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Regioselective Synthesis and Slow-Release Suzuki–Miyaura Cross-Coupling of MIDA Boronate-Functionalized Isoxazoles and Triazoles

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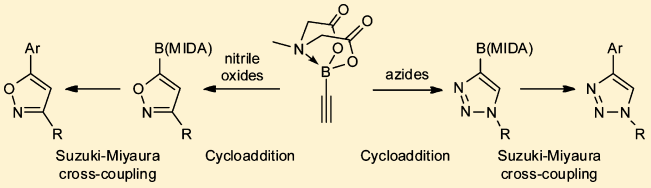
Supporting Information

ABSTRACT: The efficient preparation of heterocycles with a range of substitutions ortho to heteroatoms remains as a challenge in organic synthesis, particularly relevant to the construction of druglike molecules due to the ubiquitous presence of such moieties in that chemical space. Modular installation of heterocyclic building blocks using Suzuki–Miyaura cross-coupling is a conceptually useful strategy to address this challenge, though this has historically been met with technical difficulty due to issues of inaccessibility and instability of the requisite heterocyclic boronates. Herein we report a mild and highly regioselective cycloaddition approach which affords convenient access to stable MIDA boronate-functionalized isoxazoles and triazoles and their subsequent efficient Suzuki–Miyaura cross-coupling. This methodology is then further applied to a set of druglike compounds in an efficient one-pot telescoped sequence in line with green chemistry principles.



INTRODUCTION

Heterocyclic frameworks find ubiquitous representation in pharmaceutically active agents and other biologically relevant molecules, and methods for their synthesis and functionalization have been areas of intensive study for more than a century.[1] A more modular strategy, whereby preconstructed heterocycles are introduced to build larger molecules, constitutes a complementary synthetic approach with inherently wide versatility as well as adaptability to parallel synthesis approaches. One of the most general methods for introducing such preconstructed heterocyclic building blocks is the Suzuki–Miyaura (SM) cross-coupling.[2] However, many such heterocyclic boronic acids/esters, particularly those where boron is attached to a carbon center adjacent to the ring heteroatom, are often difficult to prepare,[3] are unstable, and are poor substrates in SM cross-couplings.[4] In particular, there have not been any reported methods for conveniently accessing 5-boronyl isoxazoles or 4-boronyl triazoles in such a way as to enable subsequent efficient cross-coupling chemistry. One practical solution to the more general problem of efficient utilization of unstable boronic acids, which was successfully applied to other heterocycles (most notably 2-pyridyl boronates), has been to introduce the boronic acid functionality in a masked form which can subsequently be liberated in a controlled release fashion into the SM reaction solution, resulting in efficient couplings.[5] This conceptual approach has been shown to be somewhat general with the use of *N*-methyliminodiacetic acid (MIDA) masked boronic acids,[6] and a number of historically difficult boronic acid cross-couplings have been successfully demonstrated with their use.[7] A remaining limitation to a broader application of this approach has been the lack of availability of convenient methods for the synthesis of heterocyclic boronic acid MIDA esters. To date, their preparation has primarily been through direct derivatization of a free boronic acid or its lithium alkoxide adduct.[8] We reasoned that by building certain 2-heterocyclic boronates from smaller prefunctionalized fragments that the aforementioned limitations might be avoided, and this powerful methodology could thereby be extended to enable a streamlined construction of heterocycle containing molecules.

RESULTS AND DISCUSSION

We chose to investigate the potential of [3 + 2] cycloadditions of ethynyl boronic acid MIDA ester **1** (Figure 1, path A), as this commercially available synthon has shown tremendous versatility as a precursor to more complex intermediates with

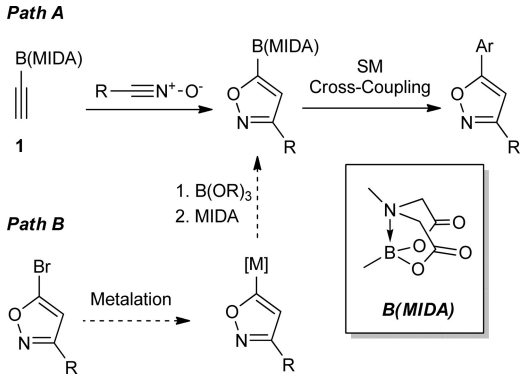


Figure 1. Two paths to the preparation of isoxazole MIDA boronates.

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a preinstalled functional handle.[7c,9] We anticipated that this method might offer a practical alternative to intercepting a metalated heterocycle with a borate ester and a subsequent requisite masking step (Figure 1, path B).

Cycloadditions of alkynyl boronates have been demonstrated by Harrity and co-workers to provide convenient access to a wide range of 5- and 6-membered ring heterocyclic boronates.[10,11] This includes precedent for [3 + 2] cycloaddition of alkynylpinacol boronate esters at elevated temperatures, giving rise to borylated isoxazoles in moderate yields and with varying degrees of regioselectivity, depending on the nature of the substitution at both the alkyne terminus and the oxime carbon. However, while Suzuki–Miyaura cross-couplings of 4-boronyl isoxazoles have found wide use in the literature, the complementary Suzuki–Miyaura cross-couplings of the unstable 5-boronyl isoxazoles are virtually unreported (Figure 2).

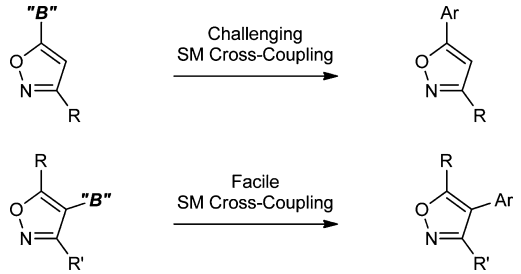
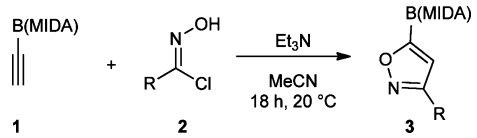


Figure 2. Divergent reactivity of boronyl isoxazoles.

Our initial results from the reaction between ethynylboronic acid MIDA ester **1** and the *in situ* generated phenyl nitrile oxide derived from chlorooxime **2** (Table 1, entry 1) demonstrated that under this protocol cycloaddition proceeded at room temperature, in high yield, and with complete regioselectivity. This transformation appears to be rather general in scope, proving to be effective on a range of aryl substituted nitrile oxides as well as heteroaryl, halogen, and carboxylate substituted nitrile oxides. In contrast to reported findings using the corresponding pinacol esters, all of the isoxazole MIDA boronates prepared in this manner were obtained as single regioisomers and were purified by silica gel chromatography with no evidence of decomposition. In order to evaluate whether the observed regioselectivity was an intrinsic property of the reacting partners or merely an artifact of the lowered reaction temperature, we tested the cycloaddition reaction at 40 °C, and still none of the 4-boronyl isoxazole was observed. We therefore hypothesize that the complete regioselectivity in the case of the MIDA ester examples stems from the presence of the sp^3-hybridized boron center which imparts a more significant steric demand in the case of the MIDA boronates relative to the sp^2-hybridized boron of the pinacol esters.

With conditions for effective cycloaddition in hand, we focused on the utilization of these new heterocyclic MIDA boronates in the SM cross-coupling. As a starting point for our optimization efforts, we turned to the conditions developed by the Burke group for unstable 2-pyridylboronic acids.[7a] Applying these conditions to the SM cross-coupling of 3-phenylisoxazole MIDA boronate **3a** with 4-chlorobenzonitrile afforded the desired cross-coupling product **5** in low yield (Table 2, entry 1), as protodeboronation of the heterocyclic boronate was a significant side product. We reasoned that an increase in the overall rate of the SM cross-coupling would lead to improvements in the observed level of selectivity for the SM cross-coupling relative to the competing protodeboronation pathway. This was investigated by replacing the aryl chloride (Table 2, entry 1) with the analogous aryl bromide **4** (Table 2, entry 2). An improvement was noted both in the yield and in the ratio of desired product **5** relative to the reduced heterocycle **6**. The selectivity of the reaction was further improved by employing Buchwald's palladacyclic precatalyst.[12] These precatalysts are known to generate a highly active Pd^0 species capable of extremely rapid uptake of the aryl halide coupling partner via oxidative addition and in this application, afforded for the first time, synthetically useful yields of SM cross-coupling product (Table 2, entry 4). In the complementary approach, we investigated the role of base and alcohol cosolvent in an attempt to modulate the rate of solvolysis of the MIDA boronate and thereby improve the performance of SM cross-coupling. In this context, reactions with weaker bases (e.g., Na_2CO_3) and more sterically hindered cosolvents (e.g., *tert*-butyl alcohol) failed to react to completion due to extremely slow solvolysis. This left only the reaction solvent as a potential variable to positively influence the efficiency of the reaction. We speculated that less polar solvents would impede the solvolysis of the isoxazole MIDA boronate as well and afford improved

Table 1. Cycloadditions with Ethynylboronic Acid MIDA Ester 1[a]



1 2 3

entry	R	base	solvent	yield (%)[b]
1	Ph–	K_3PO_4	MeCN	**3a** 90
2	Br–[c]	K_3PO_4	MeCN	**3b** 95
3	$-CO_2Et$[d]	$KHCO_3$	DCM	**3c** 73
4	4-F-Ph–	Et_3N	DCM	**3d** 90
5	2-pyridyl–	Et_3N	DCM	**3e** 72
6	4-MeO-Ph–	Et_3N	DCM	**3f** 89
7	4-Cl-Ph–	Et_3N	DCM	**3g** 75
8	2-CF_3Ph–	Et_3N	DCM	**3h** 90

[a]Unless otherwise noted, ethynylboronic acid MIDA ester **1** (1 equiv), chlorooxime **2** (2 equiv), and base (2 equiv) were allowed to react at room temperature for 18 h. [b]Isolated yield. [c]Dibromoformaldoxime was used. [d]The reaction was carried out with excess (3 equiv) chlorooxime and base.

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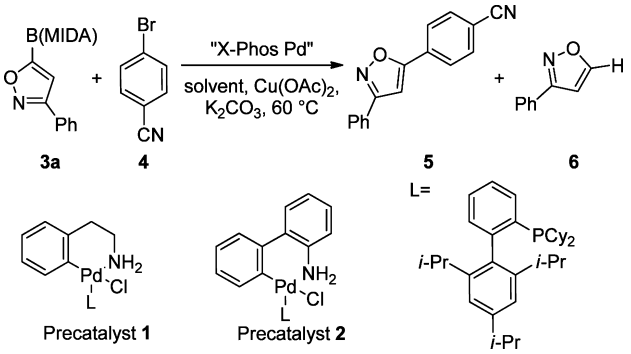
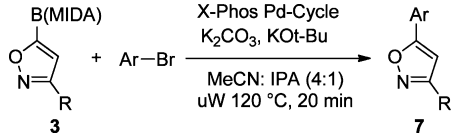
Table 2. Optimization of Suzuki–Miyaura Cross-Couplings on Isoxazole Boronic Acid MIDA Esters



entry	Pd source	solvent	5:6[a]	yield (%)[b]
1[c]	Pd_2dba_3	DMF	5:1	32
2	Pd_2dba_3	DMF	9:1	49
3[d]	Pd_2dba_3	DMF	–	0
4	precatalyst 1	DMF	7:1	59
5	precatalyst 1	MeCN	6:1	28
6	precatalyst 1[e]	MeCN	16:1	59
7	precatalyst 2	MeCN	29:1	55
8	precatalyst 1[e,f]	MeCN	14:1	63
9	precatalyst 2[f]	MeCN	15:1	69

[a]Assessed by UV-HPLC at 254 nm. [b]Isolated yield. [c]4-Chlorobenzonitrile was used. [d]Reaction was performed without the $Cu(OAc)_2$ additive. [e]With preactivation by KO*t*-Bu (0.05 equiv) at room temperature. [f]Reaction was carried out in a microwave at 120 °C for 20 min.

Table 3. Suzuki–Miyaura Cross-Couplings of Isoxazole Boronic Acid MIDA Esters



entry	method[b]	R (boronate)	Ar	yield (%)[a]
1[b]	B	**3a** Ph–	4-MeO-Ph–	**7a** 72
2	B	**3a** Ph–	4-SO_2Me-Ph–	**7b** 76
3	B	**3a** Ph–	3-Py–	**7c** 73
4	A	**3c** –CO_2Et	4-CN-Ph–	**7d** 75
5	A	**3d** 4-F-Ph–	4-CN-Ph–	**7e** 73
6	A	**3f** 4-MeO-Ph–	4-CN-Ph–	**7f** 69
7	A	**3g** 4-Cl-Ph–	4-CN-Ph–	**7g** 59
8	A	**3h** 2-CF_3-Ph–	4-CN-Ph–	**7h** 56

[a]Isolated yield. [b]Method A utilized first generation X-Phos precatalyst (5 mol %) with preactivation by KO*t*-Bu (5 mol %). Method B utilized second generation X-Phos precatalyst (5 mol %) with no preactivation.

levels of selectivity for the desired cross-coupling reaction. Initially, this approach appeared to fail as exchanging acetonitrile for DMF (Table 2, entry 5) led to a diminished yield and moderate selectivity for the desired cross-coupling. However, upon close analysis of the crude reaction mixture the presence of unactivated precatalyst was observed. This was not entirely unexpected given that precatalyst activation occurs at temperatures above 80 °C with carbonate bases. We chose to address this issue in two ways: (1) by carrying out catalyst preactivation with potassium *tert*-butoxide at room temperature in the presence of the aryl halide coupling partner[13] and (2) by investigating the second generation 2-aminobiphenyl derived precatalyst[14] which is activated at ambient temperature by carbonate bases. Both of these approaches proved effective (Table 2, entries 6 and 7) and were utilized in further optimization and evaluation of the reaction scope. We also evaluated the performance of the reaction under microwave heating and observed a further improvement in reaction efficiency for both the preactivation approach applied to the first generation precatalyst (entry 8) as well as for the second generation precatalyst with no preactivation (entry 9).

We next investigated the generality of these optimized conditions by screening substituents on the isoxazole as well as a range of aryl halide coupling partners. We observed moderate to high yields in substrates with varied electronic properties (Table 3).

Having developed the isoxazole chemistry to where it appeared to be of sufficient generality so as to be suitable for analogue synthesis in a drug discovery environment, we were also quite interested to explore whether other heterocycles might be prepared and derivatized in a similar fashion. Considering the vast precedent for [3 + 2] azide acetylene cycloaddition (AAC) reactions between alkynes and azides,[15] and encouraged by recent literature reports[16,17] on a thermal

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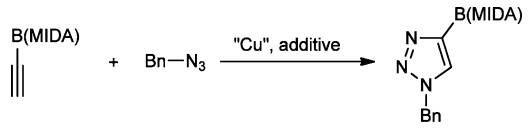
Table 4. Investigation of "Cu" and Additives on the AAC of Ethynyl MIDA Boronate 1 with Benzyl Azide 8[a]



entry	"Cu"	additive	yield (%)[b]
1	CuCl	–	0
2	CuOAc	–	0
3	$Cu(SO_4)_2$	Na-ascorbate	0
4	$Cu(OAc)_2$[c]	TBTA (10%)	78
5	$Cu(OAc)_2$[c]	–	78
6	CuI	DIPEA	60

[a]All reactions were run with equimolar amounts of alkyne and azide, 50 mol % "Cu" at 0.2 M unless otherwise indicated. [b]Isolated yield. [c]Reaction was run with 10 mol % $Cu(OAc)_2$.

cycloaddition approach to 5-boronyl triazoles and their subsequent SM cross-coupling reactions, we set out to develop a procedure that would afford ready access to triazole MIDA boronates.

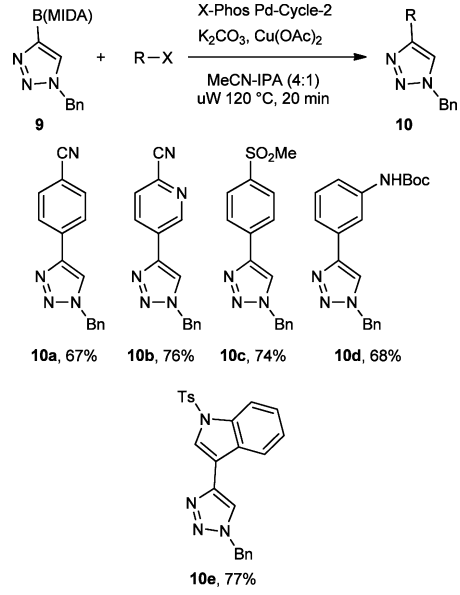
We initially surveyed some standard conditions[18] for Cu-catalyzed AAC and found three sets of conditions that provided access to triazole MIDA boronates in synthetically useful yields (Table 4). The optimal conditions were 10 mol % of $Cu(OAc)_2$-H_2O and equimolar amounts of the reaction partners heated to 60 °C for 18 h. These simple conditions enable rapid accesss to the expected and previously unreported 4-boronyl triazoles **9** as their MIDA conjugates. These air stable boronic acid surrogates are prepared with no trace of the corresponding 5-boronyl regioisomers, are isolable by standard silica gel chromatography, and for the first time enable the investigation of SM cross-coupling of these interesting heterocyclic building blocks.

In order to assess the viability of these new boronyl heterocycles as coupling partners in the SM cross-coupling, we applied the conditions developed for the 5-boronyl isoxazoles and observed an equally efficient reaction between benzyl-triazole MIDA boronate **9** and 4-bromobenzonitrile **4** as compared with the corresponding isoxazole MIDA boronate example 5. The cross-coupling was tolerant of both electron-rich and electron-poor coupling partners and proceeded in good yields in all cases (Scheme 1).

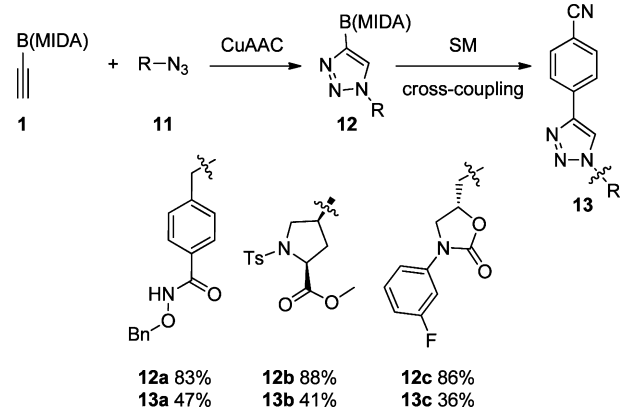
As we ultimately sought to demonstrate the utility of this method in a medicinal chemistry context, we next wished to ascertain whether this reaction might be readily applicable to the construction of a number of motifs commonly found in biologically relevant small molecules. We envisioned that this would enable a cycloaddition-SM cross-coupling sequence providing access to complex triazole products in a streamlined synthetic sequence. We selected three azide motifs for this study: a protected hydroxamic acid **11a**, a sulfonyl proline derivative **11b**, and an *N*-aryl oxazolidinone **11c**. We evaluated the performance of the CuAAC and the subsequent SM cross-coupling without modification of either protocol (Scheme 2).

All three motifs participated in the CuAAC in high yields to afford a somewhat diverse range of complex triazole MIDA boronates **12a–c** illustrative of the scope of this method. The resultant boronates performed only moderately well in the subsequent SM cross-coupling however. Yields could be improved by applying a one-pot procedure for this two-step sequence, improving the overall unoptimized yield to 49% as compared to 39% for the two-step process (**13a**). This one-pot approach while accessing the target compounds in higher yield also has the advantage of reduced waste generation by avoiding the work-up and purification of the intermediate boronyl triazole and is thus a greener and more efficient process.

Scheme 1. Slow Release SM Cross-Coupling of 4-Boronyltriazole 9 with Aryl-/Heteroaryl Halides



Scheme 2. CuAAC and SM Cross-Coupling with Druglike Azides 11



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CONCLUSION

We have developed synthetic routes useful for accessing two important classes of heterocyclic MIDA boronates—5-isoxazole and 4-triazole MIDA boronates, respectively—and demonstrated their utility in SM cross-coupling reactions. The [3 + 2] cycloaddition reactions reported herein all proceed with exceptionally high levels of regioselectivity. In the isoxazole case this is due to the relatively large steric footprint of the MIDA boronate. While in the triazole case the regioselectivity arises both from the aforementioned steric bulk as well as the reagent tolerance imparted by the MIDA boronate which enables the use of Cu catalysis, a hallmark for reliable access to the 1,4-disubstituted heterocycle. To our knowledge, this work is the first systematic study of the SM cross-couplings of 5-boronyl isoxazoles as well as the only report of the isolation, characterization, and SM cross-coupling of 4-boronyl triazoles. These cross-couplings were enabled by the stability of the MIDA boronates and the predictable slow release achieved in the course of the SM cross-coupling reactions. Further, this methodology enabled rapid access to a number of druglike molecules in a one-pot telescoped sequence. Additional ongoing investigations into synthesis and reactivity of other boronyl-functionalized heterocycles will be the subject of forthcoming communications.

EXPERIMENTAL SECTION

General Experimental Procedures. Unless otherwise stated, all reagents were used as received from commercial vendors. Ethynyl MIDA boronate was triturated with ether prior to use to remove residual DMSO. Organic solutions were concentrated via rotary evaporation under reduced pressure with a bath temperature of 35−40 °C or using a centrifugal evaporator system. Reactions were monitored by analytical HPLC-MS (electrospray ionization) using a C-18, 3 μm, 4.6 × 50 mm column with either of two eluent systems: acidic (A: water + 0.1% TFA; B: MeCN; flow rate: 2.1 mL/min gradient: 95% A to 95% B over 5 min) or basic (A: 5 mM aqueous NH_4OH; B: MeCN; flow rate: 2.1 mL/min gradient: 95% A to 95% B over 5 min). ^1H and ^{13}C NMR analyses were acquired on a 400 MHz spectrometer and referenced either to tetramethylsilane or the residual peak of solvent. Microwave reactions were carried out in 2−5 mL thick-walled glass vessels and irradiated in a variable voltage microwave instrument. Temperature was measured using an external IR sensor. All melting points are uncorrected.

Synthetic Procedures. *Synthesis of Isoxazole MIDA Boronates via [3 + 2] Cycloaddition. General Procedures for the Synthesis of Isoxazole MIDA Boronates.* To a reaction vessel containing ethynyl MIDA boronate **1** (1 equiv) and chlorooxime **2** (2 equiv) in dichloromethane or acetonitrile (0.1 M) was added triethylamine or tripotassium phosphate (2 equiv). The reaction was allowed to stir at ambient temperature for 18 h, at which time the reaction solvent was removed *in vacuo*, and the residue was purified by flash chromatography (ethyl acetate isocratic or dichloromethane−acetonitrile).

Synthesis of Triazole MIDA Boronates via CuAAC. General Procedure for the Synthesis of Triazole MIDA Boronates. To a reaction vessel containing ethynyl MIDA boronate **1** (1 equiv), azide (1 equiv), and copper(II) acetate monohydrate (0.1 equiv) was added acetonitrile (0.1 M). The reaction was heated at 60 °C for 18 h, at which time the reaction solvent was removed *in vacuo* and the residue was purified by flash chromatography (ethyl acetate isocratic or dichloromethane−acetonitrile).

MIDA Boronates Suzuki Coupling. General Procedure A for the SM Cross-Coupling of Heterocyclic MIDA Boronates. To a reaction vessel containing phenethylamine derived X-Phos palladacycle precatalyst-1 (0.05 equiv), aryl halide (1.25 equiv), and dry acetonitrile (0.75 mL) was added potassium *tert*-butoxide (0.1 M in THF, 0.05 equiv); this mixture was allowed to stir at ambient temperature for 5 min before being added to a second reaction vessel containing heterocyclic MIDA boronate (1 equiv), potassium carbonate (7 equiv), copper(II) acetate monohydrate (0.5 equiv), and acetonitrile (1 mL). 2-Propanol was then added (in sufficient quantity to achieve a 4:1 ratio of acetonitrile:2-propanol), and the reaction was subjected to microwave irradiation at 120 °C for 20 min. The reaction solvent was removed *in vacuo*, and the residue was dissolved in dichloromethane and was purified by flash chromatography (heptanes/ethyl acetate).

General Procedure B for the SM-Cross-Coupling of Heterocyclic MIDA Boronates. To a microwave vial containing 2-aminobiphenyl derived X-Phos palladacycle precatalyst-2 (0.05 equiv), aryl halide (1.25 equiv), heterocyclic MIDA boronate (1 equiv), potassium carbonate (7 equiv), and copper(II) acetate monohydrate (0.5 equiv) was added acetonitrile and 2-propanol (4:1, 0.1 M), and the reaction was subjected to microwave irradiation at 120 °C for 20 min. The reaction solvent was removed *in vacuo*, and the residue was dissolved in dichloromethane and was purified by flash chromatography (heptanes/ethyl acetate).

*3-Phenylisoxazol-5-ylboronic Acid MIDA Ester (**3a**).* A general procedure was followed using ethynyl MIDA boronate (381 mg, 2.1 mmol) and *N*-hydroxybenzimidoyl chloride (421 mg, 2.2 mmol) and tripotassium phosphate (993 mg, 4.5 mmol), affording desired product as an off-white powder (560 mg, 90% yield). Melting point: 158−159 °C. ^1H NMR (acetonitrile-d_3, 400 MHz): δ = 7.85−7.95 (m, 2 H), 7.47−7.58 (m, 3 H), 7.09 (s, 1 H), 4.17 (d, J = 17.6 Hz, 2 H), 4.01 (d, J = 18.1 Hz, 2 H), 2.78 ppm (s, 3 H). ^{13}C NMR (acetonitrile-d_3, 101 MHz): δ = 169.2, 162.6, 131.3, 130.42, 130.40, 128.1, 111.5, 63.1, 48.7 ppm. HRMS (ESI-TOF) $[M + H]^+$ calculated for $C_{14}H_{13}BN_2O_5$: 301.0990; found: 301.1000.

*3-Bromoisoxazol-5-ylboronic Acid MIDA Ester (**3b**).* A general procedure was followed using ethynyl MIDA boronate (423 mg, 2.3 mmol), dibromoformaldoxime (726 mg, 3.4 mmol), and tripotassium phosphate (1.1 g, 5 mmol), affording desired product as an off-white powder (626 mg, 90% yield). Melting point: 177−178 °C decomposed. ^1H NMR (acetonitrile-d_3, 400 MHz): δ = 6.81 (s, 1 H), 4.15 (d, J = 17.1 Hz, 2 H), 3.98 (d, J = 18.1 Hz, 2 H), 2.75 ppm (s, 3 H). ^{13}C NMR (acetonitrile-d_3, 101 MHz): δ = 168.9, 140.9, 116.8, 63.3, 48.8 ppm. HRMS (ESI-TOF) $[M + H]^+$ calculated for $C_8H_8BBrN_2O_5$: 302.9782; found: 302.9788.

*(3-(Ethoxycarbonyl)isoxazol-5-yl)boronic Acid MIDA Ester (**3c**).* A general procedure was followed using ethynyl MIDA boronate (3.1 g, 17.1 mmol) and ethyl 2-chloro-2-(hydroxyimino) acetate (7.8 g, 51.4 mmol) and potassium bicarbonate (5.15 g, 51.4 mmol) in 300 mL of acetonitrile (0.06 M), affording desired product as an off-white powder (3.75 g, 73% yield). Melting point: 159−162 °C. ^1H NMR (acetonitrile-d_3, 400 MHz): δ = 7.02 (s, 1 H), 4.42 (d, J = 7.1 Hz, 2 H), 4.20 (d, J = 18.2 Hz, 2 H), 4.04 (d, J = 16.2 Hz, 2 H), 2.75 (s, 3 H), 1.38 ppm (t, J = 7.3 Hz, 3 H). ^{13}C NMR (DMSO-d_6, 101 MHz): δ = 168.6, 159.5, 155.0, 112.0, 61.8, 61.6, 47.4, 13.8 ppm. HRMS (ESI-TOF) $[M + H]^+$ calculated for $C_{11}H_{13}BN_2O_7$: 297.0889; found: 297.0892.

*(3-(4-Fluorophenyl)isoxazol-5-yl)boronic Acid MIDA Ester (**3d**).* General procedure A was followed using ethynyl MIDA boronate (543 mg, 3 mmol) and 4-fluoro-*N*-hydroxybenzimidoyl chloride (1.04 g, 6 mmol) and triethylamine (607 mg, 6 mmol), affording desired product as an off-white powder (940 mg, 99% yield). Melting point: 139−141 °C. ^1H NMR (DMSO-d_6, 400 MHz): δ = 7.98 (dd, J = 8.5, 5.5 Hz, 2 H), 7.35 (t, J = 9.0 Hz, 2 H), 7.24 (s, 1 H), 4.46 (d, J = 17.1 Hz, 2 H), 4.23 (d, J = 17.1 Hz, 2 H), 2.74 ppm (s, 3 H). ^{13}C NMR (101 MHz, DMSO-d_6): δ =168.7, 161.8 (d, J = 247.0 Hz), 159.8, 129.1 (d, J = 8.4 Hz), 125.2 (d, J = 2.9 Hz), 116.1 (d, J = 21.6 Hz), 110.0, 61.7, 47.4 ppm. HRMS (ESI-TOF) $[M + H]^+$ calculated for $C_{14}H_{12}BFN_2O_5$: 319.0896; found: 319.0905.

*(3-(Pyridin-2-yl)isoxazol-5-yl)boronic Acid MIDA Ester (**3e**).* A general procedure was followed using ethynyl MIDA boronate (63 mg, 0.35 mmol) and *N*-hydroxypicolinimidoyl chloride (0.35 mmol) and triethylamine (106 mg, 1.05 mmol), affording desired product as a white powder which was an inseparable admixture with ethynyl MIDA boronate (100 mg, 72% yield, purity 85%). ^1H NMR (acetonitrile-d_3, 400 MHz): δ = 8.61−8.71 (m, 1 H), 8.00−8.11 (m, 1 H), 7.87 (td, J =

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7.8, 2.0 Hz, 8 H), 7.36−7.48 (m, 1 H), 7.19 (s, 1 H), 4.18 (d, J = 17.1 Hz, 2 H), 4.03 (d, J = 17.1 Hz, 2 H), 2.77 ppm (s, 3 H). ^{13}C NMR (acetonitrile-d_3, 101 MHz): δ = 168.7, 163.2, 150.8, 149.2, 138.1, 125.5, 122.6, 111.5, 62.8, 48.3 ppm. HRMS (ESI-TOF) [M + H]$^+$ calculated for $C_{13}H_{12}BN_3O_5$: 302.0943; found: 302.0954.

*(3-(4-Methoxyphenyl)isoxazol-5-yl)boronic Acid MIDA Ester (**3f**).* A general procedure was followed using ethynyl MIDA boronate (50 mg, 0.276 mmol) and *N*-hydroxy-4-methoxybenzimidoyl chloride (51 mg, 0.276 mmol) and triethylamine (28 mg, 0.276 mmol), affording desired product as white foam (81 mg, 89% yield). ^{1}H NMR (DMSO-d_6, 400 MHz): δ = 7.85 (d, J = 9.0 Hz, 2 H), 7.15 (s, 1 H), 7.05 (d, J = 8.5 Hz, 2 H), 4.44 (d, J = 17.1 Hz, 2 H), 4.21 (d, J = 19.1 Hz, 2 H), 3.81 (s, 3 H), 2.74 ppm (s, 3 H). ^{13}C NMR (DMSO-d_6, 101 MHz): δ = 168.8, 160.5, 160.2, 128.2, 121.0, 114.4, 109.7, 61.7, 55.2, 47.4 ppm. HRMS (ESI-TOF) [M + H]$^+$ calculated for $C_{15}H_{15}BN_2O_6$: 331.1096; found: 331.1100.

*(3-(4-Chlorophenyl)isoxazol-5-yl)boronic Acid MIDA Ester (**3g**).* A general procedure was followed using ethynyl MIDA boronate (50 mg, 0.276 mmol) and *N*-hydroxy-4-chlorobenzimidoyl chloride (53 mg, 0.276 mmol) and triethylamine (28 mg, 0.276 mmol), affording desired product as an off-white powder (69 mg, 75% yield). Melting point: 194−195 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ = 7.95 (d, J = 8.5 Hz, 2 H), 7.58 (d, J = 8.5 Hz, 2 H), 7.27 (s, 1 H), 4.44 (d, J = 16.1 Hz, 2 H), 4.18−4.27 (m, 2 H), 2.74 ppm (s, 3 H). ^{13}C NMR (DMSO-d_6, 101 MHz): δ = 168.7, 168.6, 159.8, 134.6, 129.2, 128.5, 127.5, 110.1, 61.7, 47.4 ppm. HRMS (ESI-TOF) [M + H]$^+$ calculated for $C_{14}H_{12}BClN_2O_5$: 335.0601; found: 335.0605.

*(3-(2-Trifluoromethylphenyl)isoxazol-5-yl)boronic Acid MIDA Ester (**3h**).* A general procedure was followed using ethynyl MIDA boronate (153 mg, 0.85 mmol) and 2-trifluoromethyl-*N*-hydroxybenzimidoyl chloride (378 mg, 1.69 mmol) and triethylamine (171 mg, 1.69 mmol), affording desired product as an off-white powder (280 mg, 90% yield). Melting point: 144−145 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ = 7.93 (d, J = 7.5 Hz, 1 H), 7.81 (d, J = 7.5 Hz, 1 H), 7.72−7.78 (m, 1 H), 7.68 (d, J = 7.5 Hz, 1 H), 6.86 (s, 1 H), 4.45 (d, J = 17.6 Hz, 2 H), 4.25 (d, J = 18.1 Hz, 2 H), 2.75 ppm (s, 3 H). ^{13}C NMR (DMSO-d_6, 101 MHz): δ = 168.7, 159.7, 132.7, 131.8, 130.2, 128.0−126.4 (m), 125.1, 122.3, 112.7, 61.9, 47.4 ppm. HRMS (ESI-TOF) [M + H]$^+$ calculated for $C_{15}H_{12}BF_3N_2O_5$: 369.0864; found: 369.0880.

*4-(3-Phenylisoxazol-5-yl)benzonitrile (**5**).* General procedure B was followed using **3a** (60 mg, 0.20 mmol) and 4-bromobenzonitrile (45 mg, 0.25 mmol), affording desired product (34 mg, 69% yield). Melting point: 166−167 °C. ^{1}H NMR (chloroform-*d*, 400 MHz): δ = 7.96 (d, J = 8.5 Hz, 2 H), 7.87 (dd, J = 6.3, 3.3 Hz, 2 H), 7.80 (d, J = 8.5 Hz, 2 H), 7.44−7.56 (m, 3 H), 6.98 ppm (s, 1 H). ^{13}C NMR (chloroform-*d*, 101 MHz): δ = 168.1, 163.3, 132.9, 132.2, 131.1, 130.4, 129.1, 128.5, 128.0, 126.8, 126.3, 118.2, 113.6, 99.7 ppm. HRMS (ESI-TOF) [M + H]$^+$ calculated for $C_{16}H_{10}N_2O$: 247.0866; found: 247.0876.

*5-(4-Methoxyphenyl)-3-phenylisoxazole (**7a**).* General procedure B was followed using **3a** (65 mg, 0.22 mmol) and 4-bromoanisole (51 mg, 0.27 mmol), affording desired product as an off-white powder (39 mg, 72% yield). Melting point: 127−128 °C. ^{1}H NMR (methanol-d_4, 400 MHz): δ = 7.85−7.93 (m, 2 H), 7.79−7.85 (m, 2 H), 7.46−7.53 (m, 3 H), 7.02−7.11 (m, 3 H), 3.86 ppm (s, 3 H). ^{13}C NMR (methanol-d_4, 101 MHz): δ = 172.0, 164.5, 163.0, 131.2, 130.4, 130.1, 128.5, 127.8, 121.4, 115.6, 97.4, 55.9 ppm. HRMS (ESI-TOF) [M + H]$^+$ calculated for $C_{16}H_{13}NO_2$: 252.1019; found: 252.1026.

*5-(4-(Methylsulfonyl)phenyl)-3-phenylisoxazole (**7b**).* General procedure B was followed using **3a** (65 mg, 0.22 mmol) and 1-bromo-4-(methylsulfonyl)benzene (64 mg, 0.27 mmol), affording desired product as a yellow powder (49 mg, 76% yield). Melting point: 200−201 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ = 8.16−8.23 (m, 2 H), 8.09−8.16 (m, 2 H), 7.91−7.98 (m, 2 H), 7.87 (s, 1 H), 7.52−7.62 (m, 3 H), 3.31 ppm (s, 3 H). ^{13}C NMR (DMSO-d_6, 101 MHz): δ = 168.0, 162.9, 142.0, 131.0, 130.5, 129.2, 128.2, 128.0, 126.6, 126.4, 100.9, 43.3 ppm. HRMS (ESI-TOF) [M + H]$^+$ calculated for $C_{16}H_{13}NO_3S$: 300.0689; found: 300.0691.

*3-Phenyl-5-(pyridin-3-yl)isoxazole (**7c**).* General procedure B was followed using **3a** (65 mg, 0.22 mmol) and 3-bromopyridine (26 μL, 0.27 mmol), affording desired product as a yellow powder (35 mg, 73% yield). Melting point: 133−136 °C. ^{1}H NMR (methanol-d_4, 400 MHz): δ = 9.04−9.18 (m, 1 H), 8.65 (dd, J = 4.8, 1.3 Hz, 1 H), 8.34 (dt, J = 8.1, 2.0 Hz, 1 H), 7.86−7.99 (m, 2 H), 7.61 (dd, J = 8.1, 5.6 Hz, 1 H), 7.47−7.57 (m, 3 H), 7.45 ppm (s, 1 H). ^{13}C NMR (methanol-d_4, 101 MHz): δ = 168.7, 164.7, 151.6, 147.4, 135.0, 131.5, 130.2, 130.0, 127.9, 125.7, 125.6, 100.5 ppm. HRMS (ESI-TOF) [M + H]$^+$ calculated for $C_{14}H_{10}N_2O$: 223.0866; found: 223.0874.

*Ethyl 5-(4-Cyanophenyl)isoxazole-3-carboxylate (**7d**).* General procedure A was followed using **3c** (64 mg, 0.22 mmol) and 4-bromobenzonitrile (49 mg, 0.27 mmol), affording desired product as a brownish powder (39 mg, 75% yield). Melting point: 170−173 °C. ^{1}H NMR (chloroform-*d*, 400 MHz): δ = 7.93 (d, J = 8.6 Hz, 2 H), 7.80 (d, J = 8.6 Hz, 2 H), 7.04 (s, 1 H), 4.50 (q, J = 7.1 Hz, 2 H), 1.46 ppm (t, J = 7.1 Hz, 3 H). ^{13}C NMR (chloroform-*d*, 101 MHz): δ = 169.4, 159.6, 157.2, 133.0, 130.3, 126.4, 118.0, 114.3, 102.1, 62.6, 14.2 ppm. HRMS (ESI-TOF) [M + H]$^+$ calculated for $C_{13}H_{10}N_2O_3$: 243.0764; found: 243.0775.

*4-(3-(4-Fluorophenyl)isoxazol-5-yl)benzonitrile (**7e**).* General procedure A was followed using **3f** (63 mg, 0.19 mmol) and 4-bromobenzonitrile (45 mg, 0.25 mmol), affording desired product as an off-white solid (40 mg, 72% yield). Melting point: 160−161 °C. ^{1}H NMR (chloroform-*d*, 400 MHz): δ = 7.95 (d, J = 7.5 Hz, 2 H), 7.86 (dd, J = 8.8, 5.3 Hz, 2 H), 7.80 (d, J = 8.5 Hz, 2 H), 7.20 (t, J = 8.8 Hz, 2 H), 6.94 ppm (s, 1 H). ^{13}C NMR (101 MHz, chloroform-*d*): δ ppm 168.3, 164.0 (d, J = 250.5 Hz), 162.4, 132.9, 131.0, 128.8 (d, J = 8.4 Hz), 126.3, 124.7 (d, J = 3.3 Hz), 118.2, 116.3 (d, J = 22.0 Hz), 113.7, 99.5. HRMS (ESI-TOF) [M + H]$^+$ calculated for $C_{16}H_9FN_2O$: 265.0783; found: 265.0772.

*4-(3-(4-Methoxyphenyl)isoxazol-5-yl)benzonitrile (**7f**).* General procedure A was followed using **3f** (62 mg, 0.19 mmol) and 4-bromobenzonitrile (41 mg, 0.23 mmol), affording desired product as a yellowish powder (36 mg, 69% yield). Melting point: 163−164 °C. ^{1}H NMR (MeOD, 400 MHz): δ = 8.07 (d, J = 8.0 Hz, 2 H), 7.90 (d, J = 9.0 Hz, 2 H), 7.85 (d, J = 9.0 Hz, 2 H), 7.40 (s, 1 H), 7.06 (d, J = 9.0 Hz, 2 H), 3.86 ppm (s, 3 H). ^{13}C NMR (MeOD, 101 MHz): δ = 169.5, 164.5, 163.0, 134.2, 132.7, 129.4, 127.5, 122.2, 119.2, 115.5, 114.7, 101.1, 55.9 ppm. HRMS (ESI-TOF) [M + H]$^+$ calculated for $C_{17}H_{12}N_2O_2$: 277.0972; found: 277.0983.

*4-(3-(4-Chlorophenyl)isoxazol-5-yl)benzonitrile (**7g**).* General procedure A was followed using **3g** (53 mg, 0.158 mmol) and 4-bromobenzonitrile (35 mg, 0.19 mmol), affording desired product as a yellowish powder (26 mg, 59% yield). Melting point: 158−161 °C. ^{1}H NMR (chloroform-*d*, 400 MHz): δ = 7.96 (d, J=8.0 Hz, 2 H), 7.77−7.86 (m, 4 H), 7.49 (d, J = 8.5 Hz, 2 H), 6.95 ppm (s, 1 H). ^{13}C NMR (chloroform-*d*, 101 MHz): δ = 168.5, 162.3, 136.5, 132.9, 131.0, 129.4, 128.1, 127.0, 126.3, 118.2, 113.8, 99.5 ppm. HRMS (ESI-TOF) [M + H]$^+$ calculated for $C_{16}H_9ClN_2O$: 281.0476; found: 281.0466.

*4-(3-(4-(Trifluoromethyl)phenyl)isoxazol-5-yl)benzonitrile (**7h**).* General procedure B was followed using **3h** (59 mg, 0.16 mmol) and 4-bromobenzonitrile (35 mg, 0.19 mmol), affording desired product as an off white solid (28 mg, 56% yield). Melting point: 154−155 °C. ^{1}H NMR (chloroform-*d*, 400 MHz): δ = 7.97 (d, J = 9.0 Hz, 2 H), 7.85 (d, J = 7.5 Hz, 1 H), 7.81 (d, J = 8.5 Hz, 2 H), 7.61−7.74 (m, 3 H), 6.87 ppm (s, 1 H). ^{13}C NMR (101 MHz, chloroform-*d*): δ ppm 167.7, 162.3, 132.9, 132.1, 131.8, 131.0, 130.1, 128.9 (q, J = 31.2 Hz), 128.0, 127.7 (d, J = 2.2 Hz), 126.6 (q, J = 5.5 Hz), 126.4, 123.7 (q, J = 273.6 Hz), 118.2, 113.8, 103.0 (q, J = 3.3 Hz). HRMS (ESI-TOF) [M + H]$^+$ calculated for $C_{17}H_9F_3N_2O$: 315.0740; found: 315.0739.

*(1-Benzyl-1H-1,2,3-triazol-4-yl)boronic Acid MIDA Ester (**9**).* A general procedure was followed using ethynyl MIDA boronate (55 mg, 0.3 mmol) and benzylazide (40 mg, 0.3 mmol) and copper(II) acetate monohydrate (6 mg, 0.03 mmol), affording desired product as an off-white powder (74 mg, 78% yield). Melting point: 222−225 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ = 8.10 (s, 1 H), 7.23−7.42 (m, 5 H), 5.61 (s, 2 H), 4.33 (d, J = 17.7 Hz, 2 H), 4.07 (d, J = 17.7 Hz, 2 H), 2.60 ppm (s, 3 H). ^{13}C NMR (DMSO-d_6, 101 MHz): δ = 169.0, 136.3,

129.7, 128.7, 128.0, 127.8, 61.5, 52.2, 47.4 ppm. HRMS (ESI-TOF) $[M + H]^+$ calculated for $C_{14}H_{15}BN_4O_4$: 315.1259; found: 315.1271.

*4-(1-Benzyl-1H-1,2,3-triazol-4-yl)benzonitrile (**10a**).* General procedure B was followed using **9** (65 mg, 0.21 mmol) and 4-bromobenzonitrile (47 mg, 0.26 mmol), affording desired product as a yellowish powder (36 mg, 67% yield). Melting point: 139−140 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ = 8.86 (s, 1 H), 8.05 (d, J = 8.5 Hz, 2 H), 7.92 (d, J = 8.5 Hz, 2 H), 7.32−7.50 (m, 5 H), 5.68 ppm (s, 2 H). ^{13}C NMR (DMSO-d_6, 101 MHz): δ = 145.1, 135.7, 135.1, 133.0, 128.8, 128.2, 127.9, 125.7, 123.3, 118.8, 110.1, 53.1 ppm. HRMS (ESI-TOF) $[M + H]^+$ calculated for $C_{16}H_{12}N_4$: 261.1135; found: 261.1148.

*5-(1-Benzyl-1H-1,2,3-triazol-4-yl)picolinonitrile (**10b**).* General procedure B was followed using **9** (65 mg, 0.21 mmol) and 5-bromopicolinonitrile (47 mg, 0.26 mmol). The crude product was purified by RP-HPLC (1−100% acetonitrile water with 3% 1-propanol as a modifier), affording desired product as a white solid (41 mg, 76% yield). Melting point: 163−164 °C. ^{1}H NMR (methanol-d_4, 400 MHz): δ = 9.16 (dd, J = 2.0, 1.0 Hz, 1 H), 8.60 (s, 1 H), 8.40 (dd, J = 8.1, 2.0 Hz, 1 H), 7.92 (dd, J = 8.1, 1.0 Hz, 1 H), 7.30−7.47 (m, 5 H), 5.68 ppm (s, 2 H). ^{13}C NMR (methanol-d_4, 101 MHz): δ = 149.2, 136.5, 134.9, 131.7, 130.1, 130.1, 129.7, 129.7, 129.2, 129.2, 124.2, 118.2, 55.3 ppm. HRMS (ESI-TOF) $[M + H]^+$ calculated for $C_{15}H_{11}N_5$: 262.1082; found: 262.1094.

*1-Benzyl-4-(4-(methylsulfonyl)phenyl)-1H-1,2,3-triazole (**10c**).* General procedure B was followed using **9** (65 mg, 0.21 mmol) and 1-bromo-4-(methylsulfonyl)benzene (60.8 mg, 0.259 mmol), affording desired product as an off-white powder (48 mg, 74% yield). Melting point: 177−179 °C. ^{1}H NMR (methanol-d_4, 400 MHz): δ = 8.50 (s, 1 H), 8.04−8.12 (m, 2 H), 7.95−8.04 (m, 2 H), 7.35−7.44 (m, 5 H), 5.67 (s, 2 H), 3.14 ppm (s, 3 H). ^{13}C NMR (DMSO-d_6, 101 MHz): δ = 145.1, 135.7, 135.4, 128.8, 128.2, 128.0, 127.7, 125.7, 123.1, 66.7, 53.2, 43.5 ppm. HRMS (ESI-TOF) $[M + H]^+$ calculated for $C_{16}H_{15}N_3O_2S$ 314.0958; observed: 314.0968.

*tert-Butyl (3-(1-Benzyl-1H-1,2,3-triazol-4-yl)phenyl)carbamate (**10d**).* General procedure B was followed using **9** (65 mg, 0.21 mmol) and *tert*-butyl 3-bromophenylcarbamate (70.4 mg, 0.259 mmol), affording desired product as an off-white powder (49 mg, 68% yield). Melting point: 155−156 °C. ^{1}H NMR (methanol-d_4, 400 MHz): δ = 8.26 (s, 1 H), 7.79−7.86 (m, 1 H), 7.27−7.48 (m, 8 H), 5.63 (s, 2 H), 1.52 ppm (s, 9 H). ^{13}C NMR (methanol-d_4, 101 MHz): δ = 155.3, 149.2, 141.3, 136.8, 132.2, 130.4, 130.1, 129.6, 129.1, 122.3, 120.9, 119.6, 116.8, 81.0, 55.1, 28.7 ppm. HRMS (ESI-TOF) $[M + H]^+$ calculated for $C_{20}H_{22}N_4O_2$ 351.1816; found: 351.1823.

*3-(1-Benzyl-1H-1,2,3-triazol-4-yl)-1-tosyl-1H-indole (**10e**).* General procedure B was followed using **9** (65 mg, 0.21 mmol) and 3-bromo-1-(phenylsulfonyl)-1*H*-indole (87 mg, 0.259 mmol), affording desired product as an off-white powder (66 mg, 77% yield). Melting point: 212−213 °C. ^{1}H NMR (methanol-d_4, 400 MHz): δ = 8.41 (s, 1 H), 8.09 (s, 1 H), 8.03 (d, J = 8.6 Hz, 1 H), 7.93−8.00 (m, 3 H), 7.57−7.64 (m, 1 H), 7.46−7.56 (m, 2 H), 7.28−7.44 (m, 7 H), 5.67 ppm (s, 2 H). ^{13}C NMR (methanol-d_4, 101 MHz): δ = 141.4, 139.5, 138.6, 137.5, 137.2, 132.6, 131.5, 130.9, 130.8, 130.5, 129.4, 128.1, 126.7, 126.0, 124.8, 124.5, 116.0, 96.6, 55.8 ppm. HRMS (ESI-TOF) $[M + H]^+$ calculated for $C_{23}H_{18}N_4O_2S$: 415.1223; found: 415.1226.

*(1-(4-((Benzyloxy)carbamoyl)phenyl)-1H-1,2,3-triazol-4-yl)-boronic Acid MIDA Ester (**12a**).* A general procedure was followed using ethynyl MIDA boronate (57 mg, 0.32 mmol) and 4-(azidomethyl)-*N*-(benzyloxy)benzamide (89 mg, 0.32 mmol) and copper(II) acetate monohydrate (6.3 mg, 0.032 mmol), affording desired product as an off-white powder (121 mg, 83% yield). Melting point: 158−160 °C. ^{1}H NMR (acetonitrile-d_3, 400 MHz): δ = 9.87 (br s, 1 H), 7.91 (s, 1 H), 7.69 (d, J = 8.0 Hz, 2 H), 7.45−7.51 (m, 2 H), 7.36−7.45 (m, 3 H), 7.32 (d, J = 8.0 Hz, 2 H), 5.64 (s, 2 H), 4.96 (s, 2 H), 4.10 (d, J = 16.6 Hz, 2 H), 3.93 (d, J = 18.1 Hz, 2 H), 2.64 ppm (s, 3 H). ^{13}C NMR (acetonitrile-d_3, 101 MHz): δ = 169.6, 166.1, 141.3, 137.2, 133.6, 130.9, 130.6, 129.8, 129.7, 129.1, 128.9, 79.0, 62.9, 53.7, 48.6 ppm. HRMS (ESI-TOF) $[M + H]^+$ calculated for $C_{22}H_{22}BN_5O_6$: 464.1736; found: 464.1745.

*(1-((3S,5S)-5-(Methoxycarbonyl)-1-tosylpyrrolidin-3-yl)-1H-1,2,3-triazol-4-yl)boronic Acid MIDA Ester (**12b**).* A general procedure was followed using ethynyl MIDA boronate (50 mg 0.28 mmol) and (2*S*,4*S*)-methyl 4-azido-1-tosylpyrrolidine-2-carboxylate (90 mg, 0.28 mmol) and copper(II) acetate monohydrate (5.5 mg, 0.028 mmol), affording desired product as a white foam (123 mg 88% yield). ^{1}H NMR (acetonitrile-d_3, 400 MHz): δ = 7.93 (s, 1 H), 7.78−7.83 (m, 2 H), 7.47 (d, J = 8.0 Hz, 2 H), 4.90−4.99 (m, 1 H), 4.42 (dd, J = 9.3, 5.3 Hz, 1 H), 4.12 (d, J = 17.6 Hz, 2 H), 3.90−3.98 (m, 2 H), 3.85 (d, J = 5.5 Hz, 2 H), 3.66 (s, 3 H), 2.72−2.85 (m, 1 H), 2.56−2.65 (m, 1 H), 2.61 (s, 3 H), 2.47 ppm (s, 3 H). ^{13}C NMR (acetonitrile-d_3, 101 MHz): δ = 172.7, 169.6, 146.0, 135.4, 131.3, 129.6, 129.0, 62.8, 60.6, 58.7, 54.3, 53.5, 48.6, 37.2, 21.9 ppm. HRMS (ESI-TOF) $[M + H]^+$ calculated for $C_{20}H_{24}BN_5O_8S$: 506.1511; found: 506.1511.

*(R)-(1-((3-3-4-Fluorophenyl)-2-oxooxazolidin-5-yl)methyl)-1H-1,2,3-triazol-4-yl)boronic Acid MIDA Ester (**12c**).* A general procedure was followed using ethynyl MIDA boronate (50 mg, 0.28 mmol) and (*R*)-5-(azidomethyl)-3-(4-fluorophenyl)oxazolidin-2-one (65 mg, 0.28 mmol) and copper(II) acetate monohydrate (5.5 mg, 0.028 mmol), affording desired product as a white foam (99 mg, 86% yield). ^{1}H NMR (acetonitrile-d_3, 400 MHz): δ = 7.91 (s, 6 H), 7.31−7.41 (m, 2 H), 7.19 (dd, J = 8.8, 1.8 Hz, 1 H), 6.83−6.92 (m, 1 H), 5.09 (dd, J = 9.3, 4.3 Hz, 1 H), 4.76 (dd, J = 4.3, 2.3 Hz, 2 H), 4.17 (t, J = 9.5 Hz, 1 H), 4.04 (d, J = 3.5 Hz, 1 H), 4.09 (d, J = 3.5 Hz, 1 H), 3.82−3.94 (m, 3 H), 2.46 ppm (s, 3 H). ^{13}C NMR (acetonitrile-d_3, 101 MHz): δ = 169.5, 169.5, 165.3, 162.9, 155.1, 141.3, 141.2, 131.9, 131.8, 131.7, 114.9, 114.8, 111.7, 111.4, 106.6, 106.3, 72.1, 62.8, 53.1, 48.4 ppm. HRMS (ESI-TOF) $[M + H]^+$ calculated for $C_{17}H_{17}BFN_5O_6$: 418.1329; found: 418.1335.

*N-(Benzyloxy)-4-(4-(4-cyanophenyl)-1H-1,2,3-triazol-1-yl)-benzamide (**13a**).* General procedure B was followed using **12a** (105 mg, 0.23 mmol) and 4-bromobenzonitrile (52 mg, 0.28 mmol), affording desired product as an off-white powder (44 mg, 47% yield). Melting point: 193−195 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ = 11.81 (s, 1 H), 8.87 (s, 1 H), 8.05 (d, J = 8.5 Hz, 2 H), 7.92 (d, J = 8.5 Hz, 2 H), 7.76 (d, J = 8.0 Hz, 2 H), 7.29−7.52 (m, 7 H), 5.75 (s, 2 H), 4.91 ppm (s, 2 H). ^{13}C NMR (DMSO-d_6, 101 MHz): δ = 163.7, 145.0, 139.1, 135.7, 134.9, 132.9, 132.0, 128.9, 128.2, 127.9, 127.5, 125.6, 123.3, 118.7, 110.0, 76.9, 52.6, 38.7 ppm. HRMS (ESI-TOF) $[M + H]^+$ calculated for $C_{24}H_{19}N_5O_2$: 410.1612; found: 410.1618.

*(2S,4S)-Methyl 4-(4-(4-Cyanophenyl)-1H-1,2,3-triazol-1-yl)-1-tosylpyrrolidine-2-carboxylate (**13b**).* General procedure B was followed using **12b** (101 mg, 0.20 mmol) and 4-bromobenzonitrile (46 mg, 0.25 mmol), affording desired product as a yellowish powder (37 mg, 41% yield). Melting point: 184−186 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ = 8.89 (s, 1 H), 7.98−8.03 (m, 2 H), 7.92−7.96 (m, 2 H), 7.81 (d, J = 8.0 Hz, 2 H), 7.49 (d, J = 8.0 Hz, 2 H), 5.04 (t, J = 6.3 Hz, 1 H), 4.48 (dd, J = 9.0, 5.5 Hz, 1 H), 3.86 (t, J = 6.3 Hz, 2 H), 3.59 (s, 3 H), 2.78 (dd, J = 6.8, 2.3 Hz, 1 H), 2.58−2.71 (m, 1 H), 2.43 ppm (s, 3 H). ^{13}C NMR (DMSO-d_6, 101 MHz): δ = 171.0, 144.8, 144.1, 134.9, 133.7, 133.1, 130.1, 127.5, 125.6, 122.4, 118.8, 110.2, 59.0, 57.7, 52.5, 52.3, 35.3, 21.0 ppm. HRMS (ESI-TOF) $[M + H]^+$ calculated for $C_{22}H_{21}N_5O_4S$: 452.1387; found: 452.1389.

*(R)-4-(1-((3-(3-Fluorophenyl)-2-oxooxazolidin-5-yl)methyl)-1H-1,2,3-triazol-4-yl)benzonitrile (**13c**).* General procedure B was followed using **12c** (83 mg, 0.20 mmol) and 4-bromobenzonitrile (46 mg, 0.25 mmol), affording desired product as a yellowish powder (26 mg, 36% yield). Melting point: 216−217 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ = 8.86 (s, 1 H), 8.06 (d, J = 8.0 Hz, 2 H), 7.94 (d, J = 8.5 Hz, 2 H), 7.37−7.48 (m, 2 H), 7.27 (dd, J = 7.5, 2.0 Hz, 1 H), 6.97 (td, J = 8.3, 2.0 Hz, 1 H), 5.20 (dd, J = 8.5, 5.5 Hz, 1 H), 4.91 (d, J = 5.5 Hz, 2 H), 4.29 (t, J = 9.0 Hz, 1 H), 3.96 ppm (dd, J = 9.5, 6.0 Hz, 1 H). ^{13}C NMR (DMSO-d_6, 101 MHz): δ = 163.3, 160.9, 153.3, 144.7, 139.7, 139.6, 134.8, 132.9, 130.6, 130.5, 125.7, 124.0, 118.7, 113.6, 110.2, 110.1, 110.0, 105.1, 104.8, 70.8, 52.1, 47.0, 38.7 ppm. HRMS (ESI-TOF) $[M + H]^+$ calculated for $C_{19}H_{14}FN_5O_2$: 364.1204; found: 364.1211.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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