debenzylolation protocol proved to be more straightforward. A screen of eight Pd/C catalysts from three different sources afforded in many cases examples of quantitative conversion, with ethanol identified as an appropriate solvent (Figure 4). Further investigations highlighted Evonik’s Noblyst® P1071 Pd/C catalyst as a desirable option to mediate the transformation (see Supporting Information for further details). A final optimization found that a 2.5 mol% loading of catalyst facilitated quantitative conversion under only 4 bar of hydrogen gas (Table 3, entries 1-3). It was also determined that gentle heating of the reaction mixture to 40 °C was essential for enabling full conversion (Table 3, entry 4).

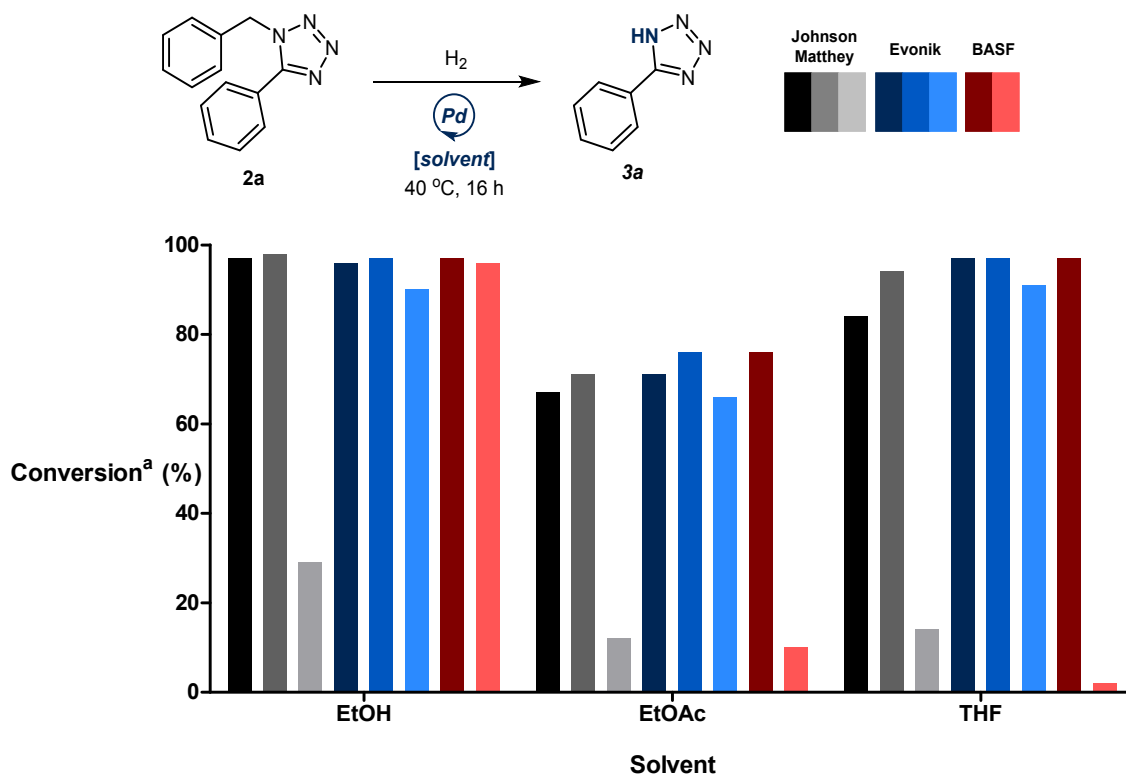


Figure 4: Preliminary screening of Pd/C catalysts generated a high degree of success ^aConversions reported as a percentage of the total peak area of **2a** and **3a**. All reactions were performed on a 63 μ mol scale using 6 bar of H₂ and 30 wt% of Pd/C at a concentration of 0.17 M.

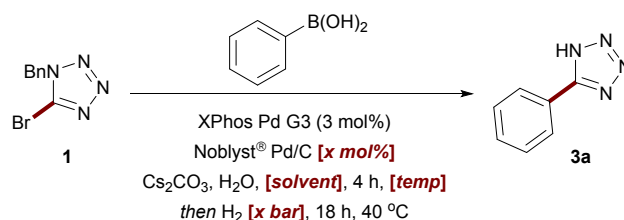
Table 3: Further optimization of hydrogenolysis conditions

Entry	H ₂ Pressure (bar)	Pd/C Loading (mol%)	Temperature (°C)	Conversion (%) ^d
1 ^a	6	7	40	97
2 ^b	4	5	40	98
3 ^b	4	2.5	40	99
4 ^c	4	2.5	rt	59

^aPerformed on a 63 μ mol scale at a concentration of 0.17 M. ^bPerformed on a 127 μ mol scale at a concentration of 0.17 M. ^cPerformed on a 0.3 mmol scale at a concentration of 0.1 M. ^dConversions were determined by LCMS with reference to caffeine as an internal standard.

Translation of this methodology into a one-pot procedure proved challenging, with preliminary attempts affording only moderate turnover. Gratifyingly, further reducing the pressure of hydrogen gas was found to increase this yield to synthetically useful levels (Table 4, entries 1 and 2). Consistent with our previous work,¹⁶ the catalyst ratio was found to be a crucial factor in maximizing product formation. While the isolated debenzoylation conditions required only a 2.5 mol% Pd/C loading, any reduction below 10% Pd/C significantly impacted conversion within the one-pot manifold (Table 4, entry 3). Attempts to circumvent the addition of ethanol as a co-solvent at the mid-point of the reaction also failed to furnish improved conversions (Table 4, entries 4 to 6). However, satisfactory conditions were identified with a total Pd catalyst loading of 13 mol%, furnishing a 65 % isolated yield of **3a** in 22 hours.

Table 4: Optimization of one-pot reaction conditions



Entry	H_2 Pressure (bar)	Pd/C Loading (mol%)	Solvent	Temperature (°C)	Conversion (%) ^b
1	4	10	PhMe ^c	100	43
2	2	10	PhMe^c	100	65 (65^d)
3	2	5	PhMe ^c	100	34
4	2	10	PhMe	100	24
5	2	10	4:1 PhMe: <i>n</i> BuOH	100	24
6	2	10	4:1 PhMe:EtOH	70	37

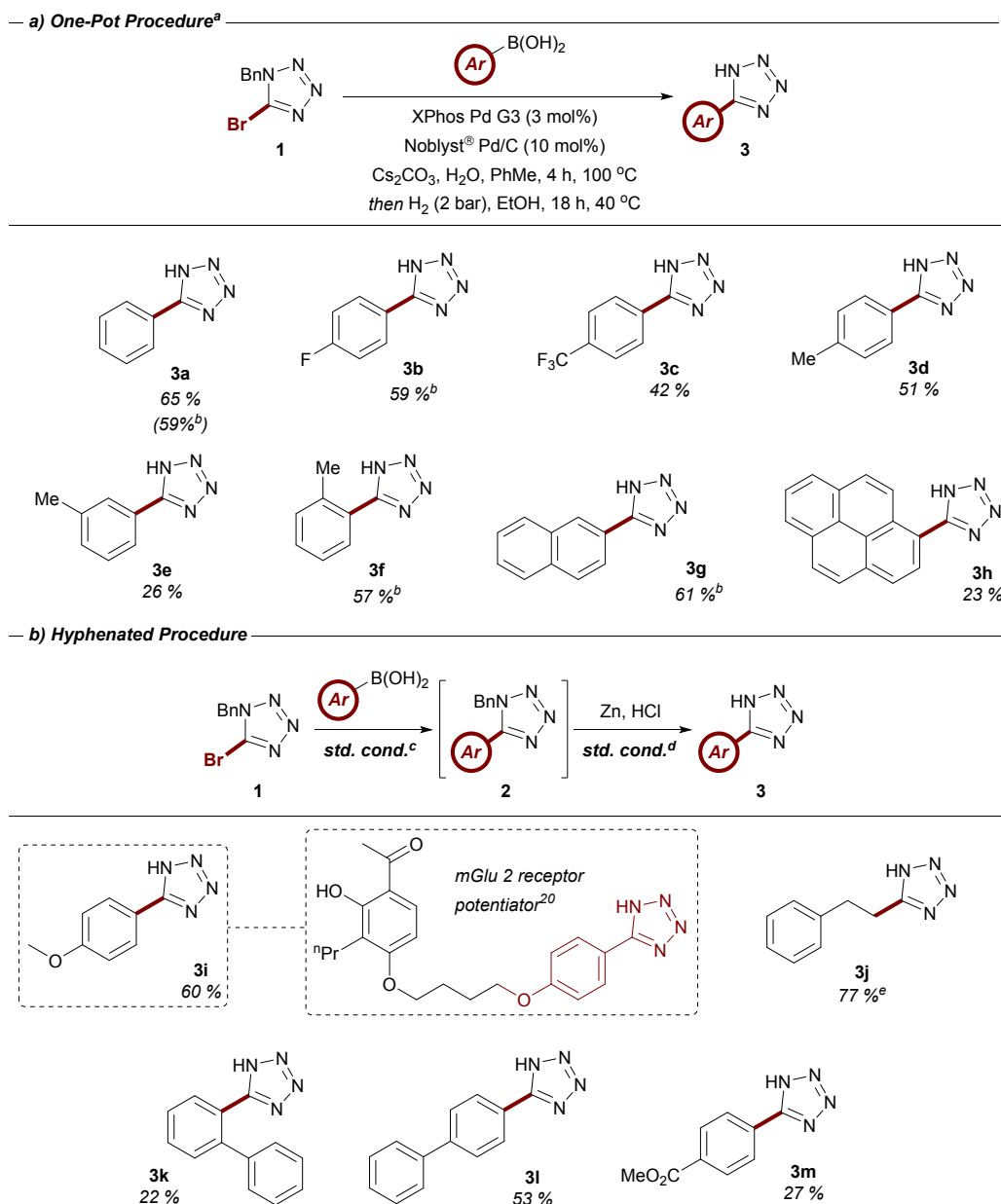
^aReactions performed on a 0.5 mmol scale using 1.3 equiv. PhB(OH)_2 , 1.5 equiv. Cs_2CO_3 and 100 equiv. H_2O at a concentration of 0.1 M. ^bConversions were determined by LCMS with reference to caffeine as an internal standard.

^cEtOH (2.5 mL) was added as a co-solvent prior to the hydrogenolysis step of the reaction. ^dIsolated yield.

With fully optimized reaction conditions in hand, we next sought to investigate the scope of this one-pot procedure with respect to the boronic acid substituent (*Table 5a*). Introduction of electronically deficient and neutral moieties were found to be well-tolerated, with minimal impact on yield (*cf.* **3b–3d**). Similarly, *meta* and *ortho*-substitution of the aryl component was found to be compatible (*cf.* **3e** and **3f**), although the reduced yield of the *meta* analogue **3e** remains more difficult to rationalize. More sterically encumbered substrates **3g** and **3h** were also successfully isolated. The modest yield associated with **3h** can likely be attributed to the increased size of the tetrazole hindering adsorption of the substrate onto the surface of the Pd/C catalyst. Reaction conditions were also found to be amenable to scale-up, with substrates **3a**, **3b**, **3f** and **3g** successfully synthesized in good yield on a 2.5 mmol scale.

While the one-pot generation of 5-aryl tetrazoles is preferable from a practical perspective, the yields of certain substrates were found to benefit from a directly related two-pot procedure (*Table 5b*). This approach enabled the robust synthesis of electron-rich analogue **3i**, a key pharmacophore of a reported allosteric potentiator of the metabotropic glutamate 2 receptor.²⁰ Vinyl boronic acids were also found to be compatible, with the synthesis of **3j** in good yield, providing access to alkyl tetrazole derivatives *via* a formal $\text{sp}^2\text{-sp}^3$ coupling. Biaryl substrates **3k** and **3l** represent examples of an important subset of nitrile imine precursors with extended π -systems, with a diminished yield in the case of the bulkier *ortho*-phenyl species. While low-yielding, methoxy-ester substrate **3m** provides a valuable functional handle for further derivatization. To exhibit the versatility of this procedure, the debenzoylation step of this scope exploited the *ex situ* generation of H_2 gas in a two-chambered reaction vessel known as COware,²¹ attaining the required pressure of H_2 without the need for more specialized apparatus.

Table 5: a) Exemplar scope of aryl boronic acids compatible with the one-pot Suzuki-hydrogenolysis coupling protocol; b) A library of boronic acids employed as part of the hyphenated two-pot synthesis of 5-aryl tetrazoles

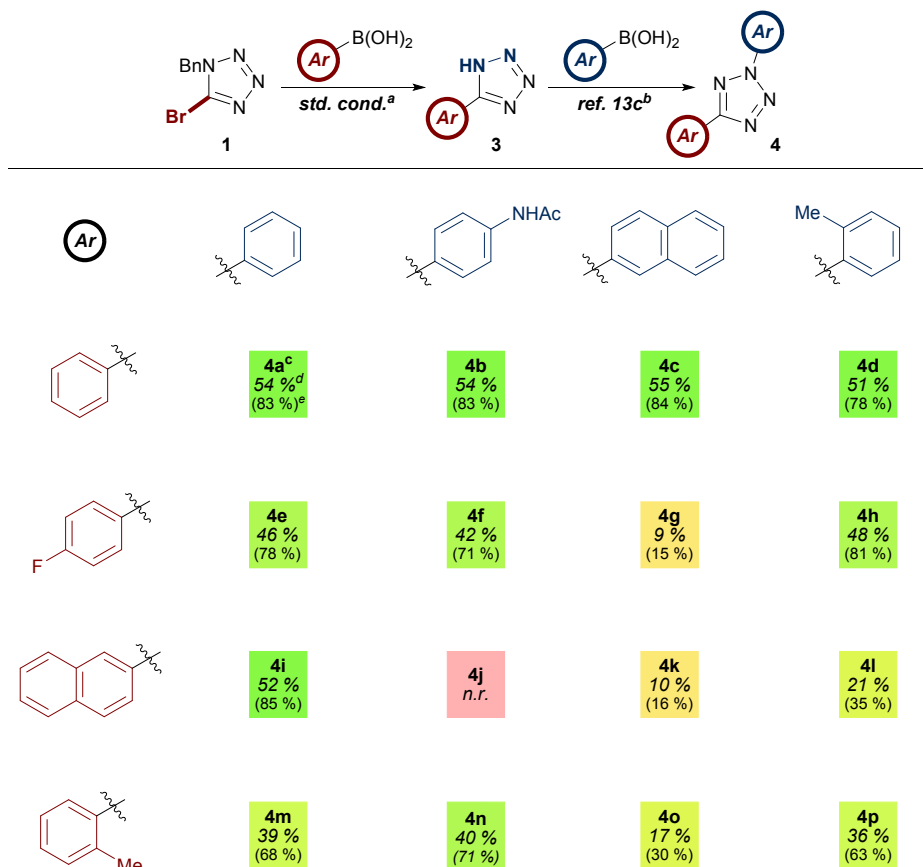


^aReactions performed on a 0.5 mmol scale using 1.3 equiv. boronic acid, 1.5 equiv. Cs_2CO_3 and 100 equiv. H_2O at a concentration of 0.1 M. ^b2.5 mmol scale. ^c1 equiv. **1**, 1.5 equiv. boronic acid, 2 equiv. Cs_2CO_3 , 3 mol% XPhos Pd G3 and 10 equiv. H_2O , heated at 100 °C in a solution of PhMe (0.2 M) for 2 hours. ^d1 equiv. **3** and 10 mol% Noblyst® Pd/C, heated at 40 °C in a solution of EtOH (0.1M) for 18 hours in the presence of 2 bar H_2 generated from Zn and HCl. ^eFrom (*E*)-styrylboronic acid.

To further exemplify the advantages afforded by this modular approach, we targeted the synthesis of a diverse matrix consisting of sixteen 2,5-diaryl tetrazoles (Table 6). *N*-aryl substituents were selected based upon their unique influence on the properties of the resulting heterocycle, such as the incorporation of a handle for further covalent modification (e.g. **4f**) or the manipulation of λ_{max} properties (e.g. **4k**). The current approach was found to be highly effective; with the synthesis of 15 of the 16 tetrazoles accomplished in good to excellent yields in conjunction with the established copper-mediated *N*-arylation protocol.^{13c} The practicality of this approach represents a significant advance over existing methods in the synthesis of a diverse library of nitrile imine precursors. One of the most beneficial aspects is the absence of time-consuming purification procedures. Owing to the acidic character of **3**, appropriate moderation of pH during reaction work-up afforded all 5-aryl-1*H*-tetrazoles at a sufficient level of purity for subsequent manipulation without the need for additional decontamination. Commencing from 5-bromotetrazole **1**, the synthesis of 2,5-tetrazoles **4a-p** required only one

chromatographic purification step prior to the isolation of the final product. The synthesis of tetrazole **4a** on a 6 mmol also demonstrated the scalability of the procedure, meaning that the entire route was shown to afford an overall yield of greater than 50 % on a multi-millimolar scale. The unexpected failure of substrate **4j** can be perhaps be attributed to a lower thermal stability of the tetrazole due to the enhanced push-pull system generated by the substituents.²²

Table 6: Synthesis of a matrix of 2,5-diaryl tetrazoles facilitated by novel Suzuki-hydrogenolysis methodology^a



^aReactions performed on a 0.5 mmol scale using the conditions described in *Table 5a*. ^bReactions performed on a 0.20-0.25 mmol scale. ^c*N*-arylation was also performed on a 6 mmol scale in an 88 % yield. ^dOverall yield. ^eYield of the individual *N*-arylation step.

Conclusions

In conclusion, we have developed a convenient and widely-applicable Suzuki-hydrogenolysis protocol enabling the expedient synthesis of 2,5-diaryl tetrazoles, valuable precursors of the nitrile imine 1,3-dipole. The scope of the reaction was shown to be tolerant of a range of steric and electronic parameters, and was further expanded through the accommodation of a hyphenated, two-pot procedure. Facile synthesis of a diverse palette of 2,5-tetrazoles in combination with existing Cu-catalyzed methodology has underlined the utility of this reaction, which offers a complementary means of accessing the 2,5-diaryl tetrazole scaffold in comparison to previous reports. We intend to further utilize this transformation in our continued investigations into the reactivity of the pleiotropic nitrile imine dipole.

Experimental Section

General Information

All reagents and solvents were obtained from commercial suppliers and were used without further purification unless otherwise stated. Purification was carried out according to standard laboratory methods. All reactions were conducted using round-bottom flasks or microwave vials of appropriate volume, unless otherwise stated. Reactions were carried out at elevated temperatures using a temperature-regulated hotplate/stirrer with a sand bath unless otherwise stated. Phase separation was conducted using IST Isolute Phase Separator Cartridges.

Flash chromatography was carried out manually using ZEOprep 60 HYD 40-63 μm silica gel, or using a Teledyne ISCO CombiFlash® RF+ apparatus with RediSep® silica cartridges.

Fourier Transformed Infra-Red (FTIR) spectra were obtained using a Perkin Elmer Spectrum One Fourier Transform spectrometer, with samples used neat. ^1H , ^{19}F and ^{13}C NMR spectra were obtained on a Bruker DRX 500, Bruker AVI, or Bruker Nano spectrometer at 400 or 500, 471 or 376, and 100 or 126 MHz, respectively. Chemical shifts are reported in ppm and coupling constants are reported in Hz with CDCl_3 referenced at 7.26 (^1H) and 77.16 ppm (^{13}C), and $\text{DMSO}-d_6$ referenced at 2.50 (^1H) and 39.52 ppm (^{13}C). Signal assignment of novel compounds was instructed using relevant 2D NMR experiments. High-resolution mass spectra were obtained on a Waters XEVO G2-XS QToF instrument (100 – 1200 AMU) in positive ionization mode. Reverse phase HPLC data was obtained using a Waters CSH C18 column. LCMS spectra were obtained using an Acquity UPLC CSH C18 column (50mm x 2.1mm i.d. 1.7 μm packing diameter) at 40 °C. The solvents employed were a 0.1 % v/v solution of formic acid in water, and a 0.1 % v/v solution of formic acid in acetonitrile. The UV detection was a summed signal from wavelengths 210 nm – 360 nm. Mass spectral data was acquired using a Waters QDA instrument (100-1000 AMU at 5 Hz) with an alternate-scan positive and negative electrospray ionization mode.

HPLC analysis was performed using a gradient method, eluting with 5 – 90% MeCN/ H_2O over 1 minute at a flow rate of 1 mL/min when employing standalone HPLC, and eluting with 3 – 98% MeCN/ H_2O (+ formic acid modifier) over 2 minutes at a flow rate of 1 mL/min when used in conjunction with MS. Reactions using an internal standard required prior HPLC calibration using samples containing varying molarities of product and caffeine, allowing calculation of the response factor by substituting values into *equation 1*. Screening reactions were then conducted using a known molarity of caffeine internal standard.

$$\text{Response Factor} = \frac{\left(\frac{\text{Area}}{\text{Molarity}}\right)_{\text{Product}}}{\left(\frac{\text{Area}}{\text{Molarity}}\right)_{\text{Standard}}} \quad \mathbf{1}$$

General Procedure for the Synthesis of Compounds **3a-3h**

To a 10 mL Biotage Endeavor reaction vessel was added Evonik Noblyst® P1071 20% palladium on carbon (10 mol%). 1-benzyl-5-bromo-1*H*-tetrazole (**1**, 1 equiv.), an aryl boronic acid (1.3 equiv.) and XPhos Pd G3 (3 mol%) were then added as a solution in toluene (0.1 M). To the resulting suspension was added cesium carbonate (1.5 equiv.) as a solution in water (100 equiv.), at which point the vessel was purged with nitrogen and stirred at 100 °C for 4 hours. Upon cooling to room temperature, ethanol (50 % volume of toluene) was added before the vessel was placed under a hydrogen atmosphere and heated at 40 °C for a further 18 hours. Upon reaction completion, the mixture was passed through celite and partitioned between ethyl acetate (30 mL) and water (30 mL). The organic phase was washed twice more with water (2 x 30 mL), before the aqueous phases were combined and acidified using 2M HCl solution (20 mL). The acidic aqueous phase was then washed three times with ethyl acetate (3 x 30 mL), before all organic layers were then combined, passed through a phase separator and concentrated under reduced pressure to yield the product.

General Procedure for the Synthesis of Compounds **3i-3m**

To a microwave vial containing 1-benzyl-5-bromo-1*H*-tetrazole (**1**, 1 equiv.), an aryl or vinyl boronic acid (1.5 equiv.) and XPhos Pd G3 (3 mol%) was added toluene (0.2 M). The vessel was purged with nitrogen, and cesium carbonate (2 equiv.) and water (10 equiv.) were added. The mixture was stirred at 100 °C for 2 hours, before being cooled to room temperature. The mixture was diluted with ethyl acetate (10 mL) and passed through a celite plug, which was then washed with a further portion of ethyl acetate (10 mL). The solution was concentrated under reduced pressure, and purified by column chromatography. Isolation of the intermediate 1-benzyl-5-aryltetrazole was confirmed by ^1H NMR spectroscopy, before the species was added to chamber A of a 2 x 10 mL COWare reaction vessel^{21a} as a solution in ethanol (0.1 M). Evonik Noblyst® P1071 20% palladium on carbon (10 mol%) was also added to chamber A, while chamber B was charged with zinc powder (1.8 mmol, 118 mg) and 36% hydrogen chloride solution (343 μL , 4 mmol). The vessel was sealed and stirred at 40 °C for 18 hours. The mixture was cooled to room temperature, diluted with ethyl acetate (10 mL) and passed through a celite plug, which was washed with a further portion of ethyl acetate (10 mL). This organic phase was washed twice with water (2 x 30 mL), before the aqueous phases were combined and acidified using 2M HCl solution (20 mL). The acidic aqueous phase was then washed three times with ethyl acetate (3 x 30 mL), before all organic layers were then combined, passed through a phase separator and concentrated under reduced pressure to yield the product.

General Procedure for the *N*-Arylation of 5-aryl tetrazoles

In accordance with previous literature precedent,^{13c} 5-aryl tetrazole (**3**, 1 equiv.), an aryl boronic acid (2 equiv.), copper (I) oxide (5 mol%), and DMSO (0.13 M) was added to a microwave vial. The reaction mixture was stirred under an oxygen atmosphere at 100 °C for 16 hours. The solution was cooled to room temperature and partitioned between ethyl acetate (20 mL) and 1M HCl solution (20 mL). The aqueous layer was backwashed with an additional portion of ethyl acetate (20 mL), before the combined organic layers were combined, washed with brine (40 mL), passed through a phase separator and concentrated under reduced pressure. The crude product was then purified by column chromatography.

Synthesis and Characterisation of Compounds **2-4**

1-benzyl-5-phenyl-1*H*-tetrazole (**2a**)

To a microwave vial containing 1-benzyl-5-bromo-1*H*-tetrazole (60 mg, 0.25 mmol), phenylboronic acid (45.7 mg, 0.38 mmol), and XPhos Pd G3 (21.2 mg, 0.025 mmol) was added toluene (2.0 mL). The vessel was purged with nitrogen, and potassium carbonate (69.1 mg, 0.5 mmol) was added as a solution in water (0.5 mL). The mixture was stirred at 100 °C for 3 hours, before being cooled to room temperature. The mixture was then diluted with ethyl acetate, passed through celite, and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (12 g silica cartridge, 0-100% EtOAc in hexane) to give 1-benzyl-5-phenyl-1*H*-tetrazole (45.2 mg, 0.19 mmol, 76 % yield) as a colorless oil.

¹H NMR (400 MHz, CDCl₃) δ 7.59 – 7.52 (m, 3H), 7.51 – 7.45 (m, 2H), 7.36 – 7.30 (m, 3H), 7.16 – 7.11 (m, 2H), 5.61 (s, 2H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 154.8, 134.0, 131.4, 129.3, 129.2, 128.9, 128.8, 127.3, 123.9, 51.5.

HRMS (ESI) *m/z*: [M+H]⁺ Calcd for C₁₄H₁₃N₄ 237.1140; Found 237.1142.

IR *v*_{max} (neat): 3065, 3033, 2937, 2857, 1529, 1497, 1458, 1401 cm⁻¹

Analytical data in agreement with the literature.¹⁷

1-benzyl-5-(4-fluorophenyl)-1*H*-tetrazole (**2b**)

To a microwave vial containing 1-benzyl-5-bromo-1*H*-tetrazole (60 mg, 0.25 mmol), (4-fluorophenyl)boronic acid (52.5 mg, 0.38 mmol), and XPhos Pd G3 (21.2 mg, 0.025 mmol) was added toluene (2.5 mL). The vessel was purged with nitrogen, and potassium carbonate (69.1 mg, 0.5 mmol) and water (0.045 mL, 2.50 mmol) were added. The mixture was stirred at 100 °C for 2 hours, before cooled to room temperature. The mixture was then diluted with ethyl acetate, passed through celite, and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (12 g silica cartridge, 0-100% EtOAc in hexane) to give 1-benzyl-5-(4-fluorophenyl)-1*H*-tetrazole (47.9 mg, 0.15 mmol, 60 % yield) as a colorless oil.

¹H NMR (400 MHz, CDCl₃) δ 7.61 – 7.54 (m, 2H), 7.37 – 7.31 (m, 3H), 7.21 – 7.09 (m, 4H), 5.61 (s, 2H).

¹⁹F NMR (376 MHz, CDCl₃) δ -107.44 – -107.60 (m).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 164.6 (d, ¹J_{C-F} = 253.2 Hz), 154.0, 133.9, 131.2 (d, ³J_{C-F} = 8.8 Hz), 129.4, 129.0, 127.2, 120.1 (d, ⁴J_{C-F} = 3.3 Hz), 116.7 (d, ²J_{C-F} = 22.2 Hz), 51.6.

HRMS (ESI) *m/z*: [M+H]⁺ Calcd for C₁₄H₁₂FN₄ 255.1046; Found 255.1051.

IR *v*_{max} (neat): 3070, 2964, 2932, 2857, 1606, 1539, 1473, 1450 cm⁻¹

Analytical data in agreement with the literature.¹⁷

1-benzyl-5-(4-(trifluoromethyl)phenyl)-1*H*-tetrazole (**2c**)

To a microwave vial containing 1-benzyl-5-bromo-1*H*-tetrazole (60 mg, 0.250 mmol), (4-(trifluoromethyl)phenyl)boronic acid (71.2 mg, 0.375 mmol), and XPhos Pd G3 (10.6 mg, 0.013 mmol) was added toluene (2.5 mL). The vessel was purged with nitrogen, and cesium carbonate (163 mg, 0.5 mmol) and water (0.450 mL, 25 mmol) were added. The mixture was stirred at 100 °C for 6 hours, before cooled to room temperature. The mixture was then diluted with ethyl acetate, passed through celite, and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (24 g silica cartridge, 0-100% EtOAc in hexane) to give 1-benzyl-5-(4-(trifluoromethyl)phenyl)-1*H*-tetrazole (43.3 mg, 0.14 mmol, 56 % yield) as a colorless oil.

¹H NMR (400 MHz, CDCl₃) δ 7.77 (d, *J* = 8.3 Hz, 2H), 7.72 (d, *J* = 8.2 Hz, 2H), 7.39 – 7.35 (m, 3H), 7.17 – 7.13 (m, 2H), 5.64 (s, 2H).

¹⁹F NMR (376 MHz, CDCl₃) δ -63.17 (s).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 153.7, 133.7, 133.4 (q, ²J_{C-F} = 33.1 Hz), 129.50, 129.45, 129.1, 127.6, 127.2, 126.3 (q, ³J_{C-F} = 3.5 Hz), 123.6 (q, ¹J_{C-F} = 272.6 Hz), 51.8.

HRMS (ESI) *m/z*: [M+H]⁺ Calcd for C₁₅H₁₂F₃N₄ 305.1014; Found 305.1018.

IR ν_{max} (neat): 3075, 3038, 2964, 1624, 1539, 1497, 1449, 1426 cm^{-1}

Analytical data in agreement with the literature.²³

1-benzyl-5-(4-methoxyphenyl)-1*H*-tetrazole (2i)

To a microwave vial containing 1-benzyl-5-bromo-1*H*-tetrazole (60 mg, 0.25 mmol), (4-methoxyphenyl)boronic acid (57.0 mg, 0.38 mmol), and XPhos Pd G3 (21.2 mg, 0.025 mmol) was added toluene (2.5 mL). The vessel was purged with nitrogen, and potassium carbonate (69.1 mg, 0.5 mmol) and water (0.045 mL, 2.50 mmol) were added. The mixture was stirred at 100 °C for 2 hours, before cooled to room temperature. The mixture was then diluted with ethyl acetate, passed through celite, and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (24 g silica cartridge, 0-100% EtOAc in hexane) to give 1-benzyl-5-(4-methoxyphenyl)-1*H*-tetrazole (48.3 mg, 0.18 mmol, 72 % yield) as a yellow oil.

¹H NMR (400 MHz, CDCl_3) δ 7.52 (d, J = 8.0 Hz, 2H), 7.34 – 7.32 (m, 3H), 7.15 – 7.13 (m, 2H), 6.98 (d, J = 8.0 Hz, 2H), 5.60 (s, 2H), 3.84 (s, 3H).

¹³C{¹H} NMR (101 MHz, CDCl_3) δ 162.0, 154.6, 134.2, 130.5, 129.3, 128.8, 127.2, 115.9, 114.8, 55.6, 51.4.

HRMS (ESI) m/z : [$\text{M}+\text{H}$]⁺ Calcd for $\text{C}_{15}\text{H}_{15}\text{ON}_4$ 267.1246; Found 267.1250.

IR ν_{max} (neat): 3081, 3027, 3006, 2958, 2937, 2841, 1611, 1581, 1477, 1446 cm^{-1}

Analytical data in agreement with the literature.²³

5-phenyl-1*H*-tetrazole (3a)

Synthesized in accordance with the general procedure using 1-benzyl-5-bromo-1*H*-tetrazole (120 mg, 0.5 mmol), phenylboronic acid (79 mg, 0.65 mmol), XPhos Pd G3 (12.7 mg, 15 μmol), Evonik P1071 Pd/C (53.2 mg, 50 μmol), cesium carbonate (244 mg, 0.75 mmol), water (901 μL , 50 mmol), toluene (5 mL) and ethanol (2.5 mL) to yield 5-phenyl-1*H*-tetrazole (47.7 mg, 0.32 mmol, 65 % yield) as a white solid.

Synthesized in accordance with the general procedure using 1-benzyl-5-bromo-1*H*-tetrazole (598 mg, 2.5 mmol), phenylboronic acid (396 mg, 3.25 mmol), XPhos Pd G3 (63.5 mg, 75 μmol), Evonik P1071 Pd/C (266 mg, 250 μmol), cesium carbonate (1220 mg, 3.75 mmol), water (4.50 mL, 250 mmol), toluene (25 mL) and ethanol (12.5 mL) to yield 5-phenyl-1*H*-tetrazole (216 mg, 1.48 mmol, 59 % yield) as a white solid.

¹H NMR (400 MHz, DMSO) δ 16.84 (br. s, 1H), 8.07 – 8.01 (m, 2H), 7.64 – 7.56 (m, 3H).

¹³C{¹H} NMR (101 MHz, DMSO) δ 155.3, 131.2, 129.4, 126.9, 124.1.

HRMS (ESI) m/z : [$\text{M}+\text{H}$]⁺ Calcd for $\text{C}_7\text{H}_7\text{N}_4$ 147.0671; Found 147.0671.

IR ν_{max} (neat): 3054, 2974, 2911, 2834, 1652, 1608, 1563, 1485, 1465, 1409 cm^{-1} .

Analytical data in agreement with the literature.²⁴

5-(4-fluorophenyl)-1*H*-tetrazole (3b)

Synthesized in accordance with the general procedure using 1-benzyl-5-bromo-1*H*-tetrazole (598 mg, 2.5 mmol), 4-fluorophenylboronic acid (455 mg, 3.25 mmol), XPhos Pd G3 (63.5 mg, 75 μmol), Evonik P1071 Pd/C (266 mg, 250 μmol), cesium carbonate (1220 mg, 3.75 mmol), water (4.50 mL, 250 mmol), toluene (25 mL) and ethanol (12.5 mL) to yield 5-(4-fluorophenyl)-1*H*-tetrazole (245 mg, 1.48 mmol, 59 % yield) as a white solid.

¹H NMR (400 MHz, DMSO) δ 16.84 (br. s, 1H), 8.13 – 8.06 (m, 2H), 7.46 (app. t, J = 8.9 Hz, 2H).

¹⁹F{¹H} NMR (376 MHz, DMSO) δ -108.98 (s).

¹³C{¹H} NMR (101 MHz, DMSO) δ 163.6 (d, $^1J_{\text{C-F}}$ = 249.0 Hz), 154.8, 129.4 (d, $^3J_{\text{C-F}}$ = 9.0 Hz), 120.9, 116.5 (d, $^2J_{\text{C-F}}$ = 22.3 Hz).

HRMS (ESI) m/z : [$\text{M}+\text{H}$]⁺ Calcd for $\text{C}_7\text{H}_6\text{FN}_4$ 165.0576; Found 165.0579.

IR ν_{max} (neat): 3070, 2985, 2916, 2841, 1609, 1498, 1446, 1410 cm^{-1}

Analytical data in agreement with the literature.²⁵

5-(4-(trifluoromethyl)phenyl)-1*H*-tetrazole (3c)

Synthesized in accordance with the general procedure using 1-benzyl-5-bromo-1*H*-tetrazole (120 mg, 0.5 mmol), (4-(trifluoromethyl)phenyl)boronic acid (123 mg, 0.65 mmol), XPhos Pd G3 (12.7 mg, 15 μmol), Evonik P1071 Pd/C (53.2 mg, 50 μmol), cesium carbonate (244 mg, 0.75 mmol), water (901 μL , 50 mmol), toluene (5 mL) and ethanol (2.5 mL) to yield 5-(4-(trifluoromethyl)phenyl)-1*H*-tetrazole (47.1 mg, 0.21 mmol, 42 % yield) as a white solid.

¹H NMR (400 MHz, DMSO) δ 17.08 (br. s, 1H), 8.26 (d, J = 7.9 Hz, 2H), 7.98 (d, J = 7.9 Hz, 2H).

¹⁹F{¹H} NMR (376 MHz, DMSO) δ -61.53 (s).

¹³C{¹H} NMR (101 MHz, DMSO) δ 155.3, 130.9 (q, $^2J_{\text{C-F}}$ = 32.1 Hz), 128.4, 127.7, 126.3, 123.8 (q, $^1J_{\text{C-F}}$ = 271.0 Hz)

HRMS (ESI) m/z : [$\text{M}+\text{H}$]⁺ Calcd for $\text{C}_8\text{H}_6\text{F}_3\text{N}_4$ 215.0545; Found 215.0547.

IR ν_{\max} (neat): 3070, 2990, 2916, 2852, 1682, 1573, 1506, 1441 cm^{-1}

Analytical data in agreement with the literature.²⁴

5-(*p*-tolyl)-1*H*-tetrazole (3d)

Synthesized in accordance with the general procedure using 1-benzyl-5-bromo-1*H*-tetrazole (120 mg, 0.5 mmol), *p*-tolylboronic acid (88 mg, 0.65 mmol), XPhos Pd G3 (12.7 mg, 15 μmol), Evonik P1071 Pd/C (53.2 mg, 50 μmol), cesium carbonate (244 mg, 0.75 mmol), water (901 μL , 50 mmol), toluene (5 mL) and ethanol (2.5 mL) to yield 5-(*p*-tolyl)-1*H*-tetrazole (41.2 mg, 0.26 mmol, 51 % yield) as a white solid.

^1H NMR (400 MHz, DMSO) δ 16.71 (br. s, 1H), 7.96 – 7.90 (m, 2H), 7.45 – 7.39 (m, 2H), 2.39 (s, 3H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, DMSO) δ 141.1, 129.9, 126.8, 121.3, 21.0, 1C not observed.

HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_8\text{H}_9\text{N}_4$ 161.0827; Found 161.0828.

IR ν_{\max} (neat): 3043, 2964, 2917, 2848, 1612, 1570, 1504, 1432, 1404 cm^{-1}

Analytical data in agreement with the literature.²⁴

5-(*m*-tolyl)-1*H*-tetrazole (3e)

Synthesized in accordance with the general procedure using 1-benzyl-5-bromo-1*H*-tetrazole (120 mg, 0.5 mmol), *m*-tolylboronic acid (88 mg, 0.65 mmol), XPhos Pd G3 (12.7 mg, 15 μmol), Evonik P1071 Pd/C (53.2 mg, 50 μmol), cesium carbonate (244 mg, 0.75 mmol), water (901 μL , 50 mmol), toluene (5 mL) and ethanol (2.5 mL) to yield 5-(*m*-tolyl)-1*H*-tetrazole (21.3 mg, 0.13 mmol, 26 % yield) as a white solid.

^1H NMR (400 MHz, DMSO) δ 16.77 (br. s, 1H), 7.87 (s, 1H), 7.83 (d, $J = 7.6$ Hz, 1H), 7.48 (t, $J = 7.6$ Hz, 1H), 7.40 (d, $J = 7.6$ Hz, 1H), 2.41 (s, 3H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, DMSO) δ 155.3, 138.8, 131.8, 129.3, 127.4, 124.1, 20.9, 1C not observed.

HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_8\text{H}_9\text{N}_4$ 161.0827; Found 161.0828.

IR ν_{\max} (neat): 3065, 2980, 2918, 2847, 1651, 1599, 1560, 1485, 1456, 1415, 1400, cm^{-1}

Analytical data in agreement with the literature.²⁶

5-(*o*-tolyl)-1*H*-tetrazole (3f)

Synthesized in accordance with the general procedure using 1-benzyl-5-bromo-1*H*-tetrazole (598 mg, 2.5 mmol), *o*-tolylboronic acid (442 mg, 3.25 mmol), XPhos Pd G3 (63.5 mg, 75 μmol), Evonik P1071 Pd/C (266 mg, 250 μmol), cesium carbonate (1222 mg, 3.75 mmol), water (4.5 mL, 250 mmol), toluene (25 mL) and ethanol (12.5 mL) to yield 5-(*o*-tolyl)-1*H*-tetrazole (229 mg, 1.41 mmol, 57 % yield) as a white solid.

^1H NMR (400 MHz, DMSO) δ 16.63 (br. s, 1H), 7.69 (d, $J = 7.6$ Hz, 1H), 7.52 – 7.36 (m, 3H), 2.48 (s, 3H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, DMSO) δ 155.2, 137.1, 131.3, 130.7, 129.3, 126.2, 123.8, 20.4.

HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_8\text{H}_9\text{N}_4$ 161.0827; Found 161.0827.

IR ν_{\max} (neat): 3065, 3027, 2964, 2921, 2847, 2714, 1654, 1606, 1561, 1484, 1464, 1404 cm^{-1}

Analytical data in agreement with the literature.²⁴

5-(naphthalen-2-yl)-1*H*-tetrazole (3g)

Synthesized in accordance with the general procedure using 1-benzyl-5-bromo-1*H*-tetrazole (598 mg, 2.5 mmol), naphthalen-2-ylboronic acid (559 mg, 3.25 mmol), XPhos Pd G3 (63.5 mg, 75 μmol), Evonik P1071 Pd/C (266 mg, 250 μmol), cesium carbonate (1222 mg, 3.75 mmol), water (4.50 mL, 50 mmol), toluene (25 mL) and ethanol (12.5 mL) to yield 5-(naphthalen-2-yl)-1*H*-tetrazole (331 mg, 1.53 mmol, 61 % yield) as a white solid.

^1H NMR (400 MHz, DMSO) δ 16.96 (br. s, 1H), 8.66 (d, $J = 0.8$ Hz, 1H), 8.17 – 8.07 (m, 3H), 8.05 – 8.01 (m, 1H), 7.69 – 7.61 (m, 2H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, DMSO) δ 133.9, 132.6, 129.2, 128.6, 127.8, 127.8, 127.2, 126.9, 123.6, 121.6, 1C not observed

HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{11}\text{H}_9\text{N}_4$ 197.0827; Found 197.0831.

IR ν_{\max} (neat): 3128, 3059, 2990, 2921, 2889, 2841, 1635, 1609, 1564, 1510, 1417 cm^{-1}

Analytical data in agreement with the literature.²⁴

5-(pyren-1-yl)-1*H*-tetrazole (3h)

Synthesized in accordance with the general procedure using 1-benzyl-5-bromo-1*H*-tetrazole (120 mg, 0.5 mmol), pyren-1-ylboronic acid (160 mg, 0.65 mmol), XPhos Pd G3 (12.7 mg, 15 μmol), Evonik P1071 Pd/C (53.2 mg, 50 μmol), cesium carbonate (244 mg, 0.75 mmol), water (901 μL , 50 mmol), toluene (5 mL) and ethanol (2.5 mL) to yield 5-(pyren-1-yl)-1*H*-tetrazole (37.6 mg, 0.11 mmol, 23 % yield) as a white solid.

¹H NMR (400 MHz, DMSO) δ 17.12 (br. s, 1H), 8.95 (d, J = 9.3 Hz, 1H), 8.49 (s, 2H), 8.44 (d, J = 2.9 Hz, 1H), 8.42 (d, J = 2.9 Hz, 1H), 8.39 (d, J = 9.4 Hz, 1H), 8.36 (d, J = 8.9 Hz, 1H), 8.30 (d, J = 8.9 Hz, 1H), 8.21 – 8.15 (m, 1H).

¹³C{¹H} NMR (101 MHz, DMSO) δ 132.5, 130.7, 130.1, 129.2, 129.1, 128.8, 128.5, 128.1, 127.3, 127.2, 126.9, 126.4, 126.1, 125.0, 124.2, 124.0, 123.4.

HRMS (ESI) m/z : [M+H]⁺ Calcd for C₁₇H₁₁N₄ 271.0984; Found 271.0988.

IR ν_{\max} (neat): 3022, 2921, 2847, 1577, 1454, 1421 cm⁻¹

Analytical data in agreement with the literature.²⁷

5-(4-methoxyphenyl)-1H-tetrazole (3i)

Synthesized in accordance with the general procedure using 1-benzyl-5-bromo-1H-tetrazole (120 mg, 0.5 mmol), 4-methoxyphenylboronic acid (114 mg, 0.75 mmol), XPhos Pd G3 (12.7 mg, 15 μ mol), cesium carbonate (326 mg, 1.0 mmol), water (90 μ L, 5.0 mmol), toluene (2.5 mL), Evonik P1071 Pd/C (36.3 mg, 34 μ mol), and ethanol (2.5 mL) to yield 5-(4-methoxyphenyl)-1H-tetrazole (49.4 mg, 0.28 mmol, 60 % yield) as a white solid.

¹H NMR (400 MHz, DMSO) δ 7.98 (d, J = 8.9 Hz, 2H), 7.16 (d, J = 8.9 Hz, 2H), 3.84 (s, 3H) 1H not observed (exchangeable).

¹³C{¹H} NMR (101 MHz, DMSO) δ 161.4, 128.6, 127.0, 116.3, 114.8, 55.4.

HRMS (ESI) m/z : [M+H]⁺ Calcd for C₈H₉ON₄ 177.0776; Found 177.0770.

IR ν_{\max} (neat): 3160, 3081, 3022, 2919, 2843, 1610, 1585, 1499, 1470, 1443, 1405 cm⁻¹

Analytical data in agreement with the literature.²⁴

5-phenethyl-1H-tetrazole (3j)

Synthesized in accordance with the general procedure using 1-benzyl-5-bromo-1H-tetrazole (120 mg, 0.5 mmol), (*E*)-styrylboronic acid (111 mg, 0.75 mmol), XPhos Pd G3 (12.7 mg, 15 μ mol), cesium carbonate (326 mg, 1.0 mmol), water (90 μ L, 5.0 mmol), toluene (2.5 mL), Evonik P1071 Pd/C (29.6 mg, 28 μ mol), and ethanol (2.5 mL) to yield 5-phenethyl-1H-tetrazole (48.9 mg, 0.28 mmol, 77 % yield) as a white solid.

¹H NMR (500 MHz, DMSO) δ 11.07 (br. s, 1H), 7.28 – 7.35 (m, 2H), 7.23 – 7.15 (m, 3H), 3.18 (t, J = 7.8 Hz, 2H), 3.06 (t, J = 7.7 Hz, 2H).

¹³C{¹H} NMR (126 MHz, DMSO) δ 155.4, 140.0, 128.4, 128.3, 126.3, 32.7, 24.6.

HRMS (ESI) m/z : [M+H]⁺ Calcd for C₉H₁₁N₄ 175.0984; Found 175.0977.

IR ν_{\max} (neat): 3030, 3007, 2992, 2972, 2922, 2857, 1560, 1491, 1454, 1425, 1408 cm⁻¹

Analytical data in agreement with the literature.²⁸

5-([1,1'-biphenyl]-2-yl)-1H-tetrazole (3k)

Synthesized in accordance with the general procedure using 1-benzyl-5-bromo-1H-tetrazole (120 mg, 0.5 mmol), [1,1'-biphenyl]-2-ylboronic acid (150 mg, 0.75 mmol), XPhos Pd G3 (12.7 mg, 15 μ mol), cesium carbonate (326 mg, 1.0 mmol), water (90 μ L, 5.0 mmol), toluene (2.5 mL), Evonik P1071 Pd/C (36.3 mg, 34 μ mol), and ethanol (2.5 mL) to yield 5-([1,1'-biphenyl]-2-yl)-1H-tetrazole (24.1 mg, 0.11 mmol, 22 % yield) as a white solid. Column chromatography (0-100% ethyl acetate in petroleum ether) following the hydrogenolysis step was required for this substrate.

¹H NMR (400 MHz, DMSO) δ 7.72 – 7.65 (m, 2H), 7.61 – 7.54 (m, 2H), 7.34 – 7.28 (m, 3H), 7.12 – 7.07 (m, 2H) 1H not observed (exchangeable).

¹³C{¹H} NMR (101 MHz, DMSO) δ 141.5, 139.2, 131.1, 130.6, 128.7, 128.2, 127.7, 127.4, 123.4, 2C not observed.

HRMS (ESI) m/z : [M+H]⁺ Calcd for C₁₃H₁₁N₄ 223.0978; Found 223.0979.

IR ν_{\max} (neat): 3059, 2963, 2918, 2886, 2845, 2822, 1601, 1572, 1560, 1477, 1454, 1437 cm⁻¹

Analytical data in agreement with the literature.²⁸

5-([1,1'-biphenyl]-4-yl)-1H-tetrazole (3l)

Synthesized in accordance with the general procedure using 1-benzyl-5-bromo-1H-tetrazole (120 mg, 0.5 mmol), [1,1'-biphenyl]-4-ylboronic acid (150 mg, 0.75 mmol), XPhos Pd G3 (12.7 mg, 15 μ mol), cesium carbonate (326 mg, 1.0 mmol), water (90 μ L, 5.0 mmol), toluene (2.5 mL), Evonik P1071 Pd/C (27.3 mg, 26 μ mol), and ethanol (2.5 mL) to yield 5-([1,1'-biphenyl]-4-yl)-1H-tetrazole (56.7 mg, 0.26 mmol, 53 % yield) as a white solid.

¹H NMR (500 MHz, DMSO) δ 8.15 (d, J = 8.3 Hz, 2H), 7.91 (d, J = 8.3 Hz, 2H), 7.76 (d, J = 7.5 Hz, 2H), 7.50 (app. t, J = 7.6 Hz, 2H), 7.43 – 7.40 (m, 1H).

¹³C{¹H} NMR (126 MHz, DMSO) δ 155.0, 151.0, 142.7, 138.9, 129.1, 128.2, 127.6, 126.8, 123.1.

HRMS (ESI) m/z : [M+H]⁺ Calcd for C₁₃H₁₁N₄ 223.0978; Found 223.0979.

IR ν_{\max} (neat): 3092, 3059, 3003, 2982, 2922, 2851, 1614, 1560, 1522, 1501, 1483, 1452, 1425 cm⁻¹

Analytical data in agreement with the literature.²⁴

Methyl 4-(1*H*-tetrazol-5-yl)benzoate (3m)

Synthesized in accordance with the general procedure using 1-benzyl-5-bromo-1*H*-tetrazole (120 mg, 0.5 mmol), (4-(methoxycarbonyl)phenyl)boronic acid (135 mg, 0.75 mmol), XPhos Pd G3 (12.7 mg, 15 μ mol), cesium carbonate (326 mg, 1.0 mmol), water (90 μ L, 5.0 mmol), toluene (2.5 mL), Evonik P1071 Pd/C (10.6 mg, 10 μ mol), and ethanol (1.5 mL) to yield methyl 4-(1*H*-tetrazol-5-yl)benzoate (20.3 mg, 0.10 mmol, 27 % yield) as a yellow solid.

¹H NMR (400 MHz, DMSO) δ 8.19 (d, *J* = 8.6 Hz, 2H), 8.15 (d, *J* = 8.7 Hz, 2H), 3.89 (s, 3H).

¹³C{¹H} NMR (101 MHz, DMSO) δ 165.6, 155.7, 145.3, 131.5, 130.1, 127.2, 52.4.

HRMS (ESI) *m/z*: [M+H]⁺ Calcd for C₉H₉N₄O₂ 205.0720; Found 205.0720.

IR ν_{\max} (neat): 3154, 3098, 3073, 3046, 3019, 2953, 2928, 2855, 1709, 1686, 1566, 1499, 1427 cm⁻¹

Analytical data in agreement with the literature.²⁸

2,5-diphenyl-2*H*-tetrazole (4a)

Synthesized in accordance with the general procedure using tetrazole **3a** (29 mg, 0.2 mmol), phenylboronic acid (49 mg, 0.4 mmol), copper(I) oxide (1.4 mg, 10 μ mol) and DMSO (2 mL) to yield 2,5-diphenyl-2*H*-tetrazole (36.7 mg, 0.17 mmol, 83 % yield) as a white solid.

Synthesized in accordance with the general procedure using tetrazole **3a** (877 mg, 6.0 mmol), phenylboronic acid (1.5 g, 12 mmol), copper(I) oxide (43 mg, 0.3 mmol) and DMSO (10 mL) to yield 2,5-diphenyl-2*H*-tetrazole (1.2 g, 5.3 mmol, 88 % yield) as a white solid.

¹H NMR (400 MHz, CDCl₃) δ 8.30 – 8.24 (m, 2H), 8.24 – 8.18 (m, 2H), 7.62 – 7.47 (m, 6H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 165.4, 137.1, 130.7, 129.8, 129.8, 129.1, 127.3, 127.2, 120.0.

HRMS (ESI) *m/z*: [M+H]⁺ Calcd for C₁₃H₁₂N₄ 223.0984; Found 223.0986.

IR ν_{\max} (neat): 3066, 1595, 1530, 1497, 1470, 1447 cm⁻¹

Analytical data in agreement with the literature.²⁹

N-(4-(5-phenyl-2*H*-tetrazol-2-yl)phenyl)acetamide (4b)

Synthesized in accordance with the general procedure using tetrazole **3a** (29 mg, 0.2 mmol), (4-acetamidophenyl)boronic acid (72 mg, 0.4 mmol), copper(I) oxide (1.4 mg, 10 μ mol) and DMSO (2 mL) to yield *N*-(4-(5-phenyl-2*H*-tetrazol-2-yl)phenyl)acetamide (49.7 mg, 0.18 mmol, 83 % yield) as a brown solid.

¹H NMR (400 MHz, DMSO) δ 10.32 (s, 1H), 8.18 – 8.13 (m, 2H), 8.09 (d, *J* = 9.0 Hz, 2H), 7.88 (d, *J* = 9.0 Hz, 2H), 7.63 – 7.58 (m, 3H), 2.11 (s, 3H).

¹³C{¹H} NMR (101 MHz, MeOD) δ 162.4, 156.8, 132.3, 124.3, 122.3, 120.7, 118.9, 118.4, 112.1, 112.0, 14.5.

HRMS (ESI) *m/z*: [M+H]⁺ Calcd for C₁₅H₁₄N₅O 280.1193; Found 280.1196.

IR ν_{\max} (neat): 3265, 3144, 3073, 2961, 2926, 1667, 1605, 1557, 1531, 1510, 1468, 1452, 1418 cm⁻¹

Analytical data in agreement with the literature.²⁹

2-(naphthalen-2-yl)-5-phenyl-2*H*-tetrazole (4c)

Synthesized in accordance with the general procedure using tetrazole **3a** (29 mg, 0.2 mmol), 2-naphthylboronic acid (69 mg, 0.4 mmol), copper(I) oxide (1.4 mg, 10 μ mol) and DMSO (2 mL) to yield 2-(naphthalen-2-yl)-5-phenyl-2*H*-tetrazole (46 mg, 0.17 mmol, 84 % yield) as a yellow solid.

¹H NMR (400 MHz, CDCl₃) δ 8.65 (d, *J* = 2.0 Hz, 1H), 8.34 – 8.28 (m, 3H), 8.02 (d, *J* = 8.9 Hz, 1H), 7.98 (dd, *J* = 6.5, 2.7 Hz, 1H), 7.91 (dd, *J* = 6.3, 2.9 Hz, 1H), 7.62 – 7.48 (m, 5H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 165.4, 134.4, 133.5, 133.2, 130.7, 130.0, 129.1, 128.8, 128.1, 127.6, 127.5, 127.3, 127.2, 118.3, 118.0.

HRMS (ESI) *m/z*: [M+H]⁺ Calcd for C₁₇H₁₃N₄ 273.1140; Found 273.1143.

IR ν_{\max} (neat): 3067, 3051, 2922, 1599, 1514, 1495, 1472, 1449 cm⁻¹

5-phenyl-2-(*o*-tolyl)-2*H*-tetrazole (4d)

Synthesized in accordance with the general procedure using tetrazole **3a** (29 mg, 0.2 mmol), *o*-tolylboronic acid (54 mg, 0.4 mmol), copper(I) oxide (1.4 mg, 10 μ mol) and DMSO (2 mL) to yield 5-phenyl-2-(*o*-tolyl)-2*H*-tetrazole (37 mg, 0.16 mmol, 78 % yield) as an off-white solid.

¹H NMR (400 MHz, CDCl₃) δ 8.29 – 8.22 (m, 2H), 7.70 – 7.65 (m, 1H), 7.57 – 7.49 (m, 3H), 7.48 – 7.38 (m, 3H), 2.44 (s, 3H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 165.1, 136.7, 133.3, 132.1, 130.7, 130.5, 129.1, 127.4, 127.2, 127.1, 125.4, 18.9.

HRMS (ESI) m/z : $[M+H]^+$ Calcd for $C_{14}H_{13}N_4$ 237.1140; Found 237.1141.

IR ν_{\max} (neat): 3051, 2959, 2920, 2853, 1585, 1530, 1497, 1468, 1450 cm^{-1}

Analytical data in agreement with the literature.^{13c}

5-(4-fluorophenyl)-2-phenyl-2H-tetrazole (4e)

Synthesized in accordance with the general procedure using tetrazole **3b** (39 mg, 0.24 mmol), phenylboronic acid (49 mg, 0.48 mmol), copper(I) oxide (1.7 mg, 12 μmol) and DMSO (2 mL) to yield 5-(4-fluorophenyl)-2-phenyl-2H-tetrazole (45 mg, 0.19 mmol, 78 % yield) as a white solid.

^1H NMR (400 MHz, CDCl_3) δ 8.28 – 8.21 (m, 2H), 8.20 – 8.15 (m, 2H), 7.61 – 7.54 (m, 2H), 7.53 – 7.47 (m, 1H), 7.24 – 7.17 (m, 2H).

^{19}F NMR (471 MHz, CDCl_3) δ -109.57 (tt, J = 8.6, 5.3 Hz).

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 164.6, 164.4 (d, $^1J_{\text{C-F}}$ = 250.9 Hz), 137.0, 129.9, 129.2 (d, $^3J_{\text{C-F}}$ = 8.8 Hz), 123.6 (d, $^4J_{\text{C-F}}$ = 3.1 Hz), 120, 116.2 (d, $^2J_{\text{C-F}}$ = 22.0 Hz).

HRMS (ESI) m/z : $[M+H]^+$ Calcd for $C_{13}H_{10}FN_4$ 241.0889; Found 241.0891.

IR ν_{\max} (neat): 3082, 3069, 3045, 3026, 2924, 1597, 1541, 1495, 1491, 1474, 1458, 1423 cm^{-1}

Analytical data in agreement with the literature.³⁰

N-(4-(5-(4-fluorophenyl)-2H-tetrazol-2-yl)phenyl)acetamide (4f)

Synthesized in accordance with the general procedure using tetrazole **3b** (32.8 mg, 0.2 mmol), (4-acetamidophenyl)boronic acid (71.6 mg, 0.4 mmol), copper(I) oxide (1.4 mg, 12 μmol) and DMSO (2 mL) to yield N-(4-(5-(4-fluorophenyl)-2H-tetrazol-2-yl)phenyl)acetamide (42 mg, 0.14 mmol, 71 % yield) as a white solid.

^1H NMR (400 MHz, DMSO) δ 10.31 (s, 1H), 8.20 (dd, J = 8.5, 5.6 Hz, 2H), 8.08 (d, J = 8.9 Hz, 2H), 7.87 (d, J = 8.9 Hz, 2H), 7.45 (app. t, J = 8.8 Hz, 2H), 2.10 (s, 3H).

^{19}F NMR (471 MHz, DMSO) δ -109.54 – -109.62 (m).

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 168.8, 163.6 (d, $^1J_{\text{C-F}}$ = 248.1 Hz), 163.5, 141.0, 131.0, 129.0 (d, $^3J_{\text{C-F}}$ = 8.8 Hz), 123.1 (d, $^4J_{\text{C-F}}$ = 2.9 Hz), 120.7, 119.7, 116.5 (d, $^2J_{\text{C-F}}$ = 22.0 Hz), 24.1.

HRMS (ESI) m/z : $[M+H]^+$ Calcd for $C_{15}H_{13}FN_5O$ 298.1099; Found 298.1101.

IR ν_{\max} (neat): 3310, 3277, 3208, 3150, 3088, 1665, 1609, 1541, 1508, 1466, 1423, 1414 cm^{-1}

5-(4-fluorophenyl)-2-(naphthalen-2-yl)-2H-tetrazole (4g)

Synthesized in accordance with the general procedure using tetrazole **3b** (39.2 mg, 0.24 mmol), 2-naphthylboronic acid (68.8 mg, 0.42 mmol), copper(I) oxide (1.7 mg, 12 μmol) and DMSO (2 mL) to yield 5-(4-fluorophenyl)-2-(naphthalen-2-yl)-2H-tetrazole (10 mg, 0.04 mmol, 15 % yield) as a yellow solid.

^1H NMR (400 MHz, CDCl_3) δ 8.66 (d, J = 2.0 Hz, 1H), 8.35 – 8.26 (m, 3H), 8.04 (d, J = 9.0 Hz, 1H), 8.02 – 7.98 (m, 1H), 7.96 – 7.91 (m, 1H), 7.65 – 7.56 (m, 2H), 7.24 (dd, J = 13.6, 4.9 Hz, 2H).

^{19}F NMR (471 MHz, CDCl_3) δ -109.41 – -109.65 (m).

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 164.7, 163.4 (d, $^1J_{\text{C-F}}$ = 250.8 Hz), 134.4, 133.6, 133.2, 130.1, 129.3 (d, $^3J_{\text{C-F}}$ = 8.6 Hz), 128.8, 128.2, 127.7, 127.6, 123.6 (d, $^4J_{\text{C-F}}$ = 4.2 Hz), 118.4, 118.0, 116.3 (d, $^2J_{\text{C-F}}$ = 22.3 Hz).

HRMS (ESI) m/z : $[M+H]^+$ Calcd for $C_{17}H_{12}FN_4$ 291.1046; Found 291.1046.

IR ν_{\max} (neat): 3061, 2953, 2922, 2851, 1607, 1603, 1539, 1510, 1476, 1460, 1447, 1423 cm^{-1}

5-(4-fluorophenyl)-2-(o-tolyl)-2H-tetrazole (4h)

Synthesized in accordance with the general procedure using tetrazole **3b** (32.8 mg, 0.20 mmol), o-tolylboronic acid (54 mg, 0.4 mmol), copper(I) oxide (1.4 mg, 10 μmol) and DMSO (2 mL) to yield 5-(4-fluorophenyl)-2-(o-tolyl)-2H-tetrazole (41.4 mg, 0.16 mmol, 81 % yield) as an off-white solid.

^1H NMR (400 MHz, CDCl_3) δ 8.27 – 8.21 (m, 2H), 7.66 (dd, J = 7.7, 1.1 Hz, 1H), 7.50 – 7.37 (m, 3H), 7.25 – 7.18 (m, 2H), 2.43 (s, 3H).

^{19}F NMR (471 MHz, CDCl_3) δ -109.70 (tt, J = 8.6, 5.3 Hz).

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 164.33 (d, $^1J_{\text{C-F}}$ = 250.7 Hz), 164.31, 136.6, 133.2, 132.1, 130.5, 129.2 (d, $^3J_{\text{C-F}}$ = 8.6 Hz), 127.1, 125.4, 123.7 (d, $^4J_{\text{C-F}}$ = 2.9 Hz), 116.3 (d, $^2J_{\text{C-F}}$ = 22.3 Hz), 18.9.

HRMS (ESI) m/z : $[M+H]^+$ Calcd for $C_{14}H_{12}FN_4$ 255.1046; Found 255.1051.

IR ν_{\max} (neat): 3088, 2984, 2963, 2924, 2853, 1603, 1497, 1472, 1458, 1423 cm^{-1}

5-(naphthalen-2-yl)-2-phenyl-2H-tetrazole (4i)

Synthesized in accordance with the general procedure using tetrazole **3g** (39.2 mg, 0.20 mmol), phenylboronic acid (49 mg, 0.4 mmol), copper(I) oxide (1.4 mg, 10 μ mol) and DMSO (2 mL) to yield 5-(naphthalen-2-yl)-2-phenyl-2H-tetrazole (46.4 mg, 0.17 mmol, 85 % yield) as a beige solid.

¹H NMR (500 MHz, CDCl₃) δ 8.80 (s, 1H), 8.32 (dd, J = 8.5, 1.6 Hz, 1H), 8.26 – 8.22 (m, 2H), 8.02 – 7.97 (m, 2H), 7.92 – 7.87 (m, 1H), 7.61 – 7.54 (m, 4H), 7.51 (app. t, J = 7.4 Hz, 1H).

¹³C{¹H} NMR (126 MHz, CDCl₃) δ 165.5, 137.1, 134.5, 133.4, 129.81, 129.77, 128.93, 128.87, 128.0, 127.4, 127.1, 126.9, 124.6, 124.1, 120.0.

HRMS (ESI) m/z : [M+H]⁺ Calcd for C₁₇H₁₃N₄ 273.1140; Found 273.1143.

IR ν_{\max} (neat): 3051, 2930 2853, 1595, 1522, 1503, 1468, 1436 cm⁻¹

2,5-di(naphthalen-2-yl)-2H-tetrazole (4k)

Synthesized in accordance with the general procedure using tetrazole **3g** (39.2 mg, 0.20 mmol), 2-naphthylboronic acid (69 mg, 0.4 mmol), copper(I) oxide (1.4 mg, 10 μ mol) and DMSO (2 mL) to yield 2,5-di(naphthalen-2-yl)-2H-tetrazole (10.2 mg, 0.03 mmol, 16 % yield) as a white solid.

¹H NMR (400 MHz, CDCl₃) δ 8.85 (s, 1H), 8.72 (d, J = 1.7 Hz, 1H), 8.39 (dd, J = 4.5, 1.8 Hz, 1H), 8.37 (dd, J = 4.1, 1.8 Hz, 1H), 8.07 (d, J = 9.0 Hz, 1H), 8.05 – 7.99 (m, 3H;), 7.97 – 7.90 (m, 2H;), 7.66 – 7.55 (m, 4H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 165.6, 134.6, 134.5, 133.6, 133.4, 133.3, 130.1, 129.0, 128.9, 128.85, 128.2, 128.1, 127.7, 127.6, 127.4, 127.2, 126.9, 124.6, 124.2, 118.5, 118.1.

HRMS (ESI) m/z : [M+H]⁺ Calcd for C₂₁H₁₅N₄ 323.1297; Found 323.1299.

IR ν_{\max} (neat): 3055, 3030, 1630, 1603, 1524, 1501, 1474, 1437 cm⁻¹

5-(naphthalen-2-yl)-2-(o-tolyl)-2H-tetrazole (4l)

Synthesized in accordance with the general procedure using tetrazole **3g** (39.2 mg, 0.20 mmol), o-tolylboronic acid (54 mg, 0.4 mmol), copper(I) oxide (1.4 mg, 10 μ mol) and DMSO (2 mL) to yield 5-(naphthalen-2-yl)-2-(o-tolyl)-2H-tetrazole (20.0 mg, 0.07 mmol, 35 % yield) as a beige solid.

¹H NMR (500 MHz, CDCl₃) δ 8.80 (s, 1H), 8.32 (dd, J = 8.5, 1.6 Hz, 1H), 8.00 (d, J = 8.5 Hz, 1H), 8.00 – 7.97 (m, 1H), 7.93 – 7.88 (m, 1H), 7.71 (d, J = 7.9 Hz, 1H), 7.59 – 7.53 (m, 2H), 7.51 – 7.39 (m, 3H), 2.47 (s, 3H).

¹³C{¹H} NMR (126 MHz, CDCl₃) δ 165.2, 136.7, 134.5, 133.4, 133.3, 132.1, 130.5, 129.0, 128.9, 128.0, 127.3, 127.07, 127.05, 126.9, 125.4, 124.7, 124.1, 19.0.

HRMS (ESI) m/z : [M+H]⁺ Calcd for C₁₈H₁₅N₄ 287.1297; Found 287.1299.

IR ν_{\max} (neat): 3061, 2924, 2853, 1605, 1522, 1493, 1464, 1435 cm⁻¹

2-phenyl-5-(o-tolyl)-2H-tetrazole (4m)

Synthesized in accordance with the general procedure using tetrazole **3f** (32.0 mg, 0.20 mmol), phenylboronic acid (49 mg, 0.4 mmol), copper(I) oxide (1.4 mg, 10 μ mol) and DMSO (2 mL) to yield 2-phenyl-5-(o-tolyl)-2H-tetrazole (32.0 mg, 0.14 mmol, 68 % yield) as an off-white solid.

¹H NMR (400 MHz, DMSO) δ 8.19 – 8.13 (m, 2H), 8.04 (dd, J = 7.6, 1.2 Hz, 1H), 7.73 – 7.66 (m, 2H), 7.64 – 7.59 (m, 1H), 7.50 – 7.36 (m, 3H), 2.64 (s, 3H).

¹³C{¹H} NMR (101 MHz, DMSO) δ 164.9, 137.0, 136.2, 131.5, 130.4, 130.1, 129.2, 126.3, 125.6, 119.9, 21.2, 1C not observed.

HRMS (ESI) m/z : [M+H]⁺ Calcd for C₁₄H₁₃N₄ 237.1135; Found 237.1134.

IR ν_{\max} (neat): 3076, 3030, 2980, 2959, 2926, 1595, 1522, 1497, 1479, 1456, 1418 cm⁻¹

N-(4-(5-(o-tolyl)-2H-tetrazol-2-yl)phenyl)acetamide (4n)

Synthesized in accordance with the general procedure using tetrazole **3f** (32.0 mg, 0.20 mmol), (4-acetamidophenyl)boronic acid (71.6 mg, 0.4 mmol), copper(I) oxide (1.4 mg, 10 μ mol) and DMSO (2 mL) to yield N-(4-(5-(o-tolyl)-2H-tetrazol-2-yl)phenyl)acetamide (41.2 mg, 0.14 mmol, 71 % yield) as a white solid.

¹H NMR (400 MHz, CDCl₃) δ 8.17 – 8.13 (m, 2H), 8.13 – 8.09 (m, 1H), 7.75 (d, J = 8.9 Hz, 2H), 7.56 (br. s, 1H), 7.43 – 7.31 (m, 3H), 2.71 (s, 3H), 2.23 (s, 3H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 168.6, 165.7, 139.3, 137.8, 133.0, 131.6, 130.3, 129.7, 126.3, 126.2, 120.7, 120.5, 24.8, 21.9.

HRMS (ESI) m/z : [M+H]⁺ Calcd for C₁₆H₁₆N₅O 294.1349; Found 294.1351.

IR ν_{\max} (neat): 3294, 3269, 3211, 3148, 3075, 2957, 2926, 1661, 1611, 1535, 1510, 1481, 1450, 1414cm⁻¹

2-(naphthalen-2-yl)-5-(*o*-tolyl)-2*H*-tetrazole (4o)

Synthesized in accordance with the general procedure using tetrazole **3f** (32.0 mg, 0.20 mmol), 2-naphthylboronic acid (69 mg, 0.4 mmol), copper(I) oxide (1.4 mg, 10 μ mol) and DMSO (2 mL) to yield 2-(naphthalen-2-yl)-5-(*o*-tolyl)-2*H*-tetrazole (17.3 mg, 0.06 mmol, 30 % yield) as an off-white solid.

¹H NMR (400 MHz, CDCl₃) δ 8.68 (d, *J* = 2.0 Hz, 1H, 8.35 (dd, *J* = 9.0, 2.2 Hz, 1H), 8.18 (dd, *J* = 8.0, 1.5 Hz, 1H), 8.05 (d, *J* = 9.0 Hz, 1H), 8.03 – 7.99 (m, 1H), 7.97 – 7.91 (m, 1H), 7.65 – 7.57 (m, 2H), 7.45 – 7.35 (m, 3H), 2.77 (s, 3H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 165.9, 137.9, 134.5, 133.5, 133.3, 131.6, 130.3, 130.1, 129.8, 128.8, 128.2, 127.7, 127.5, 126.4, 126.3, 118.3, 118.0, 22.0.

HRMS (ESI) *m/z*: [M+H]⁺ Calcd for C₁₈H₁₅N₄ 287.1291; Found 287.1288.

IR ν_{\max} (neat): 3049, 3034, 2959, 2922, 2851, 1603, 1514, 1474, 1449 cm⁻¹

2,5-di-*o*-tolyl-2*H*-tetrazole (4p)

Synthesized in accordance with the general procedure using tetrazole **3f** (32.0 mg, 0.20 mmol), *o*-tolylboronic acid (54 mg, 0.4 mmol), copper(I) oxide (1.4 mg, 10 μ mol) and DMSO (2 mL) to yield 2,5-di-*o*-tolyl-2*H*-tetrazole (31.4 mg, 0.13 mmol, 63 % yield) as a yellow oil.

¹H NMR (500 MHz, CDCl₃) δ 8.19 – 8.16 (m, 1H), 7.71 (d, *J* = 7.9 Hz, 1H), 7.49 – 7.34 (m, 6H), 2.72 (s, 3H), 2.47 (s, 3H).

¹³C{¹H} NMR (126 MHz, CDCl₃) δ 165.4, 137.7, 136.7, 133.0, 132.1, 131.6, 130.3, 130.2, 129.7, 127.1, 126.4, 126.2, 125.3, 22.0, 19.1.

HRMS (ESI) *m/z*: [M+H]⁺ Calcd for C₁₅H₁₅N₄ 251.1291; Found 251.1290.

IR ν_{\max} (neat): 3063, 3032, 2961, 2924, 1607, 1584, 1520, 1495, 1476, 1452 cm⁻¹

Supporting Information

Supporting information (general procedures, optimization experiments, and the NMR spectra of selected compounds) is available for this manuscript.

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Conflicts of Interest

There are no conflicts to declare.

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