METHOD FOR ITERATIVE N-C AND C-C BOND FORMATION

RELATED APPLICATIONS

This application claims the benefit of priority to U.S. Provisional Application No. 63/569,496, filed March 25, 2024; the contents of which is incorporated by reference.

STATEMENT OF GOVERNMENT SUPPORT

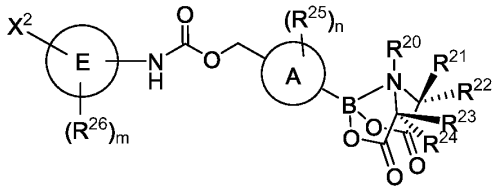
This invention was made with government support under 2019897 awarded by the National Science Foundation. The government has certain rights in the invention.

BACKGROUND

MIDA and TIDA boronates are used as carbon-based iteration-enabling groups that reversibly attenuate the reactivity of carbon atoms and enable generalized purification via catch and release chromatography. This enables modules to be linked iteratively via C-C bonds. Module-linking N-C bonds also appear in many types of medicines, materials, and other functional molecules, but the ability to iteratively connect modules with a nitrogen, instead of a carbon, atom as the iteration handle, remained an unresolved challenge. The required bifunctional halo-amino building blocks would undergo uncontrolled oligomerization under cross-coupling conditions and known N-protecting groups would not enable generalized purification compatible with automation. In view of the foregoing, there is an unmet need to develop a nitrogen iteration handle.

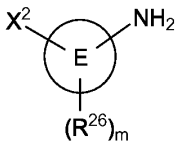
SUMMARY OF THE INVENTION

In certain aspects, provided herein are methods of making a compound of formula (I):



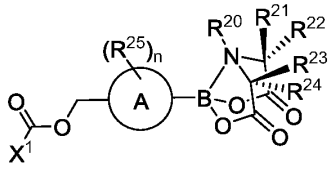
(I);

comprising combining a compound of formula (II):



(**II**);

and a compound of formula (III):



(**III**);

thereby forming the compound of Formula I;

wherein:

A is aryl or heteroaryl;

E is aryl or heteroaryl;

B is a boron having sp^3 hybridization;

n is an integer selected from 1, 2, 3, or 4;

m is an integer selected from 0, 1, 2, 3, or 4;

X^1 is halogen or $-OR^j$;

X^2 is halogen;

R^j is selected from the group consisting of alkyl, nitrophenyl, pentafluorophenyl, and $-N(C(O)CH_2)_2$;

R^{20} is selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, and aryl;

R^{21} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, and heteroaralkyl;

R^{22} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, and heteroaralkyl;

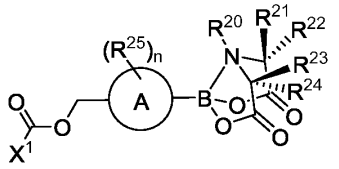
R^{23} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, and heteroaralkyl;

R^{24} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, and heteroaralkyl;

R^{25} is, independently for each occurrence, selected from the group consisting of H, alkyl, cycloalkyl, alkoxy, hydroxyl, halogen, acyl, aryl, heteroaryl, heterocyclyl, cyano, nitro, and sulfonyl; and

R^{26} is, independently for each occurrence, selected from the group consisting of H, alkyl, cycloalkyl, alkoxy, hydroxyl, acyl, aryl, heteroaryl, heterocyclyl, cyano, nitro, and sulfonyl.

In further aspects, provided herein are compounds of Formula (I):



(I)

or a salt thereof;

wherein:

A is aryl or heteroaryl;

B is a boron having sp^3 hybridization;

n is an integer selected from 1, 2, 3, or 4;

X^1 is halogen or OR^j;

R^j is selected from the group consisting of alkyl, nitrophenyl, pentafluorophenyl, and $-N(C(O)CH_2)_2$;

R^{20} is selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, and aryl;

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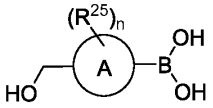
R^{22} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, and heteroaryl;

R^{23} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, and heteroaryl;

R^{24} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, and heteroaryl; and

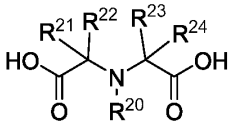
R^{25} is, independently for each occurrence, selected from the group consisting of H, alkyl, cycloalkyl, alkoxy, hydroxyl, halogen, acyl, aryl, heteroaryl, heterocyclyl, cyano, nitro, and sulfonyl.

In yet further aspects, provided are methods of making a compound of Formula (I), wherein the method comprises combining a compound of Formula (XII):



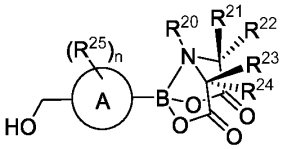
(**XII**);

and a compound of Formula (XIII):



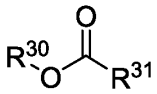
(**XIII**);

thereby forming a compound of Formula (XIV):



(**XIV**);

and further combining the compound of Formula (XIV) and a compound of Formula (XV):



(**XV**);

thereby forming the compound of Formula (I);

wherein:

A is aryl or heteroaryl;

B is a boron having sp^3 hybridization;

n is an integer selected from 1, 2, 3, or 4;

X^1 is halogen or OR^j;

R^j is nitrophenyl;

R^{20} is selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, and aryl;

R^{21} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, and heteroaralkyl;

R^{22} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, and heteroaralkyl;

R^{23} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, and heteroaralkyl;

R^{24} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, and heteroaralkyl;

R^{25} is, independently for each occurrence, selected from the group consisting of H, alkyl, cycloalkyl, alkoxy, hydroxyl, halogen, acyl, aryl, heteroaryl, heterocyclyl, cyano, nitro, and sulfonyl;

R^{30} is haloalkyl or nitrophenyl; and

R^{31} is –(O)haloalkyl or halogen.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1A shows molecules inaccessible via iterative cross-coupling due to lack of an N-iteration-enabling group.

FIG. 1B shows a schematic of the installation of CBzT-Cl on free amines.

FIG. 1C shows a schematic demonstrating that CBzT enables iterative and automated N-C bond formation.

FIG. 1D shows a schematic of iterative automated C-N bond formation as enabled by CBzT.

FIG. 2A shows a schematic of the synthesis and installation of CBzT.

FIG. 2B shows an example of catch-and-release purification of a CBzT-amine.

FIG. 2C shows thin-layer chromatography results of a catch-and-release purification of a CBzT-amine.

FIG. 2D shows an example of catch-and-release purification for a Buchwald-Hartwig coupling.

FIG. 3A shows a schematic of the purification of amines with a tolBTIDA byproduct.

FIG. 3B shows an example of the purification of amines with a *p*-cresol byproduct.

FIG. 3C shows an example of "catch and kill" purification.

FIG. 4 shows images of the automated platform for iterative N-C and C-C bond formation.

FIG. 5 shows the crystal structure of CBzT-Cl, as solved through X-ray diffraction.

FIG. 6 shows the crystal structure of compound **5**, as solved through X-ray diffraction.

FIG. 7 shows the crystal structure of compound **8**, as solved through X-ray diffraction.

FIG. 8 shows the crystal structure of compound **19**, as solved through X-ray diffraction.

FIG. 9A shows the results of a thin-layer chromatography experiment demonstrating that CBzT-amines show binary elution properties on silica gel.

FIG. 9B shows the results of a thin-layer chromatography experiment demonstrating that CBz-amines lack binary elution properties on silica gel.

FIG. 10 shows the design of the anhydrous automated reaction module.

FIG. 11 shows the design of the aqueous automated reaction module.

FIG. 12 shows the design of the catch-and-release purification module.

FIG. 13 shows proton NMR spectra comparing an imatinib standard to a sample produced via automated synthesis.

DETAILED DESCRIPTION OF THE INVENTION

Small molecule solutions to many contemporary societal challenges await discovery, but the artisanal and manual process via which this class of chemical manner is typically accessed limits the discovery of new functions. Automated iterative cross-coupling with MIDA or TIDA boronates alternatively enables generalized and automated preparation of many different types of small molecules. But in its current form, this engine cannot leverage nitrogen atoms as iteration handles. Here, a new *iteration-enabling group*, CbzT, is disclosed, that reversibly attenuates the reactivity of nitrogen atoms and enables generalized catch and release purification. CBzT is leveraged to achieve the automated modular synthesis of Imatinib (Gleevec), an archetypical clinically approved kinase inhibitor, in which building blocks are iteratively linked by both N-C and C-C bonds. This work substantially expands the types of small molecules that can be made in an automated modular fashion. It also advances the concept of intentionally developing chemistry that machines can do.

Small molecules are represented as powerful tools with largely untapped potential to help solve frontier societal challenges in the fields of medicine, materials, energy, agriculture, and more. Many such compounds can be viewed as collections of functional modules connected via C-C and N-C bonds (**FIG. 1A**). However, the highly customized, specialist-dependent, and manual process typically utilized to synthesize such compounds hinders the ability to rapidly discover novel small molecule functions. In contrast, the synthesis of biopolymers/oligomers such as polypeptides, oligonucleotides, and oligosaccharides can now be performed automatically. These

platforms represent modular synthesis engines in which prefabricated building blocks are iteratively linked using a bounded set of chemical reactions and a general purification strategy. A similar approach to generate small molecules, dubbed iterative cross-coupling (ICC), has emerged and its modularity makes it inherently automatable. This platform has enabled the modular synthesis of many different types of small molecules with myriad functions. Considering that multi-step synthesis automation has the potential to accelerate the discovery of new functional molecules while also allowing non-experts to construct molecules for their unique applications, the expansion of ICC and automation to new functional spaces represents an important step towards democratizing small molecule synthesis. ICC leverages halogen- and boron-containing bifunctional building blocks (called haloboronic acids), increasingly general iterative Suzuki-Miyaura cross-coupling reactions, and a general purification strategy. Specifically, MIDA and TIDA boronates are used as carbon-based iteration-enabling groups that reversibly attenuate the reactivity of carbon atoms and enable generalized purification via "catch-and-release" chromatography. This enables functional modules to be linked iteratively via C-C bonds using iterative cycles of coupling (C), purification (P), and deprotection (D).

Module-linking N-C bonds also appear in many types of medicines, materials, and other functional molecules (**FIG. 1A**), but the ability to iteratively connect modules with a nitrogen, instead of a carbon, atom as the iteration handle remained an unresolved challenge. The required bifunctional halo-amine building blocks would undergo potential uncontrolled oligomerization and other undesired side reactions under cross-coupling conditions, and known N-protecting groups would not enable generalized purification compatible with automation (**FIG. 1B**). Herein, a novel reagent, p-TIDA boronate-substituted benzyl chloroformate (CbzT-Cl) (**1**) (**FIG. 1C**), is described that enables iterative N-C bond formation by reversibly attenuating the reactivity of amines and permitting automation-friendly generalized purification via "catch-and-release" chromatography (**FIG. 1D**). To add N-C bond formation into the ICC strategy, incorporation of a general purification handle, in the form of the highly stable TIDA boronate group, into a robust and well-characterized nitrogen protecting group was specifically envisioned. It was anticipated that such an iteration enabling group would both prevent undesired oligomerization and enable generalized and automated purification due to the remarkably general binary elution properties of TIDA boronates on silica gel. After surveying common amine protecting groups, benzyl chloroformate was identified as an especially promising scaffold due to its easily modifiable core

structure, ease of introduction with a wide range of amines, the expected stability of the corresponding benzyl carbamates under cross-coupling conditions, and the facility with which such motifs can be removed under orthogonal conditions.

Synthesis of CbzT chloride (**1**) proceeded via TIDA complexation of (4-(hydroxymethyl)phenyl)boronic acid followed by nucleophilic substitution of triphosgene (**FIG. 2A**). CbzT-Cl is a crystalline, bench stable solid that was prepared on gram scale and stored on a benchtop in a sealed vial under air. Additionally, it can be prepared and used directly after concentration of the crude reaction mixture without further purification. A variety of bases were tested for the installation of CbzT onto 3-bromoaniline (**4**), but most of these provided a mixture of undesired byproducts such as the benzyl chloride, akin to previous reports. Potassium phosphate provided 66% yield of the desired CbzT protected amine (**5**), but exogenous base-free conditions afforded the highest yield of 90% (**FIG. 2B**). Additionally, in some cases it was found that CbzT-carbonate (**S2**) can provide increased yields compared to the CbzT-Cl (**1**), although **1** is more general across the scope of amines tested. With bifunctional block **5** in hand, it was first tested if the targeted chemoselective coupling step could be achieved. It was specifically asked if bifunctional halo-CbzT-amines could be engaged as electrophiles in cross-coupling with chemoselective reactivity at the halide terminus without undesired oligomerization at the amine-terminus. Buchwald-Hartwig cross-coupling of **6** with bifunctional bromo-CbzT-amine **5** proceeded with high efficiency for the desired product **7** (**FIG. 2C**). The purification step was next tested.

It was hypothesized that CbzT groups would exhibit the same binary affinity for silica gel that enable C-centered MIDA and TIDA boronates to be purified via general and machine-friendly "catch-and-release" chromatography (**FIG. 2D**). This hypothesis was confirmed via TLC analysis of a variety of CbzT-amines, while Cbz-amines submitted to the same conditions did not show binary elution properties. "Catch-and-release" purification of the crude reaction mixture from the reaction of **5** and **6** was also attempted and **7** was obtained in 70% yield and high purity. Specifically, the mixture derived from the coupling of **5** and **6** was loaded onto a silica gel plug and then byproducts/impurities were removed by eluting with diethyl ether. During this step, the cross-coupling product (**7**) containing the CbzT-group was retained on the silica gel. A second elution with a more polar solvent (ethyl acetate) was then performed, releasing purified product **7** (**FIG. 2D**) (Similar results were obtained using acetone as the release solvent). The deprotection

of TIDA boronates only yields TIDA as a byproduct, which is easily removed during an aqueous work-up. To complete the targeted iterable sequence of coupling, purification, and deprotection sequence, ways to deprotect CbzT-amines while creating product mixtures that could be purified in a simple and automation-friendly manner were explored. Two alternative strategies relying on conversion of CbzT into volatile CO_2 and other easily removed byproduct were ideated. In the first approach, the use of Pd-mediated hydrogenation to cleave the CbzT group and generate tolyl TIDA boronate (tolBTIDA, **10**) (**FIG. 3A**) was targeted.

Simple removal of **10** using silica gel as a capture resin was anticipated. After screening a variety of conditions (**Example 2**), it was found that the deprotection of **8** was achieved in an automation-friendly way via treatment with catalytic palladium on carbon and sodium borohydride in >90% yield (**Example 2** entries 2,3). Similar results were obtained with **7** (**Example 2**). Subsequent purification of product **12** was achieved by running the optimized deprotection conditions on **7**, loading the crude reaction mixture onto a silica plug with hexanes and flushing with Et_2O to elute the free amine **12** while retaining TIDA boronate-containing **10** on the silica plug. This simple procedure afforded purified 12 in 93% isolated yield and excellent purity. In the second approach, an alternative protocol to provide flexibility for substrates that may not be compatible with reactions mediated by unligated palladium, such as those that are rich in heteroatoms, was sought. Conditions that would similarly liberate CO_2 but alternatively generate p-cresol **11** as a byproduct (**FIG. 3B**), which could presumably be separated with a silica gel plug due to its anticipated decreased polarity relative to free amine products, were specifically envisioned. In this vein, it was found that hydrolysis and oxidation of the TIDA boronic ester using $LiOH/H_2O_2$ liberated p-cresol **11** and desired free amine products for both **8** and **7** (**Example 2**). The corresponding free amine products were readily purified via silica plug by first eluting p-cresol and other undesired reaction byproducts with hexanes, and then releasing the free amine using diethyl ether.

Having developed methods to complete the targeted couple, purify, and deprotect sequences, it was tested if the CbzT protecting group could enable iterative N-C and/or C-C bond formation. Two trimers were first aimed to be manually generated, the first of these requiring two iterative N-C bond forming reactions and the second requiring C-C bond followed by N-C bond formation (**Example 3**). Synthesis of the first trimer proceeded via the previously described Buchwald-Hartwig cross-coupling of **6** with bifunctional CbzT-protected haloamine **5** followed

by "catch-and-release" purification to provide **7**. Deprotection of **7** with removal of **10** using silica gel as a capture resin proceeded smoothly to provide purified **12**. The free amine product (**12**) was then submitted to amide bond formation conditions with benzoic acid (**13**) to forge trimer **14** in 45% yield. Synthesis of the second trimer proceeded via Suzuki-Miyaura cross-coupling of pinacol boronic ester **15** with **5** and then "catch-and-release" purification to obtain the purified dimeric coupling product (**16**) in >90% yield. Deprotection and silica gel capture-mediated removal of **10** provided free amine **17** in >90% yield. Subsequent Buchwald-Hartwig coupling with bromobenzene (**18**) produced the desired trimer product (**19**) in 95% yield. In most cases, "catch-and-release" purification yields products with very high purity. In cases where minor impurities are present, they are not significant enough to affect the outcome of subsequent reactions.

Having established the viability of the newly developed N-C and/or C-C bond forming iterative cross-coupling platform, a new synthesis machine capable of automatically executing the coupling, deprotection, and purification steps described above was constructed (**FIG. 5**). Building on previous advances from the group, the synthesis machine integrates several key components via a LabVIEW interface: 40 mL scintillation vials as reaction vessels, hot plates with aluminum blocks for heating and magnetic stirring, disposable "catch-and-release" cartridges, a syringe pump for liquid transfer, multiport valve assemblies, and a rotary evaporator system for solvent evaporation. The system maintains an argon atmosphere through an automated Schlenk protocol enabled by a high vacuum pump that also serves vacuum-driven fluid transfer. Leveraging this synthesis machine and the established coupling, purification, and deprotection protocols, an additional three trimers were set out to be constructed, this time in a fully automated manner (**Example 5**). First, trimers **25**, **30** and **36** were synthesized manually with intermediate isolated and characterized. Then, these synthetic procedures were translated to the synthesis machine and performed in series without any characterization of intermediates. Synthesis of the trimer **25** proceeded via Suzuki-Miyaura cross-coupling of pinacol boronic ester **20** with bifunctional CbzT-protected haloamine **21** and then "catch-and-release" purification to obtain the purified dimer product (**20**) in >90% yield. Deprotection and silica gel capture-mediated to remove **10** provided free amine **23** in 90% yield. Subsequent amide coupling with benzoyl chloride (**24**) resulted in the desired trimer product (**25**) in 88% yield.

Synthesis of trimer **30** proceeded via Suzuki-Miyaura cross-coupling of boronic acid neopentylglycol ester **26** with bifunctional CbzT-protected haloamine **5** and then "catch-and-release" purification to obtain the dimeric coupling product (**27**) in >90% yield. Deprotection provided free amine **28** in 40% yield. Amide coupling with pentanoyl chloride (**29**) produced the desired trimer product (**30**) in 35% yield. Synthesis of trimer **36** proceeded via the Buchwald-Hartwig cross-coupling of **31** with bifunctional CbzT-protected haloamine **32** followed by "catch-and-release" purification to provide **33** in 84% yield. Deprotection of **33** provided **34** in 38% yield. The free amine product (**34**) was submitted to another Buchwald-Hartwig cross-coupling with halogen **35** to forge the trimer **36** in 52% yield. Notably, all three of these automated modular syntheses afforded >10 mg of the purified trimer products. Finally, an FDA approved kinase inhibitor rich in N-C and C-C bond-based module connections was set out to be automatically synthesized. Kinase inhibitors represent a very important subset of anticancer drugs that could in theory be rapidly accessed via the automated iterative cross-coupling strategy. Notably, more than 90% of the 538 human kinases have not yet been drugged. Imatinib (Gleevec®) was identified as an archetypical test for the new platform (**Example 6**).

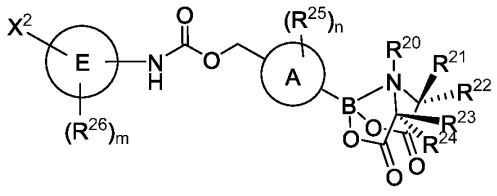
This molecule posed a notable challenge because it required three difficult coupling reactions with heterocyclic building blocks, highly polar and thus challenging-to-purify intermediates, and many heteroatom-rich intermediates that could be incompatible with hydrogenation-based deprotection mediated by unligated palladium. Before fully automating the process, the proposed route was tested by hand and then each step was automated independently. Common Suzuki-Miyaura conditions were found to be unproductive for the coupling of **37** and **38**, likely due to well established challenges representative of heterocyclic substrates. Use of a variant of Denmark and coworkers' TMSOK-promoted coupling conditions, recently shown to be compatible with TIDA boronate-enabled automated synthesis, provided the desired coupling product (**39**) in 54% manual yield and 42% automated yield. Removal of the CbzT-group via treatment with Pd/NaBH4 followed by a modified sequence of eluents appropriate for such a polar product, generated free amine **40** in 75% manual yield and 50% automated yield. This amine was then engaged in a Buchwald-Hartwig coupling with CbzT-protected bifunctional haloamine **41** followed by "catch-and-release" purification providing the coupling product **42** in 60% manual yield and 55% automated yield. Heteroatom-rich intermediate (**42**) exhibited resistance to deprotection when using the Pd-mediated conditions. An opportunity to use the alternative

$LiOH/H_2O_2$ procedure and telescope into the final amide bond formation was recognized. The hydrolysis-oxidation-deprotection was successful, providing **43** in 60% manual yield and 49% automated yield.

Free amine **43** was subjected to amide bond-forming conditions with **44**, providing Imatinib in 68% manual yield and 60% automated yield. The lower automated yield may be due to loss of material that occurs when solutions are transferred between vessels through tubing. This process was then performed in a fully automated manner on the next-generation synthesis machine described above without any analytics or isolation of intermediates to yield 2 mg of imatinib after a final HPLC-based purification. This product was suitable in quantity and purity for what is required for testing in biological assays, which are now routinely conducted in miniaturized formats. In conclusion, a novel automation friendly iteration enabling group that reversibly attenuates the reactivity of amines while simultaneously enabling automated purification by "catch-and-release" chromatography was developed. The utility of this synthetic platform was demonstrated via the automated modular synthesis of imatinib, an archetypical kinase inhibitor. This expanded automated modular synthesis approach stands to enable the on-demand synthesis and testing of a wide range of drug candidates and incorporation of such capacity into AI-guided closed-loop discovery engines, similar to the way organic materials discovery has recently been enabled by automated modular small molecule synthesis. The CbzT group also has potential applications in the simplified prefabrication of diverse amine-containing building blocks. Finding increasingly general conditions for coupling, deprotection, and purification is a frontier and unmet challenge in chemical reaction development that will broadly enable automation. Together, this work emphasizes the impact of intentionally developing new synthetic methods explicitly to enable the automation of small molecule synthesis.

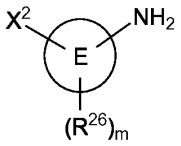
Methods of C-C/C-N Bond Formation

In certain aspects, disclosed herein are methods of making a compound of formula (I):



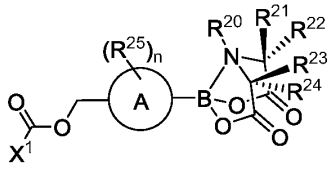
(I);

comprising combining a compound of formula (II):



(**II**);

and a compound of formula (III):



(**III**);

thereby forming the compound of Formula I;

wherein:

A is aryl or heteroaryl;

E is aryl or heteroaryl;

B is a boron having sp^3 hybridization;

n is an integer selected from 1, 2, 3, or 4;

m is an integer selected from 0, 1, 2, 3, or 4;

X^1 is halogen or $-OR^j$;

X^2 is halogen;

R^j is selected from the group consisting of alkyl, nitrophenyl, pentafluorophenyl, and $-N(C(O)CH_2)_2$;

R^{20} is selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, and aryl;

R^{21} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, and heteroaralkyl;

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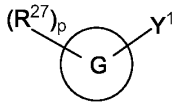
R^{24} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, and heteroaralkyl;

R^{25} is, independently for each occurrence, selected from the group consisting of H, alkyl, cycloalkyl, alkoxy, hydroxyl, halogen, acyl, aryl, heteroaryl, heterocyclyl, cyano, nitro, and sulfonyl; and

R^{26} is, independently for each occurrence, selected from the group consisting of H, alkyl, cycloalkyl, alkoxy, hydroxyl, acyl, aryl, heteroaryl, heterocyclyl, cyano, nitro, and sulfonyl.

In certain embodiments, the methods further comprise a base selected from the group consisting of triethylamine, pyridine, 2,6-lutidine, 1,8-diazabicyclo[5.4.0]undec-7-ene, 2,2,6,6-tetramethylpiperidine, $NaHCO_3$, K_2CO_3, $CsCO_3$, and K_3PO_4. In further embodiments, A is phenyl. In yet further embodiments, each of R^{21}, R^{22}, R^{23}, and R^{24} is methyl. In yet further embodiments, each of R^{20}, R^{21}, R^{22}, R^{23}, and R^{24} is methyl. In still further embodiments, R^{25} is H. In certain embodiments, X^1 is chloro or fluoro. In further embodiments, X^1 is chloro. In yet further embodiments, X^1 is OR^j. In still further embodiments, R^j is selected from the group consisting of methyl, ethyl, nitrophenyl, pentafluorophenyl, and $-N(C(O)CH_2)_2$. In certain embodiments, X^2 is bromo or iodo.

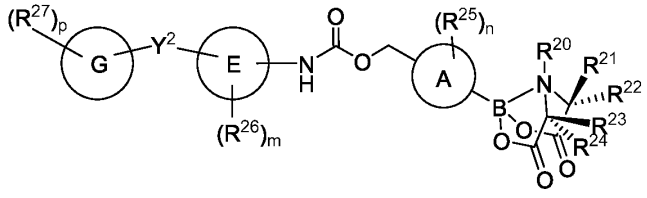
In further embodiments, the methods further comprise combining the compound of Formula (I), a compound of Formula (V):



(**V**);

a palladium catalyst, and a base;

thereby forming a compound of Formula (IV):



(**IV**);

wherein:

G is aryl or heteroaryl;

p is an integer selected from 0, 1, 2, 3, and 4;

R^{27} is, independently for each occurrence, selected from the group consisting of H, alkyl, cycloalkyl, alkoxy, hydroxyl, halogen, acyl, aryl, heteroaryl, heterocyclyl, cyano, nitro, and sulfonyl;

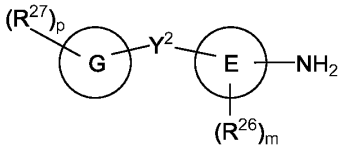
Y^1 is selected from the group consisting of -NH_2, -B(pin), -B(neop), -B(dan), -B(MIDA), and -$B(OH)_2$; and

Y^2 is -NH- or is a bond.

In yet further embodiments, Y^1 is -NH_2. In still further embodiments, Y^1 is -$B(OH)_2$. In certain embodiments, Y^2 is -NH-. In further embodiments, Y^2 is a bond. In yet further embodiments, the palladium catalyst is a Buchwald precatalyst. Buchwald precatalysts are transition metal complexes used in, for example, cross-coupling reactions, and are of the general form (L(M) G1–G4), wherein L is a ligand, M is a transition metal, such as palladium, and G indicates the generational series, for example, (XPhos)Pd G3. A list of transition metal catalysts, including Buchwald precatalysts, used in this disclosure and their standard nomenclature follows below. In still further embodiments, the palladium catalyst is selected from the group consisting of (t-Bu-XPhos)Pd G3 [(2-dicyclohexylphosphino-2′,4′,6′-triisopropyl-1,1′-biphenyl)[2-(2′-amino-1,1′-biphenyl)] palladium(II) methanesulfonate], (t-Bu-XPhos)Pd G4 [(SP-4-3)-[2-di-tert-butylphosphino-2′,4′,6′-triisopropylbiphenyl[1,1′-biphenyl]-2-yl]phosphine](methanesulfonato-κO)[2′-(methylamino-κN)[1,1′-biphenyl]-2-yl-κC]palladium], (XPhos)Pd G3 [(2-dicyclohexylphosphino-2′,4′,6′-triisopropyl-1,1′-biphenyl)[2-(2′-amino-1,1′-biphenyl)] palladium(II) methanesulfonate], (XPhos)Pd G4 [(SP-4-3)-[dicyclohexyl[2′,4′,6′-tris(1-methylethyl)[1,1′-biphenyl]-2-yl]phosphine](methanesulfonato-κO)[2′-(methylamino-κN)[1,1′-biphenyl]-2-yl-κC]palladium], Pd(PPh_3)4 [tetrakis(triphenylphosphine)palladium(0)], (RuPhos)Pd G3 [(2-dicyclohexylphosphino-2′,6′-diisopropoxy-1,1′-biphenyl)[2-(2′-amino-1,1′-biphenyl)]palladium(II) methanesulfonate], (RuPhos)Pd G4 [[dicyclohexyl(2′,6′-diisopropoxy-2-biphenylyl)phosphine-κP](methanesulfonatato-κO)[2′-(methylamino-κN)-2-biphenylyl-κC2]palladium], (XantPhos)Pd G3 [[(4,5-bis(diphenylphosphino)-9,9-dimethylxanthene)-2-(2′-amino-1,1′-biphenyl)]palladium(II) methanesulfonate], (XantPhos)Pd G4 [(SP-4-3)-[[5-(diphenylphosphino)-9,9-dimethyl-9H-xanthen-4-yl]diphenylphosphine-κP](methanesulfonato-κO)[2′-(methylamino-κN)[1,1′-biphenyl]-2-yl-κC]- palladium], (t-Bu-P)$_3$Pd G3 [(tris(2-methyl-2-propanyl)phosphino-2′,6′-diisopropoxy-1,1′-biphenyl)[2-(2′-amino-1,1′-biphenyl)]palladium(II) methanesulfonate], (t-Bu-P)$_3$Pd G4 [(methanesulfonatato-κO)[2′-(methylamino-κN)-2-

biphenylyl-κC2][tris(2-methyl-2-propanyl)phosphine]palladium], (Sphos)Pd G3 [(2-dicyclohexylphosphino-2′,6′-dimethoxybiphenyl) [2-(2′-amino-1,1′-biphenyl)]palladium(II) methanesulfonate], (Sphos)Pd G4 [(methanesulfonato-κO)[2′-(methylamino)-2-biphenylyl]palladium – dicyclohexyl(2′,6′-dimethoxy-2-biphenylyl)phosphine], $Pd(Oac)_2$ [palladium(II) acetate], $(Pd)_2(DBA)_3$ [tris(dibenzylideneacetone)dipalladium(0)], and $Pd(PPh_3)_2(Cl)_2$ [bis(triphenylphosphine)palladium(II) dichloride]. In preferred embodiments, the palladium catalyst is (t-Bu-XPhos)Pd G3 or $(t\text{-Bu-P})_3Pd$ G4. In certain embodiments, the base is selected from the group consisting of potassium trimethylsilanolate, triethylamine, pyridine, 2,6-lutidine, 1,8-diazabicyclo[5.4.0]undec-7-ene, 2,2,6,6-tetramethylpiperidine, $NaHCO_3$, K_2CO_3, $CsCO_3$, and K_3PO_4. In further embodiments, the base is potassium trimethylsilanolate.

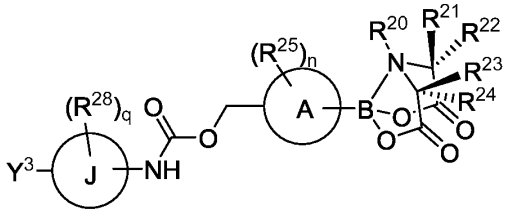
In yet further embodiments, the methods further comprise combining the compound of Formula (IV) and a reducing agent, thereby forming a compound of Formula (VI):



(**VI**).

In still further embodiments, the reducing agent is selected from the group consisting of BF_3•Oet_2, EtSH, TBAF, TMSI, Pd/C, H_2, and $NaBH_4$, or a combination of any of them. In certain embodiments, the reducing agent is the combination of Pd/C, $NaBH_4$ and H_2.

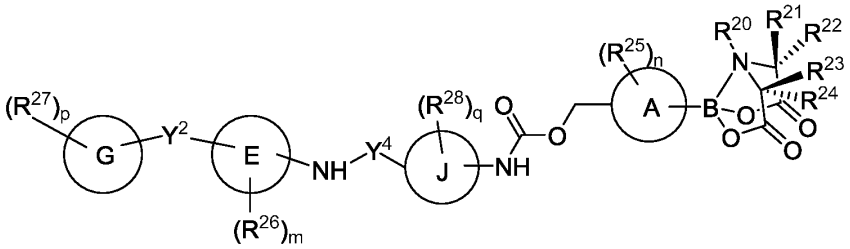
In further embodiments, the methods further comprise combining the compound of Formula (VI), a compound of Formula (VIII):



(**VIII**);

an activating agent, and a base;

thereby forming a compound of Formula (VII):



(**VII**);

wherein:

J is aryl or heteroaryl;

q is an integer selected from 0, 1, 2, 3, or 4;

R^{28} is, independently for each occurrence, selected from the group consisting of H, alkyl, cycloalkyl, alkoxy, hydroxyl, halogen, acyl, aryl, heteroaryl, heterocyclyl, cyano, nitro, and sulfonyl;

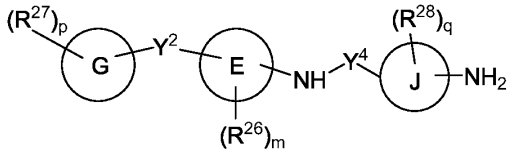
Y^3 is $-C(O)_2H$ or a carboxylate salt, and Y^4 is –C(O)-; or Y^3 is halogen, and Y^4 is a bond;

when Y^3 is $-CO_2H$ or a carboxylate salt, the activating agent is selected from the group consisting of propylphosphonic anhydride, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide, benzotriazole-1-yl-oxy-tris-(dimethylamino)-phosphonium hexafluorophosphate, 1-[(1-(cyano-2-ethoxy-2-oxoethylideneaminooxy) dimethylaminomorpholino)] uronium hexafluorophosphate, hexafluorophosphate azabenzotriazole tetramethyluronium, hexafluorophosphate benzotriazole tetramethyluronium, benzotriazol-1-yloxytripyrrolidinophosphonium hexafluorophosphate, and benzotriazol-1-yloxytris(dimethylamino)phosphonium hexafluorophosphate; and

when Y^3 is halogen, the activating agent is selected from the group consisting of $Pd(Oac)_2$, $(Sphos)Pd(Oac)_2$, (Sphos)Pd G3, and (Sphos)Pd G4.

In yet further embodiments, Y^3 is CO_2H or a carboxylate salt, and the activating agent is propylphosphonic anhydride; or wherein Y^3 is halogen, and the activating agent is $(Sphos)Pd(Oac)_2$. In still further embodiments, the base is pyridine or Cs_2CO_3.

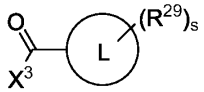
In certain embodiments, the methods disclosed herein further comprise combining the compound of Formula (VII) and an oxidizing agent, thereby forming a compound of Formula (IX):



(**IX**).

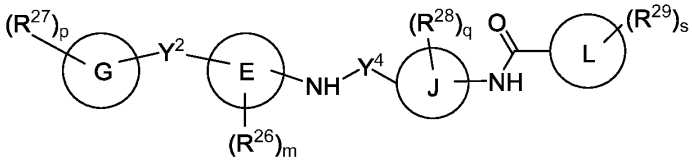
In further embodiments, the oxidizing agent is the combination of LiOH and H_2O_2.

In yet further embodiments, the methods disclosed herein further comprise combining the compound of Formula (IX), a compound of Formula (XI):



(**XI**),

and a base; thereby forming a compound of Formula (X):



(**X**);

wherein:

L is aryl or heteroaryl;

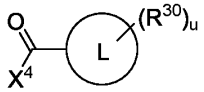
X^3 is halogen;

s is an integer selected from 0, 1, 2, 3, 4, or 5; and

R^{29} is, independently for each occurrence, selected from the group consisting of H, alkyl, cycloalkyl, heterocyclyl, heterocyclylalkyl, aryl, and heteroaryl.

In still further embodiments, the base is pyridine. In certain embodiments, X^3 is chloro. In further embodiments, L is phenyl. In yet further embodiments, R^{29} is N-methylpiperazinylmethylene. In still further embodiments, s is 1.

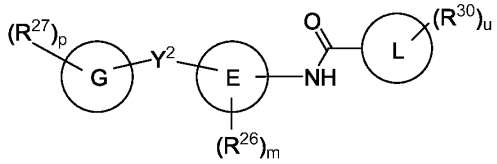
In certain embodiments, the methods disclosed herein further comprise combining the compound of Formula (VI), a compound of Formula (XII):



(**XII**);

and a base;

thereby forming a compound of Formula (XIII):



(**XIII**);

wherein:

L is aryl or heteroaryl;

X^4 is halogen;

u is an integer selected from 0, 1, 2, 3, 4, or 5; and

R^{30} is, independently for each occurrence, selected from the group consisting of H, alkyl, cycloalkyl, heterocyclyl, heterocyclylalkyl, aryl, and heteroaryl.

In further embodiments, L is aryl. In yet further embodiments, L is phenyl. In still further embodiments, X^4 is chloro. In certain embodiments, the base is pyridine.

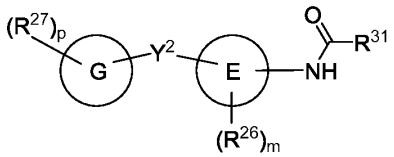
In further embodiments, the methods disclosed herein further comprise combining the compound of Formula (VI), a compound of Formula (XIV):



(**XIV**);

and a base;

thereby forming a compound of Formula (XV):



(**XV**);

wherein:

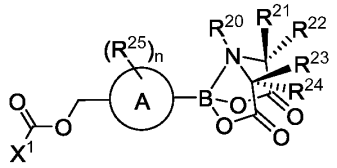
X^5 is halogen;

R^{31} is selected from the group consisting of H, alkyl, cycloalkyl, heterocyclyl, and heterocyclylalkyl.

In yet further embodiments, X^5 is chloro. In still further embodiments, R^{31} is alkyl. In certain embodiments, R^{31} is butyl. In further embodiments, the base is pyridine.

Compounds of the Disclosure, and Methods of Making Thereof

In another aspect, disclosed herein are compounds represented by Formula (I):



(I)

or a salt thereof;

wherein:

A is aryl or heteroaryl;

B is a boron having sp^3 hybridization;

n is an integer selected from 1, 2, 3, or 4;

X^1 is halogen or OR^j;

R^j is selected from the group consisting of alkyl, nitrophenyl, pentafluorophenyl, and $-N(C(O)CH_2)_2$;

R^{20} is selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, and aryl;

R^{21} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, and heteroaryl;

R^{22} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, and heteroaryl;

R^{23} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, and heteroaryl;

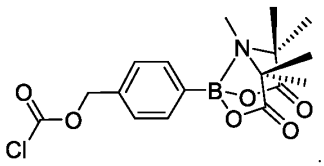
R^{24} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, and heteroaryl; and

R^{25} is, independently for each occurrence, selected from the group consisting of H, alkyl, cycloalkyl, alkoxy, hydroxyl, halogen, acyl, aryl, heteroaryl, heterocyclyl, cyano, nitro, and sulfonyl.

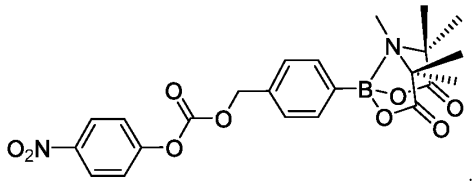
In certain embodiments, A is phenyl. In further embodiments, R^{25} is H. In yet further embodiments, at least one of R^{21}, R^{22}, R^{23}, or R^{24} is not H. In still further embodiments, at least two of R^{21}, R^{22}, R^{23}, or R^{24} are not H. In certain embodiments, at least three of R^{21}, R^{22}, R^{23}, or R^{24} are not H. In further embodiments, none of R^{21}, R^{22}, R^{23}, or R^{24} is H. In yet further embodiments, each of R^{21}, R^{22}, R^{23}, and R^{24} is methyl. In yet further embodiments, each of R^{20}, R^{21}, R^{22}, R^{23}, and R^{24} is methyl. In still further embodiments, X^1 is chloro or fluoro. In certain embodiments, X^1 is chloro. In further embodiments, X^1 is OR^j. In yet further embodiments, R^j is selected from the

group consisting of methyl, ethyl, nitrophenyl, pentafluorophenyl, and -N(C(O)CH$_2$)$_2$. In still further embodiments, R^j is 4-nitrophenyl.

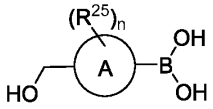
In certain embodiments, the compound is:



In further embodiments, the compound is:

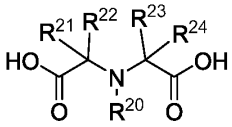


In yet another aspect, disclosed herein are methods of making a compound of Formula (I), wherein the method comprises combining a compound of Formula (XVI):



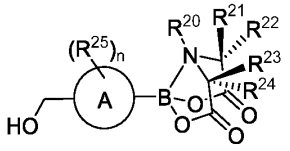
(XVI);

and a compound of Formula (XVII):



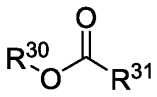
(XVII);

thereby forming a compound of Formula (XVIII):



(XVIII);

and further combining the compound of Formula (XVIII) and a compound of Formula (XIX):



(**XIX**);

thereby forming the compound of Formula (I);

wherein:

A is aryl or heteroaryl;

B is a boron having sp^3 hybridization;

n is an integer selected from 1, 2, 3, or 4;

X^1 is halogen or OR^j;

R^j is nitrophenyl;

R^{20} is selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, and aryl;

R^{21} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, and heteroaralkyl;

R^{22} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, and heteroaralkyl;

R^{23} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, and heteroaralkyl;

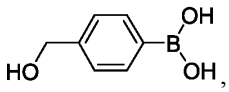
R^{24} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, and heteroaralkyl;

R^{25} is, independently for each occurrence, selected from the group consisting of H, alkyl, cycloalkyl, alkoxy, hydroxyl, halogen, acyl, aryl, heteroaryl, heterocyclyl, cyano, nitro, and sulfonyl;

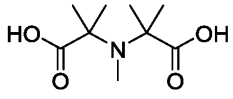
R^{30} is haloalkyl or nitrophenyl; and

R^{31} is –(O)haloalkyl or halogen.

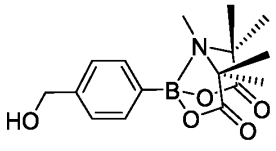
In certain embodiments, A is phenyl. In further embodiments, R^{25} is H. In yet further embodiments, X^1 is chloro or fluoro. In still further embodiments, X^1 is OR^j. In certain embodiments, R^j is 4-nitrophenyl. In yet further embodiments, each of R^{21}, R^{22}, R^{23}, and R^{24} is methyl. In further embodiments, each of R^{20}, R^{21}, R^{22}, R^{23}, and R^{24} is methyl. In yet further embodiments, R^{30} is $-C(Cl)_3$. In still further embodiments, R^{31} is $-O(C(Cl)_3)$. In certain embodiments, R^{30} is 4-nitrophenyl. In further embodiments, R^{31} is chloro. In yet further embodiments, the compound of Formula (XVI) is:


, or a salt thereof.

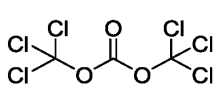
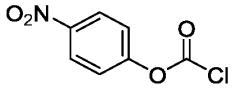
In still further embodiments, the compound of Formula (XVII) is:


, or a salt thereof.

In certain embodiments, the compound of Formula (XVIII) is:


, or a salt thereof.

In further embodiments, the compound of Formula (XIX) is selected from the group consisting of:


, and 
, or a salt thereof.

Definitions

The articles "a" and "an" are used herein to refer to one or to more than one (i.e., to at least one) of the grammatical object of the article. By way of example, "an element" means one element or more than one element.

The term "heteroatom" is art-recognized and refers to an atom of any element other than carbon or hydrogen. Illustrative heteroatoms include boron, nitrogen, oxygen, phosphorus, sulfur and selenium, and alternatively oxygen, nitrogen or sulfur.

The term "alkyl" as used herein is a term of art and refers to saturated aliphatic groups, including straight-chain alkyl groups, branched-chain alkyl groups, cycloalkyl (alicyclic) groups, alkyl substituted cycloalkyl groups, and cycloalkyl substituted alkyl groups. In certain embodiments, a straight-chain or branched-chain alkyl has about 30 or fewer carbon atoms in its backbone (e.g., C_1-C_{30} for straight chain, C_3-C_{30} for branched chain), and alternatively, about 20 or fewer, or 10 or fewer. In certain embodiments, the term "alkyl" refers to a C_1-C_{10} alkyl group.

In certain embodiments, the term "alkyl" refers to a C_1-C_6 alkyl group, for example a C_1-C_6 straight-chain alkyl group. In certain embodiments, the term "alkyl" refers to a C_3-C_{12} branched-chain alkyl group. In certain embodiments, the term "alkyl" refers to a C_3-C_8 branched-chain alkyl group. Representative examples of alkyl include, but are not limited to, methyl, ethyl, n-propyl, iso-propyl, n-butyl, sec-butyl, iso-butyl, tert-butyl, n-pentyl, isopentyl, neopentyl, and n-hexyl.

The term "cycloalkyl" means mono- or bicyclic or bridged saturated carbocyclic rings, each having from 3 to 12 carbon atoms. Certain cycloalkyls have from 5-12 carbon atoms in their ring structure, and may have 6-10 carbons in the ring structure. Preferably, cycloalkyl is (C_3-C_7)cycloalkyl, which represents a monocyclic saturated carbocyclic ring, having from 3 to 7 carbon atoms. Examples of monocyclic cycloalkyls include cyclopropyl, cyclobutyl, cyclopentyl, cyclopentenyl, cyclohexyl, cyclohexenyl, cycloheptyl, and cyclooctyl. Bicyclic cycloalkyl ring systems include bridged monocyclic rings and fused bicyclic rings. Bridged monocyclic rings contain a monocyclic cycloalkyl ring where two non-adjacent carbon atoms of the monocyclic ring are linked by an alkylene bridge of between one and three additional carbon atoms (*i.e.*, a bridging group of the form $-(CH_2)_w-$, where w is 1, 2, or 3). Representative examples of bicyclic ring systems include, but are not limited to, bicyclo[3.1.1]heptane, bicyclo[2.2.1]heptane, bicyclo[2.2.2]octane, bicyclo[3.2.2]nonane, bicyclo[3.3.1]nonane, and bicyclo[4.2.1]nonane. Fused bicyclic cycloalkyl ring systems contain a monocyclic cycloalkyl ring fused to either a phenyl, a monocyclic cycloalkyl, a monocyclic cycloalkenyl, a monocyclic heterocyclyl, or a monocyclic heteroaryl. The bridged or fused bicyclic cycloalkyl is attached to the parent molecular moiety through any carbon atom contained within the monocyclic cycloalkyl ring. Cycloalkyl groups are optionally substituted. In certain embodiments, the fused bicyclic cycloalkyl is a 5 or 6 membered monocyclic cycloalkyl ring fused to either a phenyl ring, a 5 or 6 membered monocyclic cycloalkyl, a 5 or 6 membered monocyclic cycloalkenyl, a 5 or 6 membered monocyclic heterocyclyl, or a 5 or 6 membered monocyclic heteroaryl, wherein the fused bicyclic cycloalkyl is optionally substituted.

The term "(cycloalkyl)alkyl" as used herein refers to an alkyl group substituted with one or more cycloalkyl groups. An example of cycloalkylalkyl is cyclohexylmethyl group.

The term "heterocycloalkyl" as used herein refers to a radical of a non-aromatic ring system, including, but not limited to, monocyclic, bicyclic, and tricyclic rings, which can be completely saturated or which can contain one or more units of unsaturation, for the avoidance of

doubt, the degree of unsaturation does not result in an aromatic ring system, and having 3 to 12 atoms including at least one heteroatom, such as nitrogen, oxygen, or sulfur. For purposes of exemplification, which should not be construed as limiting the scope of this invention, the following are examples of heterocyclic rings: aziridinyl, azirinyl, oxiranyl, thiiranyl, thiirenyl, dioxiranyl, diazirinyl, diazepanyl, 1,3-dioxanyl, 1,3-dioxolanyl, 1,3-dithiolanyl, 1,3-dithianyl, imidazolidinyl, isothiazolinyl, isothiazolidinyl, isoxazolinyl, isoxazolidinyl, azetyl, oxetanyl, oxetyl, thietanyl, thietyl, diazetidinyl, dioxetanyl, dioxetenyl, dithietanyl, dithietyl, dioxalanyl, oxazolyl, thiazolyl, triazinyl, isothiazolyl, isoxazolyl, azepines, azetidinyl, morpholinyl, oxadiazolinyl, oxadiazolidinyl, oxazolinyl, oxazolidinyl, oxopiperidinyl, oxopyrrolidinyl, piperazinyl, piperidinyl, pyranyl, pyrazolinyl, pyrazolidinyl, pyrrolinyl, pyrrolidinyl, quinuclidinyl, thiomorpholinyl, tetrahydropyranyl, tetrahydrofuranyl, tetrahydrothienyl, thiadiazolinyl, thiadiazolidinyl, thiazolinyl, thiazolidinyl, thiomorpholinyl, 1,1-dioxidothiomorpholinyl (thiomorpholine sulfone), thiopyranyl, trithianyl, and 2-azobicyclo[3.1.0]hexane. A heterocycloalkyl group is optionally substituted by one or more substituents as described below.

The term "(heterocycloalkyl)alkyl" as used herein refers to an alkyl group substituted with one or more heterocycloalkyl (i.e., heterocyclyl) groups.

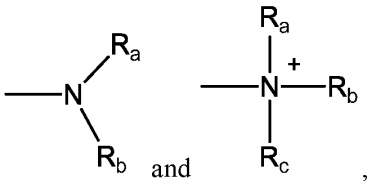
The term "alkenyl" as used herein means a straight or branched chain hydrocarbon radical containing from 2 to 10 carbons and containing at least one carbon-carbon double bond formed by the removal of two hydrogens. Representative examples of alkenyl include, but are not limited to, ethenyl, 2-propenyl, 2-methyl-2-propenyl, 3-butenyl, 4-pentenyl, 5-hexenyl, 2-heptenyl, 2-methyl-1-heptenyl, and 3-decenyl. The unsaturated bond(s) of the alkenyl group can be located anywhere in the moiety and can have either the (Z) or the (E) configuration about the double bond(s).

The term "alkynyl" as used herein means a straight or branched chain hydrocarbon radical containing from 2 to 10 carbon atoms and containing at least one carbon-carbon triple bond. Representative examples of alkynyl include, but are not limited, to acetylenyl, 1-propynyl, 2-propynyl, 3-butynyl, 2-pentynyl, and 1-butynyl.

The term "alkylene" is art-recognized, and as used herein pertains to a diradical obtained by removing two hydrogen atoms of an alkyl group, as defined above. In one embodiment an alkylene refers to a disubstituted alkane, i.e., an alkane substituted at two positions with

substituents such as halogen, azide, alkyl, arylalkyl, alkenyl, alkynyl, cycloalkyl, hydroxyl, alkoxyl, amino, nitro, sulfhydryl, imino, amido, phosphonate, phosphinate, carbonyl, carboxyl, silyl, ether, alkylthio, sulfonyl, sulfonamido, ketone, aldehyde, ester, heterocyclyl, aromatic or heteroaromatic moieties, fluoroalkyl (such as trifluromethyl), cyano, or the like. That is, in one embodiment, a "substituted alkyl" is an "alkylene".

The term "amino" is a term of art and as used herein refers to both unsubstituted and substituted amines, e.g., a moiety that may be represented by the general formulas:



,

wherein R_a, R_b, and R_c each independently represent a hydrogen, an alkyl, an alkenyl, $-(CH_2)_x-R_d$, or R_a and R_b, taken together with the N atom to which they are attached complete a heterocycle having from 4 to 8 atoms in the ring structure; R_d represents an aryl, a heteroaryl, a cycloalkyl, a cycloalkenyl, a heterocyclyl or a polycyclyl; and x is zero or an integer in the range of 1 to 8. In certain embodiments, only one of R_a or R_b may be a carbonyl, e.g., R_a, R_b, and the nitrogen together do not form an imide. In other embodiments, R_a and R_b (and optionally R_c) each independently represent a hydrogen, an alkyl, an alkenyl, or $-(CH_2)_x-R_d$. In certain embodiments, R_a and R_b are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, (cycloalkyl)alkyl, (heterocycloalkyl)alkyl, arylalkyl, heteroarylalkyl, alkoxyalkyl, or haloalkyl, any of which may be further substituted (e.g., by halogen, alkyl, alkoxy, hydroxy, and so forth). In certain embodiments, the term "amino" refers to $-NH_2$.

In certain embodiments, the term "alkylamino" refers to -NH(alkyl).

In certain embodiments, the term "dialkylamino" refers to $-N(alkyl)_2$.

The term "amido", as used herein, means -NHC(=O)-, wherein the amido group is bound to the parent molecular moiety through the nitrogen. Examples of amido include alkylamido such as $CH_3C(=O)N(H)-$ and $CH_3CH_2C(=O)N(H)-$.

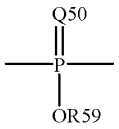
The term "acyl" is a term of art and as used herein refers to any group or radical of the form RCO- where R is any organic group, e.g., alkyl, aryl, heteroaryl, arylalkyl, and heteroarylalkyl. Representative acyl groups include acetyl, benzoyl, and malonyl.

The term "aminoalkyl" as used herein refers to an alkyl group substituted with one or more one amino groups. In one embodiment, the term "aminoalkyl" refers to an aminomethyl group, i.e., -CH_2NH_2.

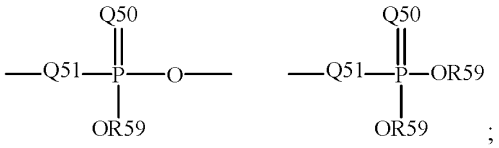
The term "aminoacyl" is a term of art and as used herein refers to an acyl group substituted with one or more amino groups.

The term "aminothionyl" as used herein refers to an analog of an aminoacyl in which the O of RC(O)- has been replaced by sulfur, hence is of the form RC(S)-.

The term "phosphoryl" is a term of art and as used herein may in general be represented by the formula:



wherein Q50 represents S or O, and R59 represents hydrogen, a lower alkyl or an aryl; for example, -P(O)(Ome)- or -$P(O)(OH)_2$. When used to substitute, e.g., an alkyl, the phosphoryl group of the phosphorylalkyl may be represented by the general formulas:



;

wherein Q50 and R59, each independently, are defined above, and Q51 represents O, S or N; for example, -O-P(O)(OH)Ome or -NH-$P(O)(OH)_2$. When Q50 is S, the phosphoryl moiety is a "phosphorothioate."

The term "aminophosphoryl" as used herein refers to a phosphoryl group substituted with at least one amino group, as defined herein; for example, -$P(O)(OH)Nme_2$.

The term "azide" or "azido", as used herein, means an $–N_3$ group.

The term "carbonyl" as used herein refers to -C(=O)-.

The term "thiocarbonyl" as used herein refers to -C(=S)-.

The term "alkylphosphoryl" as used herein refers to a phosphoryl group substituted with at least one alkyl group, as defined herein; for example, -P(O)(OH)Me.

The term "alkylthio" as used herein refers to alkyl-S-. The term "(alkylthio)alkyl" refers to an alkyl group substituted by an alkylthio group.

The term "carboxy", as used herein, means a -CO_2H group.

The term "aryl" is a term of art and as used herein refers to includes monocyclic, bicyclic and polycyclic aromatic hydrocarbon groups, for example, benzene, naphthalene, anthracene, and pyrene. Typically, an aryl group contains from 6-10 carbon ring atoms (i.e., (C_6-C_{10})aryl). The aromatic ring may be substituted at one or more ring positions with one or more substituents, such as halogen, azide, alkyl, arylalkyl, alkenyl, alkynyl, cycloalkyl, hydroxyl, alkoxyl, amino, nitro, sulfhydryl, imino, amido, phosphonate, phosphinate, carbonyl, carboxyl, silyl, ether, alkylthio, sulfonyl, sulfonamido, ketone, aldehyde, ester, heterocyclyl, aromatic or heteroaromatic moieties, fluoroalkyl (such as trifluromethyl), cyano, or the like. The term "aryl" also includes polycyclic ring systems having two or more cyclic rings in which two or more carbons are common to two adjoining rings (the rings are "fused rings") wherein at least one of the rings is an aromatic hydrocarbon, e.g., the other cyclic rings may be cycloalkyls, cycloalkenyls, cycloalkynyls, aryls, heteroaryls, and/or heterocyclyls. In certain embodiments, the term "aryl" refers to a phenyl group.

The term "heteroaryl" is a term of art and as used herein refers to a monocyclic, bicyclic, and polycyclic aromatic group having 3 to 12 total atoms including one or more heteroatoms such as nitrogen, oxygen, or sulfur in the ring structure. Exemplary heteroaryl groups include azaindolyl, benzo(b)thienyl, benzimidazolyl, benzofuranyl, benzoxazolyl, benzothiazolyl, benzothiadiazolyl, benzotriazolyl, benzoxadiazolyl, furanyl, imidazolyl, imidazopyridinyl, indolyl, indolinyl, indazolyl, isoindolinyl, isoxazolyl, isothiazolyl, isoquinolinyl, oxadiazolyl, oxazolyl, purinyl, pyranyl, pyrazinyl, pyrazolyl, pyridinyl, pyrimidinyl, pyrrolyl, pyrrolo[2,3-d]pyrimidinyl, pyrazolo[3,4-d]pyrimidinyl, quinolinyl, quinazolinyl, triazolyl, thiazolyl, thiophenyl, tetrahydroindolyl, tetrazolyl, thiadiazolyl, thienyl, thiomorpholinyl, triazolyl or tropanyl, and the like. The "heteroaryl" may be substituted at one or more ring positions with one or more substituents such as halogen, azide, alkyl, arylalkyl, alkenyl, alkynyl, cycloalkyl, hydroxyl, alkoxyl, amino, nitro, sulfhydryl, imino, amido, phosphonate, phosphinate, carbonyl, carboxyl, silyl, ether, alkylthio, sulfonyl, sulfonamido, ketone, aldehyde, ester, heterocyclyl, aromatic or heteroaromatic moieties, fluoroalkyl (such as trifluromethyl), cyano, or the like. The term "heteroaryl" also includes polycyclic ring systems having two or more cyclic rings in which two or more carbons are common to two adjoining rings (the rings are "fused rings") wherein at least one of the rings is an aromatic group having one or more heteroatoms in the ring structure, e.g., the other cyclic rings may be cycloalkyls, cycloalkenyls, cycloalkynyls, aryls, heteroaryls, and/or heterocyclyls.

The term "aralkyl" or "arylalkyl" is a term of art and as used herein refers to an alkyl group substituted with an aryl group, wherein the moiety is appended to the parent molecule through the alkyl group.

The term "heteroaralkyl" or "heteroarylalkyl" is a term of art and as used herein refers to an alkyl group substituted with a heteroaryl group, appended to the parent molecular moiety through the alkyl group.

The term "alkoxy" as used herein means an alkyl group, as defined herein, appended to the parent molecular moiety through an oxygen atom. Representative examples of alkoxy include, but are not limited to, methoxy, ethoxy, propoxy, 2-propoxy, butoxy, tert-butoxy, pentyloxy, and hexyloxy.

The term "alkoxyalkyl" refers to an alkyl group substituted by an alkoxy group.

The term "alkoxycarbonyl" means an alkoxy group, as defined herein, appended to the parent molecular moiety through a carbonyl group, represented by -C(=O)-, as defined herein. Representative examples of alkoxycarbonyl include, but are not limited to, methoxycarbonyl, ethoxycarbonyl, and *tert*-butoxycarbonyl.

The term "alkylcarbonyl", as used herein, means an alkyl group, as defined herein, appended to the parent molecular moiety through a carbonyl group, as defined herein. Representative examples of alkylcarbonyl include, but are not limited to, acetyl, 1-oxopropyl, 2,2-dimethyl-1-oxopropyl, 1-oxobutyl, and 1-oxopentyl.

The term "arylcarbonyl", as used herein, means an aryl group, as defined herein, appended to the parent molecular moiety through a carbonyl group, as defined herein. Representative examples of arylcarbonyl include, but are not limited to, benzoyl and (2-pyridinyl)carbonyl.

The term "alkylcarbonyloxy" and "arylcarbonyloxy", as used herein, means an alkylcarbonyl or arylcarbonyl group, as defined herein, appended to the parent molecular moiety through an oxygen atom. Representative examples of alkylcarbonyloxy include, but are not limited to, acetyloxy, ethylcarbonyloxy, and *tert*-butylcarbonyloxy. Representative examples of arylcarbonyloxy include, but are not limited to phenylcarbonyloxy.

The term "alkenoxy" or "alkenoxyl" means an alkenyl group, as defined herein, appended to the parent molecular moiety through an oxygen atom. Representative examples of alkenoxyl include, but are not limited to, 2-propen-1-oxyl (i.e., CH_2=CH-CH_2-O-) and vinyloxy (i.e., CH_2=CH-O-).

The term "aryloxy" as used herein means an aryl group, as defined herein, appended to the parent molecular moiety through an oxygen atom.

The term "heteroaryloxy" as used herein means a heteroaryl group, as defined herein, appended to the parent molecular moiety through an oxygen atom.

The term "carbocyclyl" as used herein means a monocyclic or multicyclic (e.g., bicyclic, tricyclic, etc.) hydrocarbon radical containing from 3 to 12 carbon atoms that is completely saturated or has one or more unsaturated bonds, and for the avoidance of doubt, the degree of unsaturation does not result in an aromatic ring system (e.g., phenyl). Examples of carbocyclyl groups include 1-cyclopropyl, 1-cyclobutyl, 2-cyclopentyl, 1-cyclopentenyl, 3-cyclohexyl, 1-cyclohexenyl and 2-cyclopentenylmethyl.

The term "cyano" is a term of art and as used herein refers to –CN.

The term "halo" is a term of art and as used herein refers to –F, –Cl, –Br, or –I.

The term "haloalkyl" as used herein refers to an alkyl group, as defined herein, wherein some or all of the hydrogens are replaced with halogen atoms.

The term "hydroxy" is a term of art and as used herein refers to –OH.

The term "hydroxyalkyl", as used herein, means at least one hydroxy group, as defined herein, is appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of hydroxyalkyl include, but are not limited to, hydroxymethyl, 2-hydroxyethyl, 3-hydroxypropyl, 2,3-dihydroxypentyl, and 2-ethyl-4-hydroxyheptyl.

The term "silyl", as used herein, includes hydrocarbyl derivatives of the silyl (H_3Si-) group (i.e., $(hydrocarbyl)_3Si$–), wherein a hydrocarbyl groups are univalent groups formed by removing a hydrogen atom from a hydrocarbon, e.g., ethyl, phenyl. The hydrocarbyl groups can be combinations of differing groups which can be varied in order to provide a number of silyl groups, such as trimethylsilyl (TMS), tert-butyldiphenylsilyl (TBDPS), tert-butyldimethylsilyl (TBS/TBDMS), triisopropylsilyl (TIPS), and [2-(trimethylsilyl)ethoxy]methyl (SEM).

The term "silyloxy", as used herein, means a silyl group, as defined herein, is appended to the parent molecule through an oxygen atom.

Certain compounds contained in compositions of the present invention may exist in particular geometric or stereoisomeric forms. In addition, compounds of the present invention may also be optically active. The present invention contemplates all such compounds, including *cis*- and *trans*-isomers, (*R*)- and (*S*)-enantiomers, diastereoisomers, (D)-isomers, (L)-isomers, the

racemic mixtures thereof, and other mixtures thereof, as falling within the scope of the invention. Additional asymmetric carbon atoms may be present in a substituent such as an alkyl group. All such isomers, as well as mixtures thereof, are intended to be included in this invention.

If, for instance, a particular enantiomer of compound of the present invention is desired, it may be prepared by asymmetric synthesis, or by derivation with a chiral auxiliary, where the resulting diastereomeric mixture is separated and the auxiliary group cleaved to provide the pure desired enantiomers. Alternatively, where the molecule contains a basic functional group, such as amino, or an acidic functional group, such as carboxyl, diastereomeric salts are formed with an appropriate optically-active acid or base, followed by resolution of the diastereomers thus formed by fractional crystallization or chromatographic means well known in the art, and subsequent recovery of the pure enantiomers.

It will be understood that "substitution" or "substituted with" includes the implicit proviso that such substitution is in accordance with permitted valence of the substituted atom and the substituent, and that the substitution results in a stable compound, e.g., which does not spontaneously undergo transformation such as by rearrangement, fragmentation, decomposition, cyclization, elimination, or other reaction.

The term "substituted" is also contemplated to include all permissible substituents of organic compounds. In a broad aspect, the permissible substituents include acyclic and cyclic, branched and unbranched, carbocyclic and heterocyclic, aromatic and nonaromatic substituents of organic compounds. Illustrative substituents include, for example, those described herein above. The permissible substituents may be one or more and the same or different for appropriate organic compounds. For purposes of this invention, the heteroatoms such as nitrogen may have hydrogen substituents and/or any permissible substituents of organic compounds described herein which satisfy the valences of the heteroatoms. This invention is not intended to be limited in any manner by the permissible substituents of organic compounds.

In certain embodiments, the optional substituents contemplated in this invention include halogen, azide, alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloalkyl, (cycloalkyl)alkyl, heterocyclyl, (heterocyclyl)alkyl, hydroxyl, alkoxyl, amino, aminoalkyl, nitro, sulfhydryl, imino, amido, phosphonate, phosphinate, carbonyl, carboxyl, silyl, ether (e.g., -alkylene-O(alkyl)), alkylthio, sulfonyl, sulfonamido, ketone (e.g., -CO(alkyl)), aldehyde (-

C(O)H), ester (e.g., -COO(alkyl)), haloalkyl, hydroxyalkyl, alkoxyalkyl, haloalkoxy, haloalkoxyalkyl, and cyano.

As used herein, the term "optionally substituted" or "substituted or unsubstituted" when it precedes a list of chemical moieties means that the list of chemical moieities that follow are each substituted or unsubstituted. For example, "substituted or unsubstituted aryl, heteroaryl, and cycloalkyl" or "optionally substituted aryl, heteroaryl, and cycloalkyl" means substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, and substituted or unsubstituted cycloalkyl.

The phrase "protecting group", as used herein, means temporary substituents which protect a potentially reactive functional group from undesired chemical transformations. Examples of such protecting groups include esters of carboxylic acids, silyl ethers of alcohols, and acetals and ketals of aldehydes and ketones, respectively. The field of protecting group chemistry has been reviewed (Greene, T.W.; Wuts, P.G.M. *Protective Groups in Organic Synthesis*, 2nd ed.; Wiley: New York, 1991). Protected forms of the inventive compounds are included within the scope of this invention.

For purposes of the invention, the chemical elements are identified in accordance with the Periodic Table of the Elements, CAS version, Handbook of Chemistry and Physics, 67th Ed., 1986-87, inside cover.

Other chemistry terms herein are used according to conventional usage in the art, as exemplified by The McGraw-Hill Dictionary of Chemical Terms (ed. Parker, S., 1985), McGraw-Hill, San Francisco, incorporated herein by reference). Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention pertains.

The term "pharmaceutically acceptable salt" as used herein includes salts derived from inorganic or organic acids including, for example, hydrochloric, hydrobromic, sulfuric, nitric, perchloric, phosphoric, formic, acetic, lactic, maleic, fumaric, succinic, tartaric, glycolic, salicylic, citric, methanesulfonic, benzenesulfonic, benzoic, malonic, trifluoroacetic, trichloroacetic, naphthalene-2-sulfonic, and other acids. Pharmaceutically acceptable salt forms can include forms wherein the ratio of molecules comprising the salt is not 1:1. For example, the salt may comprise more than one inorganic or organic acid molecule per molecule of base, such as two hydrochloric acid molecules per molecule of compound of Formula I. As another example, the salt may

comprise less than one inorganic or organic acid molecule per molecule of base, such as two molecules of compound of Formula I per molecule of tartaric acid.

The terms "carrier" and "pharmaceutically acceptable carrier" as used herein refer to a diluent, adjuvant, excipient, or vehicle with which a compound is administered or formulated for administration. Non-limiting examples of such pharmaceutically acceptable carriers include liquids, such as water, saline, and oils; and solids, such as gum acacia, gelatin, starch paste, talc, keratin, colloidal silica, urea, and the like. In addition, auxiliary, stabilizing, thickening, lubricating, flavoring, and coloring agents may be used. Other examples of suitable pharmaceutical carriers are described in *Remington's Pharmaceutical Sciences* by E.W. Martin, herein incorporated by reference in its entirety.

As used herein, the term "oxidizing agent" refers to a reagent that accepts one or more electrons from a substrate. Certain oxidizing agents may also induce the formation of new bonds to oxygen. Illustrative examples of oxidizing agent include, but are not limited to, oxygen, ozone, hydrogen peroxide, periodic acid, sodium periodate, Dess-Martin periodinane, peracetic acid, *meta*-chloroperbenzoic acid, fluorine, chlorine, bromine, iodine, nitric acid, potassium nitrate, potassium chlorate, peroxydisulfuric acid, peroxymonosulfuric acid, sodium hypochlorite, interhalogen compounds (such as Icl), chromic acids, chromium trioxide, pyridinium chlorochromate, sodium dichromate, potassium permanganate, manganese heptoxide, sodium perborate, nitrous oxide, nitrogen dioxide, dinitrogen tetroxide, ceric ammonium nitrate, and ceric sulfate.

As used herein, the term "reducing agent" refers to a reagent that donates one or more electrons to a substrate. Illustrative examples of reducing agents include, but are not limited to, lithium, sodium, potassium, magnesium, aluminum, iron, tin, copper, zinc, sodium hydride, lithium aluminum hydride, sodium borohydride, lithium borohydride, sodium tetraacetoxyborohydride, $NaAlH_2(OCH_2CH_2OCH_3)_2$, Na(Hg), Zn(Hg), diborane, nickel boride, sodium dithionate, diisobutylaluminum hydride, and ascorbic acid.

EXAMPLES

The invention now being generally described, it will be more readily understood by reference to the following examples which are included merely for purposes of illustration of

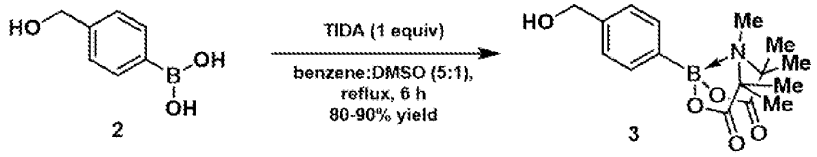
certain aspects and embodiments of the present invention, and are not intended to limit the invention.

General Synthetic Methods

Reaction mixtures were stirred magnetically. Air- and moisture-sensitive reactions were carried out in flame-dried glassware under nitrogen atmosphere by using standard Schlenk manifold techniques. Fine chemicals were purchased from Acros Organics, Alfa Aesar, Frontier Scientific, Combi-Blocks, or Sigma Aldrich and were used as received unless otherwise mentioned. Anhydrous THF, CH_2Cl_2, toluene, hexane, acetonitrile and Et_2O were dried by passing through a modified Grubbs system of alumina columns, manufactured by Anhydrous Engineering and were transferred under nitrogen via syringe. 1H Nuclear Magnetic Resonance (NMR) spectra were recorded in $CDCl_3$ at 400 or 500 Mhz on either a Varian Unity 400, Varian Unity 500, Varian Unity Inova 500NB or Bruker 500-MHz spectrometer with broad-band CryoProbe. Chemical shifts (δH) are quoted in parts per million (ppm) and referred to the residual protio solvent signals of CHCl3 (7.27 ppm) or acetone-d6 (2.05 ppm). ^{1}H NMR coupling constants are reported in hertz and refer to apparent multiplicities. Data are reported as follows: chemical shift, multiplicity (s = singlet, br. s = broad singlet, d = doublet, t = triplet, q = quartet, quin = quintet, sext = sextet, sept = septet, m = multiplet, dd = doublet of doublet, etc.), coupling constant, integration, and assignment. ^{13}C NMR spectra were recorded at 126 MHz. Chemical shifts (δC) are quoted in ppm and referenced to $CHCl_3$ (77.0 ppm) or acetone (29.8 ppm). ^{11}B NMR spectra were measured at 161 MHz with complete proton decoupling. ^{19}F NMR spectra were recorded at 471 MHz. Mass spectra were recorded at the University of Illinois School of Chemical Sciences Mass Spectrometry Laboratory using electron impact ionisation (EI), chemical ionisation (CI) or electrospray ionisation (ESI) techniques for high-resolution mass spectra. HRMS EI and CI were performed on a VG Analytical Autospec mass spectrometer at 70 eV. HRMS ESI was performed on either a Bruker Daltonics Apex IV, 7-Tesla FT-ICR or microTOF II.

Example 1: Synthesis of Building Blocks

*8-(4-(hydroxymethyl)phenyl)-3,3,4,5,5-pentamethyldihydro-4l4,8l4-[1,3,2]oxazaborolo[2,3-b][1,3,2]oxazaborole-2,6(3H,5H)-dione (**3**)*



To a 1 L round bottom flask with a stir bar was added the TIDA ligand (15.0 g, 100 mmol, 1 equiv), 4-(hydroxymethyl) phenylboronic acid **2** (20.0 g, 100 mmol, 1 equiv) and were dissolved in benzene (500 mL) and DMSO (100 mL). The solution was stirred and then the flask was fitted with a Dean-Stark trap and heated to reflux. After refluxing for 6 h, the reaction mixture was cooled to room temperature and then concentrated by rotary evaporation. The resultant DMSO solution was diluted with EtOAc (250 mL) and transferred to a separatory funnel, rinsing the vessel with additional EtOAc. The organic solution was washed with brine (200 mL x 3 to 6 times to ensure complete removal of DMSO), dried over MgSO4, filtered through a cotton plug, and then concentrated by rotary evaporation. The crude concentrate was dissolved in minimal hot acetone with gentle heating and added dropwise by pipette to a vigorously stirred Erlenmeyer flask containing hexanes:Et_2O (1:1, 1 L) causing precipitation of the product. Stirring continued until no further precipitation was observed. The product was collected by vacuum filtration through a fine fritted funnel and washed with Et2O (250 mL x 3) to afford a white solid (28.0 g, 88 mmol, 89% yield).

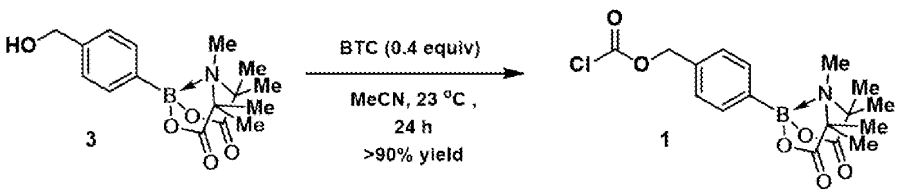
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, J = 8.1 Hz, 2H), 7.37 (d, J = 7.9 Hz, 2H), 4.59 (s, 2H), 2.49 (s, 3H), 1.85-1.74 (m, 6H), 1.60 – 1.50 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 174.82, 142.01, 134.39, 126.54, 65.35, 37.49.

^{11}B NMR (161 MHz, $CDCl_3$) δ 9.09.

HRMS (ESI+) Calculated for $C_{16}H_{23}BNO_5$ $(M+H)^+$: 320.1669, found: 320.1668

4-(3,3,4,5,5-pentamethyl-2,6-dioxotetrahydro-2H-4l4,8l4-[1,3,2]oxazaborolo[2,3-b][1,3,2]oxazaborol-8-yl)benzyl carbonochloridate (1)



To an oven dried, septa capped, glass 40 mL vial with a stir bar was added **3** (0.638 g, 2.0 mmol, 1.0 equiv), bis(trichloromethyl) carbonate (BTC, 0.237 g, 0.8 mmol, 0.4 equiv), and acetonitrile (20 mL). The vial was sealed with a teflon septum screw cap and the mixture was stirred for 24 h at 23 °C under positive pressure of nitrogen. The reaction mixture was then concentrated by rotary evaporation to afford a white solid. The solid was dissolved in acetone (10 mL) and then added dropwise by pipette to a vigorously stirred Erlenmeyer flask containing hexanes:Et_2O (1:1, 150 mL) causing precipitation of the title compound as a white solid (610 mg, 1.6 mmol, 80% yield). Alternatively, the title compound was used directly in reactions with amines without purification, by concentrating the crude reaction mixture to dryness via rotary evaporation and then adding reagents for the following step to the same vessel.

Preparation of crystals for X-ray diffraction:

To a 5 mL vial was added 10 mg of the title compound. Minimal anhydrous acetone was added to fully dissolve the solid, and then the vial was sealed with a septum cap. A needle was used to pierce the cap and allow slow evaporation of the acetone. The solution was allowed to sit at 23 °C until colorless crystals were observed (CCDC 2291420).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, J = 8.0 Hz, 2H), 7.37 (d, J = 7.9 Hz, 2H), 5.30 (s, 2H), 2.49 (s, 3H), 1.83-1.73 (m, 6H), 1.63 – 1.44 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 174.65, 150.79, 134.57, 134.22, 128.37, 73.40, 37.50.

^{11}B NMR (161 MHz, $CDCl_3$) δ 10.24.

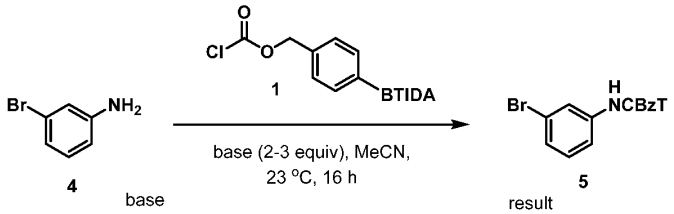
HRMS (ESI+) Calculated for $C_{17}H_{22}BClNO_6$ $(M+H)^+$: 382.1229, found: 382.1219.

General Protection Procedure A: Protection of amines with CbzT-Cl

To an oven dried glass 40 mL vial with a stir bar CbzT-Cl was added (1.0 mmol, 1.0 equiv) followed by the free amine (1.1 mmol, 1.1 equiv). The vessel was sealed with a septum cap. Using a needle attached to a Schlenk line, the vessel was evacuated and backfilled with nitrogen (3x) and then anhydrous acetonitrile (20 mL) was added by syringe. The mixture was stirred for 16 h at 23 °C and was then concentrated by rotary evaporation to afford a solid. To the solid was added EtOAc (30 mL) and then the solution was washed with H_2O (30 mL x 3) directly in the vial by adding water, sealing of the vial, shaking rigorously, and then opening the vial to remove water via pipette in between washes. The organic layer was dried with anhydrous magnesium sulfate, filtered through a cotton plug, and then concentrated by rotary evaporation to obtain the crude product

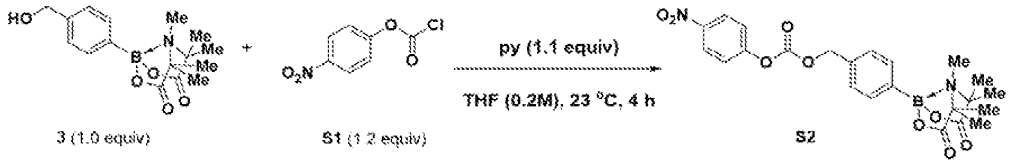
mixture. The crude mixture was purified by silica gel column chromatography eluting with 0 to 50% EtOAc/hexanes to yield the CbzT-amine compound.

Optimization of CbzT installation for general protection procedure A



base	result
triethyl amine, pyridine, 2,6-lutidine, DBU, DIPEA, 2,2,6,6-TMP, $NaHCO_3$,K_2CO_3, $CsCO_3$	low product formation, mixture of byproducts
K_3PO_4	66%
none	90%

*4-nitrophenyl(4-(3,3,4,5,5-pentamethyl-2,6-dioxotetrahydro-2H-4l4,8l4-[1,3,2]oxazaborolo[2,3-b][1,3,2]oxazaborol-8-yl)benzyl) carbonate (**S2**)*



To an oven dried, septa capped, glass 40 mL vial with a stir bar was added **S1** (0.241 g, 1.2 mmol, 1.2 equiv), **3** (0.319 g, 1.0 mmol, 1.0 equiv), THF (5 mL), and pyridine (88 µL, 1.1 equiv). The vial was sealed with a Teflon septum screw cap and the mixture was stirred for 4 h at 23 °C under positive pressure of nitrogen. After the completion of the reaction, the crude mixture was concentrated by rotary evaporation and then EtOAc (20 mL) was added to the vial. The organic solution was washed with H_2O (25 mL x 4), removing water with a pipette after each wash. The organic layer was dried over anhydrous MgSO4, filtered through a cotton plug, and then concentrated via rotary evaporation. The crude product mixture was purified by silica gel (10.0 g) column chromatography eluting with 0 to 50% EtOAc/hexanes to yield the title compound as a white solid (0.387 g, 0.8 mmol, 80% yield).

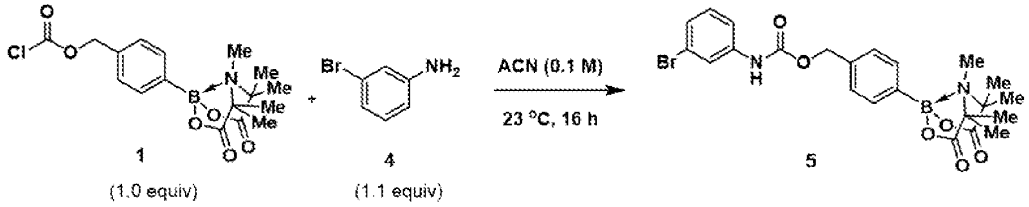
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.28 (d, J = 9.1 Hz, 2H), 7.62 (d, J = 7.6 Hz, 2H), 7.48 – 7.35 (m, 4H), 5.30 (s, 2H), 2.50 (s, 3H), 1.88 – 1.75 (m, 6H), 1.55-1.48 (m, 6H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 174.67, 155.63, 152.58, 145.56, 135.26, 134.57, 128.04, 125.47, 121.90, 70.92, 37.50.

^{11}B NMR (193 MHz, $CDCl_3$) δ 8.91.

HRMS (ESI+) Calculated for $C_{23}H_{26}BN_2O_9$ $(M+H)^+$: 485.1731, found: 485.1727.

*4-(3,3,4,5,5-pentamethyl-2,6-dioxotetrahydro-2H-4l4,8l4-[1,3,2]oxazaborolo[2,3-b][1,3,2]oxazaborol-8-yl)benzyl (3-bromophenyl)carbamate (**5**)*



Following general procedure A, to an oven dried glass 40 mL vial with a stir bar was added 1 (0.381 g, 1.0 mmol, 1.0 equiv), 4 (0.189 g, 1.1 mmol, 1.1 equiv), and then it was sealed with a septum cap. Using a needle attached to a Schlenk line, the vessel was evacuated and backfilled with nitrogen (3x) and then anhydrous acetonitrile (20 mL) was added by syringe. The mixture was stirred for 16 h at 23 °C and was then concentrated by rotary evaporation to afford a solid. To the solid was added EtOAc (30 mL) then the solution was washed with H2O (30 mL x 3) directly in the vial by adding water, sealing of the vial, shaking rigorously, and then opening the vial to remove water via pipette in between washes. The organic layer was dried with anhydrous magnesium sulfate, filtered through a cotton plug, and then concentrated by rotary evaporation to obtain an oil. The oil was purified by silica gel column chromatography eluting with 0 to 50% EtOAc/hexanes to yield the title compound as a white solid (0.464 g, 0.9 mmol, 90% yield).

Preparation of crystals for X-ray diffraction:

To a 5 mL vial was added 10 mg of the title compound. Minimal anhydrous acetone was added to fully dissolve the solid, and then the vial was sealed with a septum cap. A needle was used to pierce the cap and allow slow evaporation of the acetone. The solution was allowed to sit at 23 °C until colorless crystals were observed (CCDC 2290142).

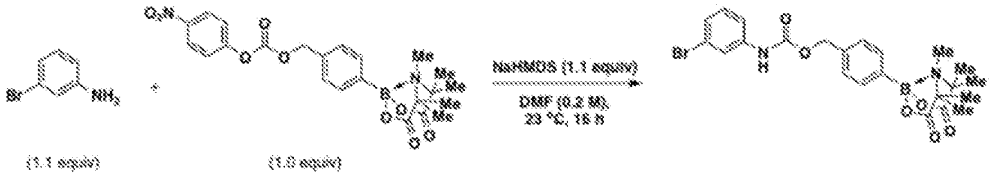
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.67 (s, 1H), 7.57 (d, J = 7.8 Hz, 2H), 7.36 (d, J = 8.0 Hz, 2H), 7.23 – 7.12 (m, 2H), 6.73 (s, 1H), 5.20 (s, 2H), 2.48 (s, 3H), 1.95 – 1.71 (m, 6H), 1.59-1.49 (m, 6H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 174.77, 138.11, 134.43, 130.49, 127.65, 126.67, 122.94, 67.09, 37.51.

^{11}B NMR (193 MHz, $CDCl_3$) δ 9.02.

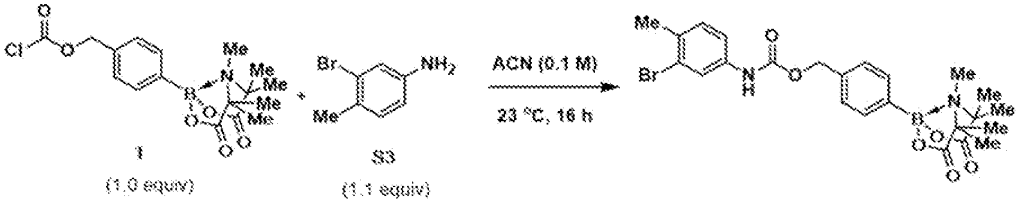
HRMS (ESI+) Calculated for $C_{23}H_{27}BBrN_2O_6$ $(M+H)^+$: 517.1146, found: 517.1149.

Use of CbzT-carbonate S2 for preparation of 4-(3,3,4,5,5-pentamethyl-2,6-dioxotetrahydro-2H-4l4,8l4-[1,3,2]oxazaborolo[2,3-b][1,3,2]oxazaborol-8-yl)benzyl (3-bromophenyl)carbamate (5)



To an oven dried glass 40 mL vial with a stir bar was added 3-bromoaniline (0.189 g, 1.1 mmol, 1.1 equiv) and **S2** (0.484 g, 1.0 mmol, 1.0 equiv), then the vial was sealed with a septum cap. The vessel was evacuated and backfilled with nitrogen (3x) via a needle attached to a Schlenk line. 2.0 M sodium bis(trimethylsilyl)amide in THF solution (0.55 mL, 1.1 mmol, 1.1 equiv) and DMF (5 mL) were added by syringe. The mixture was stirred for 16 h at 23 °C. To the solid was added EtOAc (30 mL) then the solution was washed with H_2O (30 mL x 3) directly in the vial by adding water, sealing of the vial, shaking rigorously, and then opening the vial to remove water via pipette in between washes. The organic layer was dried with anhydrous magnesium sulfate, filtered through a cotton plug, and then concentrated by rotary evaporation to obtain an oil. The oil was purified by silica gel column chromatography eluting with 50 to 100% EtOAc/hexanes to yield the title compound as a white solid (0.197 g, 0.38 mmol, 38% yield). Characterization data for **5** is the same as above.

*4-(3,3,4,5,5-pentamethyl-2,6-dioxotetrahydro-2H-4l4,8l4-[1,3,2]oxazaborolo[2,3-b][1,3,2]oxazaborol-8-yl)benzyl (3-bromo-2-methylphenyl)carbamate (**41**)*



Following general procedure A, to an oven dried, septa capped, glass 40 mL vial with a stir bar was added **1** (0.381 g, 1.0 mmol, 1.0 equiv), **S3** (0.205 g, 1.1 mmol, 1.1 equiv), and then it was sealed with a septum cap. Using a needle attached to a Schlenk line, the vessel was evacuated and backfilled with nitrogen (3x) and then anhydrous acetonitrile (20 mL) was added by syringe. The mixture was stirred for 16 h at 23 °C, and then was directly concentrated by rotary evaporation in the same vial to afford a white solid. To the solid was added EtOAc (30 mL) then the solution was washed with H_2O (30 mL x 3) directly in the vial by adding water, sealing of the vial, shaking rigorously, and then opening the vial to remove water via pipette in between washes. The organic layer was dried with anhydrous magnesium sulfate, filtered through a cotton plug, and then concentrated by rotary evaporation to obtain an oil. The oil was purified by silica gel column chromatography eluting with 0 to 50% EtOAc/hexanes to yield the title compound as a white solid (0.413 g, 0.78 mmol, 78% yield).

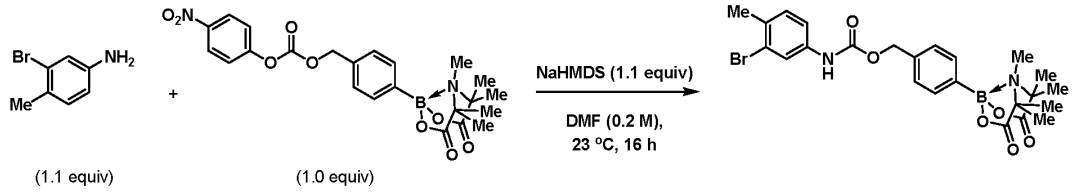
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.66 (s, 1H), 7.58 (d, J = 7.7 Hz, 2H), 7.36 (d, J = 7.8 Hz, 2H), 7.19 (d, J = 9.1 Hz, 1H), 7.14 (d, J = 8.2 Hz, 1H), 6.62 (s, 1H), 5.19 (s, 2H), 2.48 (s, 3H), 2.34 (s, 3H), 1.84-1.73 (m, 6H), 1.56-1.49 (m, 6H),

^{13}C NMR (151 MHz, $CDCl_3$) δ 174.64, 137.00, 134.29, 130.86, 127.49, 124.93, 66.88, 37.39, 22.17.

^{11}B NMR (193 MHz, $CDCl_3$) δ 9.41.

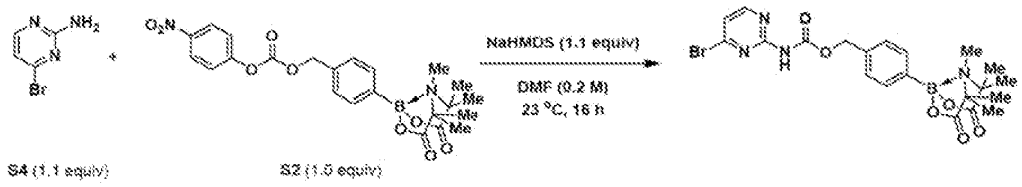
HRMS (ESI+) Calculated for $C_{24}H_{29}BBrN_2O_6$ $(M+H)^+$: 531.1302, found: 531.1302.

Use of CbzT-carbonate S2 for preparation of 4-(3,3,4,5,5-pentamethyl-2,6-dioxotetrahydro-2H-4l4,8l4-[1,3,2]oxazaborolo[2,3-b][1,3,2]oxazaborol-8-yl)benzyl(3-bromo-2-methylphenyl)carbamate (41)



To an oven dried glass 40 mL vial with a stir bar was added 3-bromo-4-methylaniline **S3** (0.205 g, 1.1 mmol, 1.1 equiv) and **S2** (0.484 g, 1.0 mmol, 1.0 equiv), then the vial was sealed with a septum cap. The vessel was evacuated and backfilled with nitrogen (3x) via a needle attached to a Schlenk line. 2.0 M sodium bis(trimethylsilyl)amide in THF solution (0.55 mL, 1.1 mmol, 1.1 equiv) and DMF (5 mL) were added by syringe. The mixture was stirred for 16 h at 23 °C. To the solid was added EtOAc (30 mL) then the solution was washed with H_2O (30 mL x 3) directly in the vial by adding water, sealing of the vial, shaking rigorously, and then opening the vial to remove water via pipette in between washes. The organic layer was dried with anhydrous magnesium sulfate, filtered through a cotton plug, and then concentrated by rotary evaporation to obtain an oil. The oil was purified by silica gel column chromatography eluting with 50 to 100% EtOAc/hexanes to yield the title compound as a white solid (0.282 g, 0.53 mmol, 53% yield). Characterization data for **41** is the same as above.

4-(3,3,4,5,5-pentamethyl-2,6-dioxotetrahydro-2H-4l4,8l4-[1,3,2]oxazaborolo[2,3-b][1,3,2]oxazaborol-8-yl)benzyl (4-bromopyrimidin-2-yl)carbamate (38)



To an oven dried glass 40 mL vial with a stir bar was added 2-amino-4-bromopyrimidine **S4** (0.191 g, 1.1 mmol, 1.1 equiv) and **S2** (0.484 g, 1.0 mmol, 1.0 equiv), then the vial was sealed with a septum cap. The vessel was evacuated and backfilled with nitrogen (3x) via a needle attached to a Schlenk line. 2.0 M sodium bis(trimethylsilyl)amide in THF solution (0.55 mL, 1.1 mmol, 1.1 equiv) and DMF (5 mL) were added by syringe. The mixture was stirred for 16 h at 23 °C. To the solid was added EtOAc (30 mL) then the solution was washed with H_2O (30 mL x 3) directly in the vial by adding water, sealing of the vial, shaking rigorously, and then opening the

vial to remove water via pipette in between washes. The organic layer was dried with anhydrous magnesium sulfate, filtered through a cotton plug, and then concentrated by rotary evaporation to obtain an oil. The oil was purified by silica gel column chromatography eluting with 50 to 100% EtOAc/hexanes to yield the title compound as a white solid (0.31 g, 0.6 mmol, 60% yield).

Preparation of crystals for X-ray diffraction:

To a 5 mL vial was added 10 mg of the title compound. Minimal anhydrous acetone was added to fully dissolve the solid, and then the vial was sealed with a septum cap. A needle was used to pierce the cap and allow slow evaporation of the acetone. The solution was allowed to sit at 23 °C until colorless crystals were observed (CCDC 2291892).

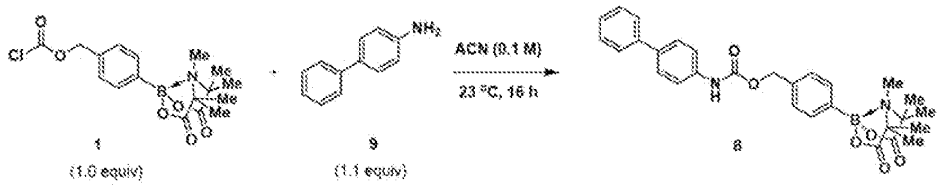
^{1}H NMR (151 MHz, $CDCl_3$) δ 8.37 (d, J = 5.2 Hz, 1H), 7.70 (s, 1H), 7.57 (d, J = 7.7 Hz, 2H), 7.39 (d, J = 7.7 Hz, 2H), 7.19 (d, J = 5.2 Hz, 1H), 5.25 (s, 2H), 2.48 (s, 3H), 1.84 – 1.77 (m, 6H), 1.55-1.48 (s, 6H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 174.77, 158.88, 156.99, 153.35, 150.94, 136.58, 134.39, 127.82, 120.49, 67.59, 37.52.

^{11}B NMR (161 MHz, $CDCl_3$) δ 9.17.

HRMS (ESI+) Calculated for $C_{21}H_{25}BBrN_4O_6$ $(M+H)^+$: 519.1051, found: 519.1047.

Synthesis of the model substrate 4-(5,5,6,7,7-pentamethyl-4,8-dioxo-1,3,6,2-dioxazaborocan-2-yl)benzyl [1,1'-biphenyl]-4-ylcarbamate (8)



Following general procedure A, to an oven dried glass 40 mL vial with a stir bar was added **1** (0.381 g, 1.0 mmol, 1.0 equiv) and 4-aminobiphenyl **9** (0.186 g, 1.1 mmol, 1.1 equiv), then it was sealed with a septum cap and evacuated and backfilled with nitrogen (3x) using a needle attached to a Schlenk line. Anhydrous acetonitrile (20 mL) was added by syringe. The mixture was stirred for 16 h at 23 °C, then was concentrated by rotary evaporation affording an oil. To oil was added EtOAc (30 mL). The solution was washed with H_2O (30 mL x 3) directly in the vial by

adding water, sealing of the vial, shaking rigorously, and then opening the vial to remove water via pipette in between washes. The organic layer was dried with anhydrous magnesium sulfate, filtered through a cotton plug, and then concentrated by rotary evaporation to obtain an oil. The oil was purified by silica gel column chromatography eluting with 0 to 50% EtOAc/hexanes to yield the title compound as a white solid (0.464 g, 0.9 mmol, 90% yield).

Preparation of crystals for X-ray diffraction:

To a 5 mL vial was added 10 mg of the title compound. Minimal anhydrous acetone was added to fully dissolve the solid, and then the vial was sealed with a septum cap. A needle was used to pierce the cap and allow slow evaporation of the acetone. The solution was allowed to sit at 23 °C until colorless crystals were observed (CCDC 2293444).

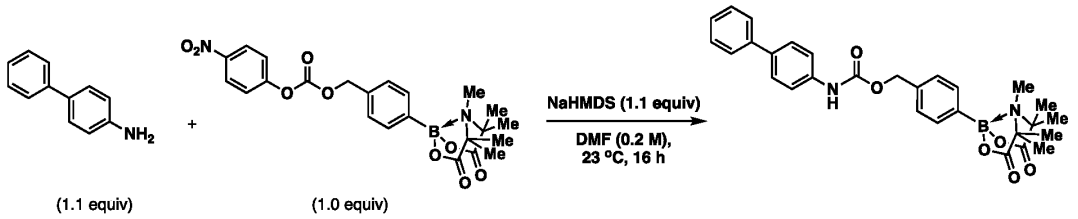
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.64 – 7.52 (m, 6H), 7.49 – 7.37 (m, 6H), 7.32 (m, 1H), 6.75 (br.s, 1H), 5.22 (s, 2H), 2.49 (s, 3H), 1.85-1.72 (s, 6H), 1.60-1.49 (s, 6H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 174.65, 140.48, 137.12, 134.29, 128.80, 127.75, 127.53, 127.08, 66.82, 37.39.

^{11}B NMR (193 MHz, $CDCl_3$) δ 9.17.

HRMS (ESI+) Calculated for $C_{29}H_{32}BN_2O_6$ $(M+H)^+$: 515.2353, found: 515.2361.

Use of CbzT-carbonate S2 for preparation of 4-(5,5,6,7,7-pentamethyl-4,8-dioxo-1,3,6,2-dioxazaborocan-2-yl)benzyl [1,1'-biphenyl]-4-ylcarbamate (8)

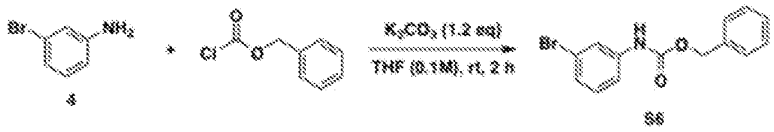


(1.1 equiv) (1.0 equiv)

To an oven dried glass 40 mL vial with a stir bar was added **9** [1,1'-biphenyl]-4-amine (0.186 g, 1.1 mmol, 1.1 equiv) and **S2** (0.484 g, 1.0 mmol, 1.0 equiv), then the vial was sealed with a septum cap. The vessel was evacuated and backfilled with nitrogen (3x) via a needle attached to a Schlenk line. 2.0 M sodium bis(trimethylsilyl)amide in THF solution (0.55 mL, 1.1 mmol, 1.1 equiv) and DMF (5 mL) were added by syringe. The mixture was stirred for 16 h at 23 °C. To the solid was added EtOAc (30 mL) then the solution was washed with H_2O (30 mL x 3)

directly in the vial by adding water, sealing of the vial, shaking rigorously, and then opening the vial to remove water via pipette in between washes. The organic layer was dried with anhydrous magnesium sulfate, filtered through a cotton plug, and then concentrated by rotary evaporation to obtain an oil. The oil was purified by silica gel column chromatography eluting with 50 to 100% EtOAc/hexanes to yield the title compound as a white solid (0.123 g, 0.24 mmol, 24% yield). Characterization data for **8** is the same as above.

Synthesis of Benzyl (3-bromophenyl)carbamate (S6)



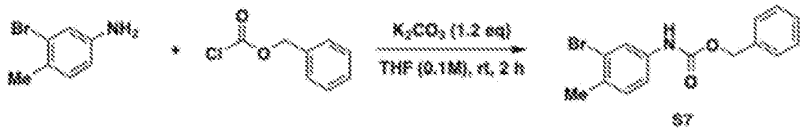
To an oven dried glass 40 mL vial with a stir bar was added **4** (0.172 g, 1.0 mmol, 1.0 equiv) and potassium carbonate (0.166 g, 1.2 mmol, 1.2 equiv) in anhydrous THF (10 mL) was added dropwise benzyl chloroformate (0.188 g, 1.1 mmol, 1.1 equiv). The mixture was stirred for 2 h at 0 °C to rt under N_2. The reaction mixture was concentrated by rotary evaporation affording an oil. To oil was added EtOAc (20 mL). The solution was washed with H_2O (20 mL x 3) directly in the vial by adding water, sealing of the vial, shaking rigorously, and then opening the vial to remove water via pipette in between washes. The organic layer was dried with anhydrous magnesium sulfate, filtered through a cotton plug, and then concentrated by rotary evaporation to obtain an oil. The oil was purified by silica gel column chromatography eluting with 0 to 50% EtOAc/hexanes to yield the title compound as a colorless oil (0.275 g, 0.9 mmol, 90% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (br s, 1H), 7.39-7.32 (m, 5H), 7.24-7.12 (m, 3H), 6.72 (br s, 1H), 5.19 (s, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 153.01, 139.05, 135.73, 130.28, 128.63, 128.45, 128.32, 126.45, 122.73, 121.51, 117.05, 67.24.

HRMS (ESI+) Calculated for $C_{14}H_{13}NO_2Br$ $(M+H)^+$: 306.0130, found: 306.0124.

Synthesis of Benzyl (3-bromo-4-methylphenyl)carbamate (S7)



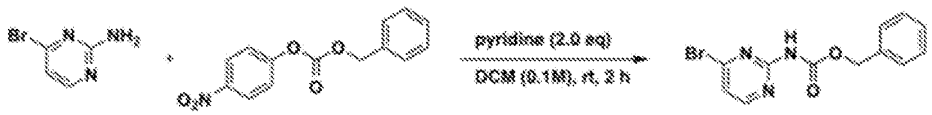
To an oven dried glass 40 mL vial with a stir bar 3-bromo-4-methylaniline **S3** (0.186 g, 1.0 mmol, 1.0 equiv) was added and potassium carbonate (0.166 g, 1.2 mmol, 1.2 equiv) in anhydrous THF (10 mL) was added dropwise benzyl chloroformate (0.188 g, 1.1 mmol, 1.1 equiv). The mixture was stirred for 2 h at 0 °C to rt under N_2. The reaction mixture was concentrated by rotary evaporation affording an oil. To oil was added EtOAc (20 mL). The solution was washed with H_2O (20 mL x 3) directly in the vial by adding water, sealing of the vial, shaking rigorously, and then opening the vial to remove water via pipette in between washes. The organic layer was dried with anhydrous magnesium sulfate, filtered through a cotton plug, and then concentrated by rotary evaporation to obtain an oil. The oil was purified by silica gel column chromatography eluting with 0 to 50% EtOAc/hexanes to yield the title compound as a colorless oil (0.272 g, 0.85 mmol, 85% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (br s, 1H), 7.41-7.33 (m, 5H), 7.22-7.17 (m, 1H), 7.14 (d, J = 10.0 Hz, 1H), 6.61 (br s, 1H), 5.19 (s, 2H), 2.34 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 153.12, 136.52, 135.86, 132.85, 130.80, 128.63, 128.42, 128.32, 124.87, 122.37, 117.60, 67.34, 67.15, 22.12.

HRMS (ESI+) Calculated for $C_{15}H_{15}NO_2Br$ $(M+H)^+$: 320.0286 , found: 320.0280.

Synthesis of Benzyl (4-bromopyrimidin-2-yl)carbamate (S8)



S8

To an oven dried glass 40 mL vial with a stir bar 4-bromopyrimidin-2-amine (0.169 g, 1.0 mmol, 1.0 equiv) was added and benzyl (4-nitrophenyl) carbonate (0.328 g, 1.2 mmol, 1.2 equiv) in anhydrous dichloromethane (10 mL) was added dropwise pyridine (0.160 g, 2.0 mmol, 2.0 equiv). The mixture was stirred for 2 h at 0 °C to rt under N_2. The reaction mixture was concentrated by rotary evaporation affording an oil. To oil was added EtOAc (20 mL). The solution was washed with H_2O (20 mL x 3) directly in the vial by adding water, sealing of the vial, shaking rigorously, and then opening the vial to remove water via pipette in between washes. The organic layer was dried with anhydrous magnesium sulfate, filtered through a cotton plug, and then concentrated by rotary evaporation to obtain an oil. The oil was purified by silica gel column

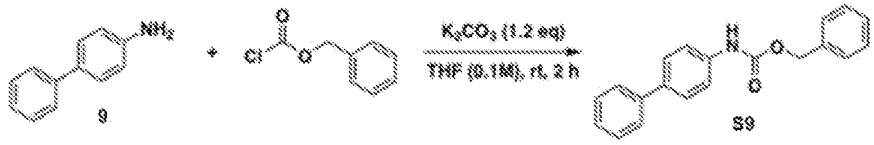
chromatography eluting with 0 to 50% EtOAc/hexanes to yield the title compound as a colorless oil (0.188 g, 0.61 mmol, 61% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.34 (d, *J* = 10.0 Hz, 1H), 7.98 (br s, 1H), 7.45-7.31 (m, 5H), 7.17 (d, *J* = 10.0 Hz, 1H), 5.25 (s, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 158.65, 156.89, 153.21, 150.81, 135.31, 128.63, 128.56, 128.54, 120.23, 67.71.

HRMS (ESI+) Calculated for $C_{12}H_{11}N_3O_2Br$ $(M+H)^+$: 308.0035, found: 308.0035.

Synthesis of Benzyl [1,1'-biphenyl]-4-ylcarbamate (S9)



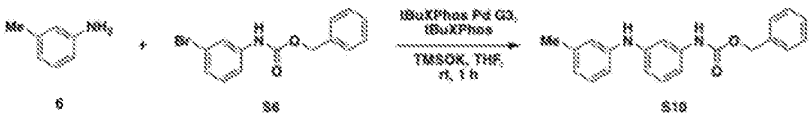
To an oven dried glass 40 mL vial with a stir bar was added **9** (0.169 g, 1.0 mmol, 1.0 equiv) and potassium carbonate (0.166 g, 1.2 mmol, 1.2 equiv) in anhydrous THF (10 mL) was added dropwise benzyl chloroformate (0.188 g, 1.1 mmol, 1.1 equiv). The mixture was stirred for 2 h at 0 °C to rt under N_2. The reaction mixture was concentrated by rotary evaporation affording an oil. To oil was added EtOAc (20 mL). The solution was washed with H_2O (20 mL x 3) directly in the vial by adding water, sealing of the vial, shaking rigorously, and then opening the vial to remove water via pipette in between washes. The organic layer was dried with anhydrous magnesium sulfate, filtered through a cotton plug, and then concentrated by rotary evaporation to obtain an oil. The oil was purified by silica gel column chromatography eluting with 0 to 50% EtOAc/hexanes to yield the title compound as a colorless oil (0.261 g, 0.86 mmol, 86% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60-7.52 (m, 4H), 7.50-7.30 (m, 10H), 6.71 (br s, 1H), 5.23 (s, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 153.25, 140.48, 137.04, 136.46, 135.98, 128.75, 128.64, 128.40, 128.35, 127.71, 127.02, 126.79, 118.93, 67.11.

HRMS (ESI+) Calculated for $C_{20}H_{18}NO_2$ $(M+H)^+$: 304.1338, found: 304.1332.

Synthesis of Benzyl (3-(m-tolylamino)phenyl)carbamate (S10)



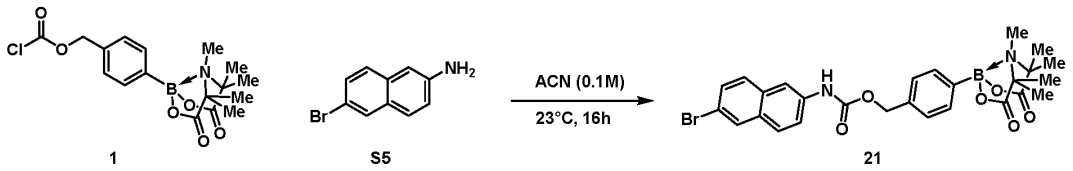
In an argon filled glovebox, an oven dried glass 40 mL vial with a stir bar was added **S6** (0.305 g, 1.0 mmol, 1.0 equiv), **6** (0.139 g, 1.3 mmol, 1.3 equiv), tBuXPhos-Pd-G3 (0.159 g, 0.2 mmol, 0.2 equiv), tBuXPhos (0.064 g, 0.15 mmol, 0.15 equiv) and TMSOK (257 mg, 2.0 mmol, 2 equiv). The vial was sealed with a PTFE septum cap. The vial was placed under positive pressure of argon via a needle attached to a Schlenk line, and then anhydrous, argon-sparged THF (10 mL) was added, and the reaction was stirred at 23 °C for 1 h. The reaction mixture was diluted with EtOAc (30 mL) and filtered through a silica plug, washing with additional EtOAc (50 mL). The EtOAc eluent was concentrated via rotary evaporation to obtain an oil. The oil was purified by silica gel column chromatography eluting with 0 to 50% EtOAc/hexanes to yield the title compound as a colorless oil (0.232 g, 0.70 mmol, 70% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42-7.32 (m, 5H), 7.17-7.14 (m, 3H), 6.93-6.88 (m, 2H), 6.85 (d, J = 10.0 Hz, 1H), 6.78 (d, J = 10.0 Hz, 2H), 6.62 (br s, 1H), 5.69 (br s, 1H), 5.19 (s, 2H), 2.32 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 144.33, 142.54, 139.26, 138.84, 136.07, 129.85, 129.19, 128.64, 128.38, 128.34, 122.36, 119.24, 115.60, 112.29, 67.02, 21.53.

HRMS (ESI+) Calculated for $C_{21}H_{21}N_2O_2$ $(M+H)^+$: 333.1603, found: 333.1608.

Synthesis of (4-((((6-bromonaphthalen-2-yl)carbamoyl)oxy)methyl)phenyl)boronic acid TIDA ester (21)



1 S5 21

Following general procedure A, to an oven dried glass 40 mL vial with a stir bar was added **1** (0.598 g, 1.73 mmol, 1.0 equiv), **S5** (0.383g, 1.57 mmol, 1.1 equiv), and then it was sealed with a septum cap. Using a needle attached to a Schlenk line, the vessel was evacuated and backfilled with nitrogen (3x) and then anhydrous acetonitrile (18 mL) was added by syringe. The mixture was stirred for 16 h at 23 °C and was then concentrated by rotary evaporation to afford a solid. To

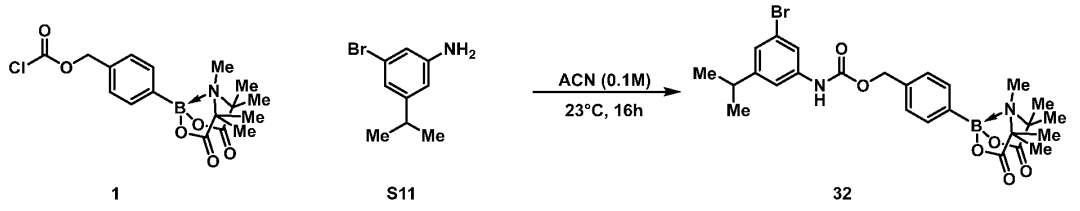
the solid was added EtOAc (30 mL) then the solution was washed with H_2O (30 mL x 3) in a separatory funnel, shaking rigorously, and then removing water in between washes. The organic layer was dried with anhydrous magnesium sulfate, filtered through a cotton plug, and then concentrated by rotary evaporation to obtain a pink solid. The pink solid was purified by silica gel column chromatography eluting with 0 to 100% EtOAc/hexanes to yield the title compound as a white solid (0.660 g, 1.16mmol, 74% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.93 (d, J=1.9Hz, 1H), 7.69 (d, J = 8.8 Hz, 1H), 7.64 (d, J=8.8, 1H), 7.59 (d, J=7.6, 2H), 7.52 (dd, J_1=1.94Hz, J_2=8.7Hz, 1H), 7.41-7.37 (m, 3H), 6.85 (s, 1H), 5.24 (s,2H), 2.49 (s, 3H), 1.80 (s, 6H), 1.54 (s, 6H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 174.60, 136.99, 135.61, 134.32, 132.41, 131.23, 129.98, 129.62, 129.08, 128.06, 127.54, 118.48, 66.96, 37.38.

HRMS (ESI+) Calculated for C27H28BBrN2O6 $(M+H)^+$: 566.1224, found: 567.1132.

Synthesis of (4-((((3-bromo-5-isopropylphenyl)carbamoyl)oxy)methyl)phenyl) boronic acid TIDA ester (32)



1 S11 32

Following general procedure A, to an oven dried glass 40 mL vial with a stir bar was added **1** (1.20 g, 3.14 mmol, 1.0 equiv), **S11** (741 mg, 3.46 mmol, 1.1 equiv), and then it was sealed with a septum cap. Using a needle attached to a Schlenk line, the vessel was evacuated and backfilled with nitrogen (3x) and then anhydrous acetonitrile (20 mL) was added by syringe. The mixture was stirred for 16 h at 23 °C and was then concentrated by rotary evaporation to afford a solid. To the solid was added EtOAc (30 mL) then the solution was washed with H_2O (30 mL x 3) directly in the vial by adding water, sealing of the vial, shaking rigorously, and then opening the vial to remove water via pipette in between washes. The organic layer was dried with anhydrous magnesium sulfate, filtered through a cotton plug, and then concentrated by rotary evaporation to obtain a pink solid. The pink solid was purified by silica gel column chromatography eluting with

0 to 100% EtOAc/hexanes to yield the title compound as a white solid (1.07 g, 1.91 mmol, 61% yield).

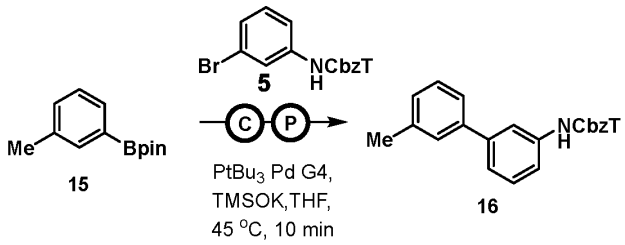
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.6 (d, *J* = 7.6 Hz, 2H), 7.5 (s, 1H), 7.4 (d, *J* = 7.8 Hz, 2H), 7.1 (s, 1H), 7.1 (t, *J* = 1.6 Hz, 1H), 6.7 (s, 1H), 5.2 (s, 2H), 3.0 – 2.7 (septet, 1H), 2.5 (s, 3H), 1.8 (s, 6H), 1.6 – 1.5 (s, 6H), 1.2 (d, *J* = 6.8 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 174.7, 153.1, 151.9, 139.0, 137.0, 134.4, 134.2, 127.4, 124.7, 122.6, 119.0, 115.5, 66.8, 46.1, 37.4, 34.1, 30.9, 23.7.

HRMS (ESI+) Calculated for $(M+H)^+$: 559.1615 , found: 559.1459.

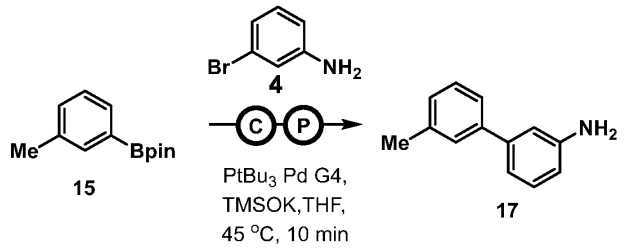
Free Amine vs. CBzT-amine coupling

Cross coupling of 15 with CbzT-amine 5



In an argon-filled glovebox, **5** (200 mg, 0.386 mmol, 1.0 equiv), **15** (169 mg, 0.773 mmol, 2.0 equiv), Pd-P(tBu)$_3$-G4 (44 mg, 0.078 mmol, 0.2 equiv), and TMSOK (99 mg, 0.78 mmol, 2.0 equiv) were added to an oven dried 20 mL vial equipped with a stir bar. The vial was sealed with a PTFE septum cap, removed from the glovebox, and placed under positive N_2 pressure via a needle attached to a Schlenk line. Anhydrous THF (5 mL) was added and the reaction was stirred at 45 °C for 10 minutes. HPLC-MS analysis showed clean conversion to the desired product with minimal remaining starting materials **5** and **15**.

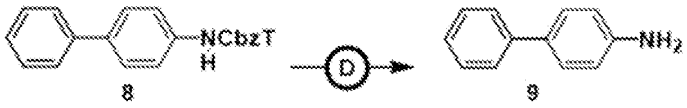
Cross coupling of 15 with free amine 4



In an argon-filled glovebox, **4** (200 mg, 1.16 mmol, 1.0 equiv), **15** (211.9 mg, 2.33 mmol, 2.0 equiv), Pd-P(tBu)$_3$-G4 (135.9 mg, 0.232 mmol, 0.2 equiv), and TMSOK (298.3 mg, 2.33 mol, 2.0 equiv) were added to an oven dried 20 mL vial equipped with a stir bar. The vial was sealed with a PTFE septum cap, removed from the glovebox, and placed under positive N_2 pressure via a needle attached to a Schlenk line. Anhydrous THF (5 mL) was added and the reaction was stirred at 45 °C for 10 minutes. HPLC-MS analysis showed minimal conversion to the desired product, remaining starting materials **15** and **4**, and numerous unidentified side products.

Example 2: Deprotection Conditions for CBzT

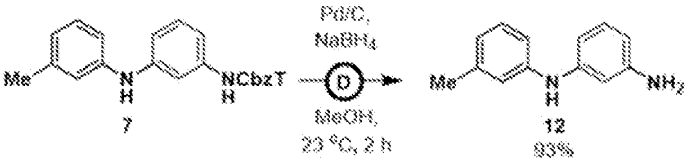
The influence of various reaction conditions on the deprotection yield of **9** is shown below.



8 9

entry	solvent	condition	temp (°C)	time (h)	yield (%)
1	MeOH	Pd/C, H_2	23	14	90
2	MeOH	Pd/C, $NaBH_4$ (30.0 equiv)	65	7	91
3	MeOH	Pd/C, $NaBH_4$ (10.0 equiv)	23	2	93
4	THF/H_2O	LiOH/H_2O_2	55	12	68

General Deprotection Procedure A



7 12
93%

To a 20 mL vial with a stir bar the CbzT-amine was added (0.037 mmol, 1.0 equiv) followed by $NaBH_4$ (37 mg, 10.0 equiv, 0.97 mmol) and 10% palladium on carbon (2 mg, 0.2 equiv). The vial was sealed with a septum cap and then evacuated and backfilled with nitrogen (3x) using a needle attached to a Schlenk line. MeOH (3 mL) was added by syringe and then an empty balloon attached to a syringe fitted with a needle was placed through the septum to minimize

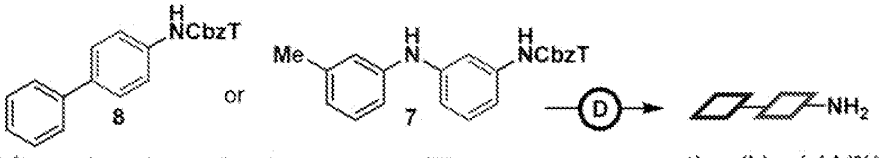
the buildup of pressure while preventing loss of generated hydrogen. The reaction was stirred at 65 °C for 7 hours. The reaction mixture was concentrated by rotary evaporation. Hexanes (30 mL) was added, and the solution was filtered through a silica plug rinsing with additional hexanes (100 mL). The hexanes layer was discarded, and the silica plug was flushed with Et_2O (100 mL). The Et_2O solution was concentrated via rotary evaporation to yield the title compound.

General Deprotection Procedure B



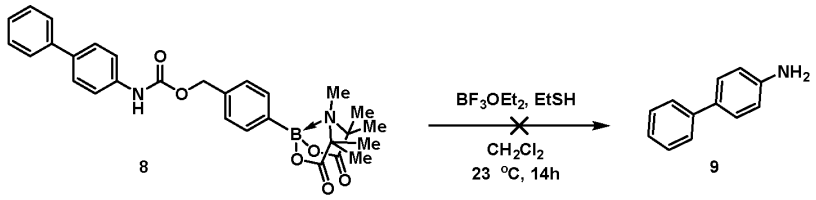
To a 40 mL vial with a stir bar the CbzT-amine wes added (0.064 mmol, 1 equiv) and then THF (5 mL) was added by syringe. The solution was vigorously stirred and then 3 M aqueous LiOH* (300 µL, 1.3 mmol, 15 equiv) was added by syringe. Aqueous 30% H_2O_2 (200 µL) was added by syringe, the vial was sealed tightly with a PTFE septum cap, the vial was placed in a pre-equilibrated 55 °C heating block, and then the reaction was stirred for 12 hours. Then hexanes was added (30 mL) and filtered through a silica plug rinsing with additional hexanes (100 mL), Et_2O (100 mL) and EtOAc (100 mL) and then the eluents were discarded. The silica plug was washed with acetone (250 mL) to elute the product. The acetone solution was concentrated via rotary evaporation and to give the desired product each time.

Optimization of CBzT deprotection procedures



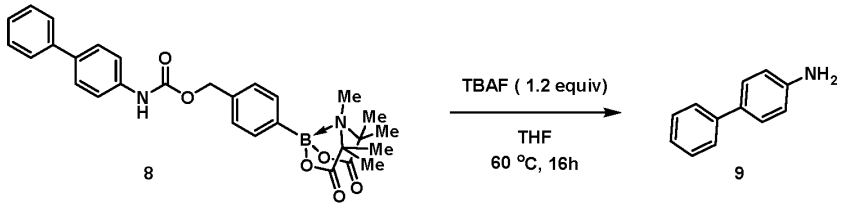
entry	substrate	solvent	condition	temp (°C)	time (h)	yield (%)
1	8	CH_2Cl_2	$BF_3{\cdot}OEt_2$, EtSH	23	14	n.d.
2	8	THF	TBAF (1.2 equiv)	82	14	65
3	8	MeCN	TMSI (2.0 equiv)	23	2	90
4	8	MeCN	TMSI (2.0 equiv)	82	1	90
5	8	MeOH	Pd/C, H_2	23	14	90
6	8	MeOH	Pd/C, $NaBH_4$ (30.0 equiv)	65	7	91
7	7	MeOH	Pd/C, $NaBH_4$ (30.0 equiv)	65	7	90
8	8	MeOH	Pd/C, $NaBH_4$ (10.0 equiv)	23	2	93
9	7	MeOH	Pd/C, $NaBH_4$ (10.0 equiv)	23	2	93
10	8	THF/H_2O	$LiOH/H_2O_2$	55	12	68
11	7	THF/H_2O	$LiOH/H_2O_2$	55	12	66

Deprotection of 8 BF_3OEt_2 with to prepare [1,1'-biphenyl]-4-amine (9)



To a 20 mL vial with a stir bar was added **8** (51 mg, 0.1 mmol, 1.0 equiv) in CH_2Cl_2 (5.0 mL), and then the vial was sealed with a septum cap. 1.0 M EtSH (0.18 g, 2.9 mmol, 29 equiv) and BF_3OEt_2 (0.145 g, 1.0 mmol, 10 equiv) were added by syringe. The mixture was stirred for 14 h at 23 °C. No desired product was observed.

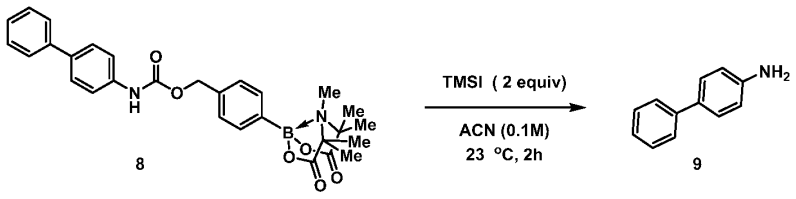
Deprotection of 8 using TBAF to prepare [1,1'-biphenyl]-4-amine (9)



To a 20 mL vial with a stir bar was added **8** (51 mg, 0.1 mmol, 1.0 equiv), and then the vial was sealed with a septum cap. 1.0 M tetrabutylammonium fluoride in THF solution (0.12 mL, 0.12 mmol, 1.2 equiv), and THF (2 mL) were added by syringe. The mixture was stirred for 16 h at 60 °C. After cooling, the mixture was concentrated by rotary evaporation affording a mixture solid. The solution was washed with H_2O (5 mL x 3) directly in the vial by adding water, sealing of the vial, shaking rigorously, and then opening the vial to remove water via pipette in between washes. The organic layer was dried with anhydrous sodium sulfate, filtered through a cotton plug, and then concentrated by rotary evaporation to obtain an oil. The oil was diluted with hexanes (30 mL) and filtered through a silica plug. The hexane was then discarded, and the silica plug was eluted with Et_2O (100 mL). The Et_2O eluent was then concentrated via rotary evaporation to yield the title compound as a light brown solid (15 mg, 0.9 mmol, 65% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, J = 7.7 Hz, 2H), 7.49 – 7.35 (m, 3H), 7.26 (d, J = 9.1 Hz, 2H), 6.76 (d, J = 6.8 Hz, 2H), 3.73 (br. s., 2H).

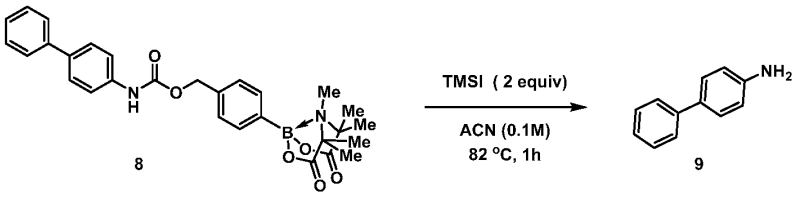
Deprotection of 8 using TMSI to prepare [1,1'-biphenyl]-4-amine (9)



8 9

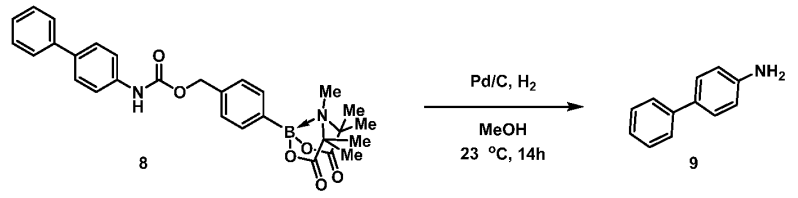
To a 20 mL vial with a stir bar was added **8** (51 mg, 0.1 mmol, 1.0 equiv) and trimethylsilyl iodide (28 µl, 0.2 mmol, 2 equiv) and acetonitrile (10 mL), then it was sealed with a septum cap. The mixture was stirred for 2 h at 23 °C and then concentrated by rotary evaporation to afford a solid. To the oil was added EtOAc (10 mL). The solution was washed with H_2O (5 mL x 3) directly in the vial by adding water, sealing of the vial, shaking rigorously, and then opening the vial to remove water via pipette in between washes. The organic layer was dried with anhydrous sodium sulfate, filtered through a cotton plug, and then concentrated by rotary evaporation to obtain an oil. The oil was diluted with hexanes (30 mL) and filtered through a silica plug. The hexane eluent was discarded, and the silica plug was washed with Et_2O (100 mL). The Et_2O eluent was then concentrated via rotary evaporation to yield the title compound as a light brown solid (15 mg, 0.9 mmol, 90% yield).

Deprotection of 8 with TMSI to prepare [1,1'-biphenyl]-4-amine (9)



To a 20 mL vial with a stir bar was added **8** (51 mg, 0.1 mmol, 1.0 equiv) and trimethylsilyl iodide (28 µl, 0.2 mmol, 2 equiv) and acetonitrile (10 mL), then it was sealed with a septum cap. The mixture was stirred for 1 h at 82 °C and then concentrated by rotary evaporation to afford a solid. To the oil was added EtOAc (10 mL). The solution was washed with H_2O (5 mL x 3) directly in the vial by adding water, sealing of the vial, shaking rigorously, and then opening the vial to remove water via pipette in between washes. The organic layer was dried with anhydrous sodium sulfate, filtered through a cotton plug, and then concentrated by rotary evaporation to obtain an oil. The oil was diluted with hexanes (30 mL) and filtered through a silica plug. The hexane eluent was discarded, and the silica plug was washed with Et_2O (100 mL). The Et_2O eluent was then concentrated via rotary evaporation to yield the title compound as a light brown solid (15 mg, 0.09 mmol, 90% yield).

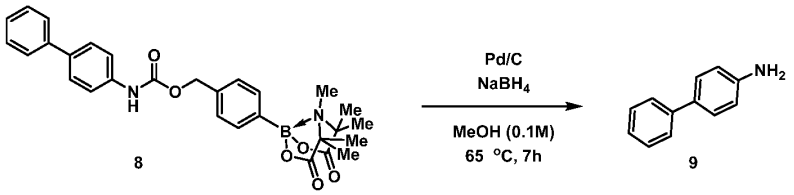
Hydrogenolysis of 8 to prepare [1,1'-biphenyl]-4-amine (9)



To a 20 mL vial with a stir bar was added **8** (20 mg, 0.037 mmol, 1.0 equiv) and 10 wt % of 10% Pd/C (2 mg, 0.2 equiv). The vial was sealed with a septum cap and was then evacuated and backfilled with nitrogen (3x) using a needle attached to a Schlenk line. MeOH (3 mL) was added by syringe and then an empty (deflated) balloon attached to a syringe fitted with a needle was placed through the septum to avoid the buildup of pressure while preventing loss of generated hydrogen. The reaction was stirred at 23 °C for 14 hours. After the reaction was completed, the solvent was removed by vacuum. Purification of the residue was conducted via

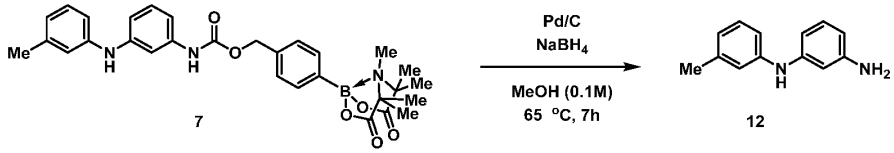
flashchromatography and afforded the desired product as light brown solid (15 mg, 0.089 mmol, 90%).

Deprotection of 8 to prepare [1,1'-biphenyl]-4-amine (9)



Following general deprotection procedure A, to a 20 mL vial with a stir bar was added **8** (20 mg, 0.037 mmol, 1.0 equiv), $NaBH_4$ (111 mg, 30.0 equiv, 2.91 mmol) and 10 wt % of 10% Pd/C (2 mg). The vial was sealed with a septum cap and was then evacuated and backfilled with nitrogen (3x) using a needle attached to a Schlenk line. MeOH (3 mL) was added by syringe and then an empty (deflated) balloon attached to a syringe fitted with a needle was placed through the septum to avoid the buildup of pressure while preventing loss of generated hydrogen. The reaction was stirred at 65 °C for 7 hours. The reaction mixture was concentrated by rotary evaporation and was then diluted with hexanes (30 mL) and filtered through a silica plug. The hexanes layer was discarded, and the silica plug was flushed with Et_2O (100 mL). The Et_2O eluent solution was concentrated via rotary evaporation to yield the title compound as a light brown solid (5.7 mg, 0.034 mmol, 91% yield).

Deprotection of 7 to prepare (m-tolyl)benzene-1,3-diamine (12)



Following general deprotection procedure A, to a 20 mL vial with a stir bar was added **7** (20 mg, 0.036 mmol, 1.0 equiv), $NaBH_4$ (111 mg, 30.0 equiv, 2.91 mmol) and 10 wt % of 10% Pd/C (2 mg). The vial was sealed with a septum cap and was then evacuated and backfilled with nitrogen (3x) using a needle attached to a Schlenk line. MeOH (3 mL) was added by syringe and then an empty (deflated) balloon attached to a syringe fitted with a needle was placed through the septum to avoid the buildup of pressure while preventing loss of generated hydrogen. The reaction was

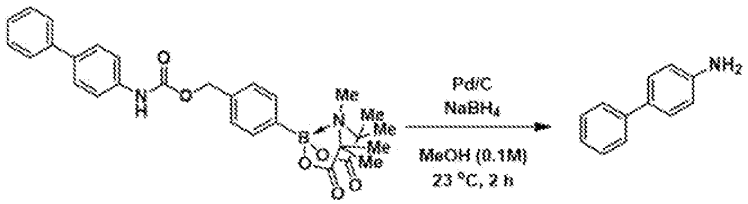
stirred at 65 °C for 7 hours. The reaction mixture was concentrated by rotary evaporation and was then diluted with hexanes (30 mL) and filtered through a silica plug. The hexanes layer was discarded, and the silica plug was flushed with Et_2O (100 mL). The Et_2O eluent solution was concentrated via rotary evaporation to yield the title compound as a light brown solid (6.4 mg, 0.032 mmol, 90% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.15 (dd, J = 8.6, 7.5 Hz, 1H), 7.04 (t, J = 7.9 Hz, 1H), 6.92 – 6.83 (m, 2H), 6.75 (d, J = 7.5 Hz, 1H), 6.46 (ddd, J = 7.9, 2.1, 0.9 Hz, 1H), 6.42 (t, J = 2.1 Hz, 1H), 6.27 (ddd, J = 7.9, 2.1, 0.9 Hz, 1H), 5.57 (s, 1H), 3.62 (br. s, 2H), 2.31 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 147.61, 144.59, 143.11, 139.29, 130.31, 129.24, 122.03, 119.14, 115.57, 108.52, 108.10, 104.15, 21.67.

HRMS (ESI+) Calculated for $C_{13}H_{15}N_2$ $(M+H)^+$: 199.1235, found: 199.1234.

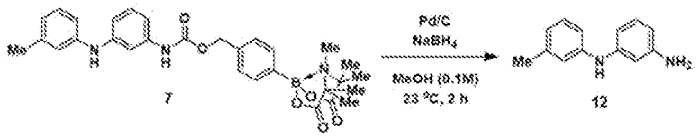
Deprotection of 8 to prepare [1,1'-biphenyl]-4-amine (9)



8 9

To a 20 mL vial with a stir bar was added **8** (20 mg, 0.037 mmol, 1.0 equiv), $NaBH_4$ (37 mg, 10.0 equiv, 0.97 mmol) and 10 wt % of 10% Pd/C (2 mg). The vial was sealed with a septum cap and was then evacuated and backfilled with nitrogen (3x) using a needle attached to a Schlenk line. MeOH (3 mL) was added by syringe and then an empty (deflated) balloon attached to a syringe fitted with a needle was placed through the septum to avoid the buildup of pressure while preventing loss of generated hydrogen. The reaction was stirred at 23 °C for 2 hours. The reaction mixture was concentrated by rotary evaporation and was then diluted with hexanes (30 mL) and filtered through a silica plug. The hexanes layer was discarded, and the silica plug was flushed with Et_2O (100 mL). The Et_2O eluent solution was concentrated via rotary evaporation to yield the title compound as a light brown solid (6.1 mg, 93 % yield).

Deprotection of 7 to prepare [1,1'-biphenyl]-4-amine (12)



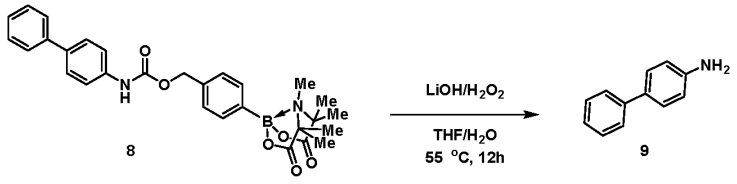
To a 20 mL vial with a stir bar was added **7** (100 mg, 0.184 mmol, 1.0 equiv), $NaBH_4$ (70 mg, 10.0 equiv, 1.84 mmol) and 10 wt % of 10% Pd/C (10 mg, 0.1 equiv). The vial was sealed with a septum cap and was then evacuated and backfilled with nitrogen (3x) using a needle attached to a Schlenk line. MeOH (5 mL) was added by syringe and then an empty (deflated) balloon attached to a syringe fitted with a needle was placed through the septum to avoid the buildup of pressure while preventing loss of generated hydrogen. The reaction was stirred at 23 °C for 2 hours. The reaction mixture was concentrated by rotary evaporation and was then diluted with hexanes (30 mL) and filtered through a silica plug. The hexanes layer was discarded, and the silica plug was flushed with Et_2O (100 mL). The Et_2O eluent solution was concentrated via rotary evaporation to yield the title compound as a light brown solid (34 mg, 91 % yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.15 (dd, J = 8.6, 7.5 Hz, 1H), 7.04 (t, J = 7.9 Hz, 1H), 6.92 – 6.83 (m, 2H), 6.75 (d, J = 7.5 Hz, 1H), 6.46 (ddd, J = 7.9, 2.1, 0.9 Hz, 1H), 6.42 (t, J = 2.1 Hz, 1H), 6.27 (ddd, J = 7.9, 2.1, 0.9 Hz, 1H), 5.57 (s, 1H), 3.62 (br. s, 2H), 2.31 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 147.61, 144.59, 143.11, 139.29, 130.31, 129.24, 122.03, 119.14, 115.57, 108.52, 108.10, 104.15, 21.67.

HRMS (ESI+) Calculated for $C_{13}H_{15}N_2$ $(M+H)^+$: 199.1235, found: 199.1234.

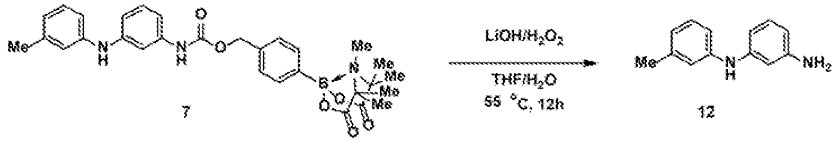
Deprotection of 8 to prepare [1,1'-biphenyl]-4-amine (9)



Following general deprotection procedure B, to a 40 mL vial with a stir bar was added **8** (33 mg, 0.064 mmol, 1 equiv) and then THF (5 mL) was added by syringe. The solution was vigorously stirred and then 3 M aqueous LiOH* (300 µL, 1.3 mmol, 15 equiv) was added by syringe. Aqueous 30% H_2O_2 (200 µL) was added by syringe, the vial was sealed tightly with a PTFE septum cap, the vial was placed in a pre-equilibrated 55 °C heating block, and then the reaction was stirred for

12hours. The reaction mixture was concentrated by rotary evaporation and was then diluted with hexanes (30 mL) and filtered through a silica plug. The hexanes layer was discarded, and the silica plug was flushed with Et_2O (100 mL). The Et_2O eluent solution was concentrated via rotary evaporation to yield the title compound as a light brown solid (7.4 mg, 0.044 mmol, 68% yield).

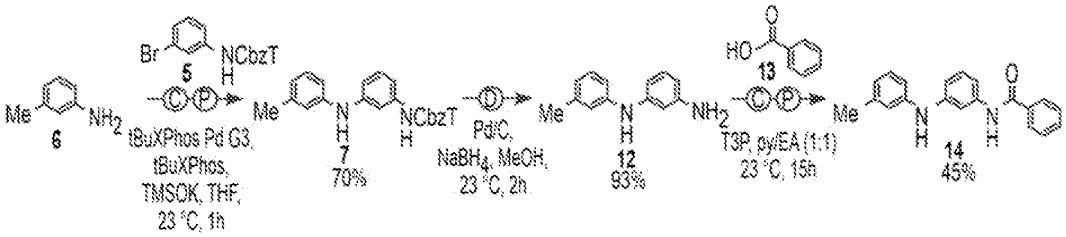
Deprotection of 7 with General Deprotection Procedure B to prepare (m-tolyl)benzene-1,3-diamine (12)



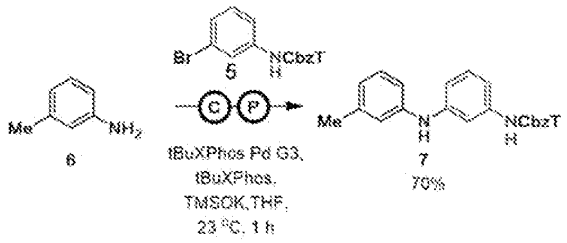
Following general deprotection procedure B, to a 40 mL vial with a stir bar was added **7** (35 mg, 0.064 mmol, 1 equiv) and then THF (5 mL) was added by syringe. The solution was vigorously stirred and then 3 M aqueous LiOH* (300 µL, 1.3 mmol, 15 equiv) was added by syringe. Aqueous 30% H_2O_2 (200 µL) was added by syringe, the vial was sealed tightly with a PTFE septum cap, the vial was placed in a pre-equilibrated 55 °C heating block, and then the reaction was stirred for 12hours. The reaction mixture was concentrated by rotary evaporation and was then diluted with hexanes (30 mL) and filtered through a silica plug. The hexanes layer was discarded, and the silica plug was flushed with Et_2O (100 mL). The Et_2O eluent solution was concentrated via rotary evaporation to yield the title compound as a light brown solid (8.7 mg, 0.044 mmol, 68% yield).

Example 3: Manual Synthesis of Oligomers

Synthesis of trimer 14



Preparation of 4-(3,3,4,5,5-pentamethyl-2,6-dioxotetrahydro-2H-4λ4,8λ4-[1,3,2]oxazaborolo[2,3-b][1,3,2]oxazaborol-8-yl)benzyl (3-(m-tolylamino)phenyl)carbamate (7)



In an argon filled glovebox, an oven dried 40 mL vial equipped with a stir bar was charged with **5** (300 mg, 0.580 mmol, 1 equiv), **6** (80 mg, 0.75 mmol, 1.3 equiv), tBuXPhos-Pd-G3 (92 mg, 0.11 mmol, 0.2 equiv), tBuXPhos (37 mg, 0.09 mmol, 0.15 equiv) and TMSOK (150 mg, 1.15 mmol, 2 equiv). The vial was sealed with a PTFE septum cap. The vial was placed under positive pressure of argon via a needle attached to a Schlenk line, and then anhydrous, argon-sparged THF (5 mL) was added and the reaction was stirred at 23 °C for 60 minutes. The reaction mixture was diluted with hexane (30 mL) and the solution was filtered through a silica plug, washing with additional hexanes (100 mL). The silica plug was then washed with Et_2O (250 mL). The hexanes and Et_2O eluents were discarded and then the silica plug was washed with EtOAc (250 mL). The EtOAc eluent was concentrated via rotary evaporation to yield the title compound as light brown solid (220 mg, 70% yield).

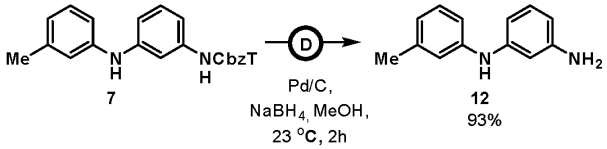
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.55 (d, J = 7.5 Hz, 2H), 7.35 (d, J = 7.4 Hz, 2H), 7.19 – 7.12 (m, 3H), 6.89 (d, J = 8.6 Hz, 2H), 6.85 (m, J = 8.1 Hz, 1H), 6.77 (t, J = 6.4 Hz, 2H), 6.72 (s, 1H), 5.71 (br. s, 1H) 5.18 (s, 2H), 2.46 (s, 3H), 2.31 (s, 3H), 1.78 (s, 6H), 1.52 (s, 6H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 174.80, 144.44, 142.63, 139.38, 134.35, 129.97, 129.30, 127.62, 122.46, 119.33, 115.67, 112.37, 66.79, 37.48, 21.65.

^{11}B NMR (161 MHz, $CDCl_3$) δ 10.87.

HRMS (ESI+) Calculated for $C_{21}H_{25}BBrN_4O_6$ $(M+H)^+$: 519.1051, found: 519.1047.

Deprotection of 7 to prepare N^1-(m-tolyl)benzene-1,3-diamine (12)



To a 20 mL vial with a stir bar was added **7** (100 mg, 0.184 mmol, 1.0 equiv), $NaBH_4$ (70 mg, 10.0 equiv, 1.84 mmol) and 10 wt % of 10% Pd/C (10 mg, 0.1 equiv). The vial was sealed

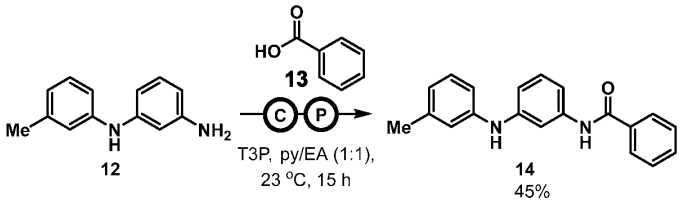
with a septum cap and was then evacuated and backfilled with nitrogen (3x) using a needle attached to a Schlenk line. MeOH (5 mL) was added by syringe and then an empty (deflated) balloon attached to a syringe fitted with a needle was placed through the septum to avoid the buildup of pressure while preventing loss of generated hydrogen. The reaction was stirred at 23 °C for 2 hours. The reaction mixture was concentrated by rotary evaporation and was then diluted with hexanes (30 mL) and filtered through a silica plug. The hexanes layer was discarded, and the silica plug was flushed with Et_2O (100 mL). The Et_2O eluent solution was concentrated via rotary evaporation to yield the title compound as a light brown solid (34 mg, 91 % yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.15 (dd, J = 8.6, 7.5 Hz, 1H), 7.04 (t, J = 7.9 Hz, 1H), 6.92 – 6.83 (m, 2H), 6.75 (d, J = 7.5 Hz, 1H), 6.46 (ddd, J = 7.9, 2.1, 0.9 Hz, 1H), 6.42 (t, J = 2.1 Hz, 1H), 6.27 (ddd, J = 7.9, 2.1, 0.9 Hz, 1H), 5.57 (s, 1H), 3.62 (br. s, 2H), 2.31 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 147.61, 144.59, 143.11, 139.29, 130.31, 129.24, 122.03, 119.14, 115.57, 108.52, 108.10, 104.15, 21.67.

HRMS (ESI+) Calculated for $C_{13}H_{15}N_2$ $(M+H)^+$: 199.1235, found: 199.1234.

Preparation of N-(3-(m-tolylamino)phenyl)benzamide (14)



An oven dried 40 mL vial equipped with a stir bar was charged with the benzoic acid **13** (10 mg, 0.81 mmol, 1.0 equiv) and then the vial was sealed with a PTFE septum cap. The vial was evacuated and backfilled with nitrogen (3x) via a needle attached to a Schlenk line and then a mixture of pyridine:EtOAc (2:1, 2 mL) was added by syringe. The solution was stirred vigorously, then T3P (50 wt% in EtOAc, 0.163mmol, 2 equiv) was added dropwise by syringe, resulting in a homogeneous yellow solution. The reaction mixture was stirred at room temperature for 15 hours. EtOAc (5 mL) was added to the reaction mixture and then the organic solution was washed with water (5 mL x 3) directly in the vial using a syringe to remove aqueous layers after each wash. The solution was washed with brine (5 mL). The organic layer was dried over anhydrous sodium sulfate, filtered through a cotton plug, and then concentrated via rotary evaporation. The crude

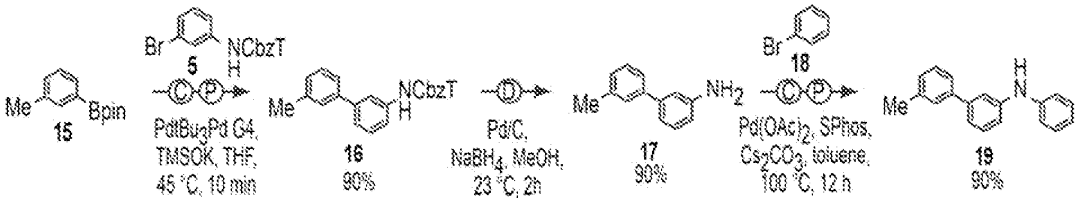
mixture was purified via silica gel column chromatography (0 to 100% hexanes/EtOAc) to yield the title compound as a light brown solid (11 mg, 0.36 mmol, 45% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.01 – 7.70 (m, 2H), 7.76 (s, 1H), 7.57 – 7.53 (m, 1H), 7.52 – 7.42 (m, 3H), 7.23 (t, J = 8.0 Hz, 1H), 7.18 (t, J = 7.7 Hz, 1H), 7.07 (dd, J = 8.0, 2.0 Hz, 1H), 6.98 – 6.92 (m, 2H), 6.91 – 6.85 (m, 1H), 6.79 (d, J = 7.5 Hz, 1H), 5.76 (s, 1H), 2.32 (s, 3H).

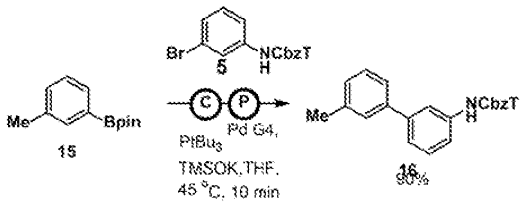
^{13}C NMR (151 MHz, $CDCl_3$) δ 165.84, 144.51, 142.62, 139.44, 139.10, 135.21, 131.99, 129.99, 129.35, 128.95, 127.14, 122.59, 119.52, 115.84, 113.35, 112.28, 109.11, 21.68.

HRMS (ESI+) Calculated for $C_{20}H_{19}N_2O$ $(M+H)^+$: 303.1497, found: 303.1495.

*Synthesis of trimer **19***



Preparation of 4-(3,3,4,5,5-pentamethyl-2,6-dioxotetrahydro-2H-4λ^4,8λ^4-[1,3,2]oxazaborolo[2,3-b][1,3,2]oxazaborol-8-yl)benzyl (3'-methyl-[1,1'-biphenyl]-3-yl)carbamate (16)



In an argon-filled glovebox, **5** (200 mg, 0.386 mmol, 1 equiv), **15** (169 mg, 0.773 mmol, 2 equiv), Pd-P(tBu)3-G4 (44 mg, 0.078 mmol, 0.2 equiv), and TMSOK (99 mg, 0.78 mmol, 2 equiv) were added to a 20 mL vial. The vial was sealed with a PTFE septum cap, removed from the glovebox, and placed under positive argon pressure via a needle attached to a Schlenk line. Anhydrous, argon-sparged THF (5 mL) was added and the reaction was stirred at 23 °C for 10 minutes. The reaction mixture was diluted with hexane (30 mL) and filtered through a silica plug. The silica plug was washed with additional hexanes (250 mL) and the hexane eluent was discarded. The silica plug was washed with Et_2O (250 mL) and then the solution was concentrated via rotary evaporation to yield **16** as a white solid (191 mg, 93% yield).

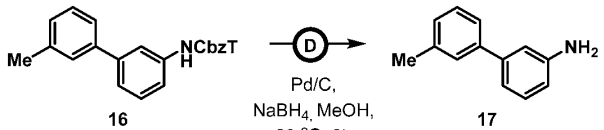
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.65 (d, J = 13.8 Hz, 1H), 7.58 (d, J = 7.6 Hz, 2H), 7.40 – 7.24 (m, 6H), 7.33 – 7.27 (m, 2H), 7.16 (d, J = 7.4 Hz, 1H), 6.79 (br. s, 1H), 5.22 (s, 2H), 2.48 (s, 3H), 2.41 (s, 3H), 1.79 (s, 6H), 1.60 (s, 6H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 174.66, 142.42, 140.66, 137.16, 134.28, 129.43, 128.68, 128.30, 127.47, 124.30, 122.48, 66.75, 37.39, 21.55.

^{11}B NMR (161 MHz, $CDCl_3$) δ 9.03.

HRMS (ESI+) Calculated for $C_{30}H_{34}BN_2O_6$ $(M+H)^+$: 529.2510, found: 529.2510.

Deprotection of 14 to prepare 3'-methyl-[1,1'-biphenyl]-3-amine (15)



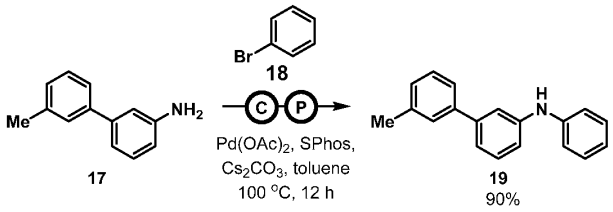
To a 20 mL vial with a stir bar was added **16** (50 mg, 0.095 mmol, 1.0 equiv), $NaBH_4$ (35 mg, 10.0 equiv, 0.95 mmol) and 10 wt % of 10% Pd/C (5 mg, 0.1 equiv). The vial was sealed with a septum cap and was then evacuated and backfilled with nitrogen (3x) using a needle attached to a Schlenk line. MeOH (3 mL) was added by syringe and then an empty (deflated) balloon attached to a syringe fitted with a needle was placed through the septum to avoid the buildup of pressure while preventing loss of generated hydrogen. The reaction was stirred at 23 °C for 2 hours. The reaction mixture was concentrated by rotary evaporation and was then diluted with hexanes (30 mL) and filtered through a silica plug. The hexanes layer was discarded, and the silica plug was flushed with Et_2O (100 mL). The Et_2O eluent solution was concentrated via rotary evaporation to yield the title compound as a light brown solid (15 mg, 90 % yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.43 – 7.38 (m, 2H), 7.35 (t, J = 7.5 Hz, 1H), 7.28 – 7.24 (m, 1H), 7.19 (d, J = 7.5 Hz, 1H), 7.03 (dt, J = 7.7, 1.4 Hz, 1H), 6.95 (q, J = 1.7 Hz, 1H), 6.72 (d, J = 7.9 Hz, 1H), 3.88 (br. s, 3H), 2.45 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 146.58, 142.73, 141.48, 138.32, 129.76, 128.68, 128.11, 128.06, 124.35, 118.00, 114.25, 114.18, 21.68.

HRMS (ESI+) Calculated for $C_{13}H_{14}N$ $(M+H)^+$: 184.1126, found: 184.1120.

Preparation of 3'-methyl-N-phenyl-[1,1'-biphenyl]-3-amine (19)



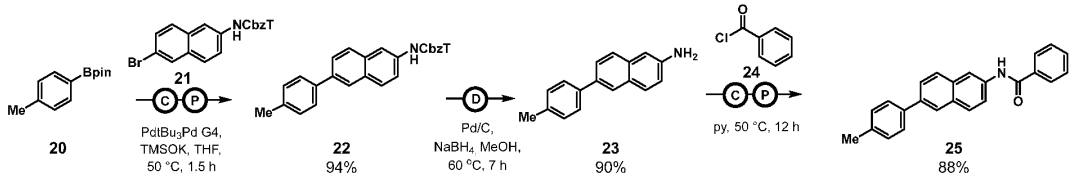
In an argon filled glovebox, an oven dried 40 mL vial equipped with a stir bar was charged with **17** (20 mg, 0.109 mmol, 1 equiv), **18** (23 mg, 0.141 mmol, 1.3 equiv), $Pd(OAc)_2$ (2.5 mg, 0.01 mmol, 0.1 equiv), SPhos (9 mg, 0.02 mmol, 0.2 equiv) and Cs_2CO_3 (50 mg, 0.15 mmol, 1.4 equiv). The vial was sealed with a PTFE septum cap, removed from the glovebox, and placed under positive pressure of argon via a needle attached to a Schlenk line. Anhydrous, argon-sparged toluene (3 mL) was added and then reaction was stirred at 100 °C for 12 hours. The reaction mixture was diluted with 5 mL of EtOAc and the organic phase washed with water (5 mL x 3) and then with brine (5 mL) directly in the vial, removing aqueous layers after each wash using a pipette. The organic layer was dried over anhydrous sodium sulfate, filtered through a cotton plug, and then concentrated via rotary evaporation. The crude mixture was purified via silica gel column chromatography (0 to 100% hexanes/EtOAc) to yield the title compound as a white solid (26 mg, 0.100 mmol, 90% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 – 7.36 (m, 2H), 7.35 – 7.27 (m, 5H), 7.19 – 7.14 (m, 2H), 7.15 – 7.12 (m, 2H), 7.08 – 7.05 (m, 1H), 6.95 (td, J = 7.4, 1.3 Hz, 1H), 2.41 (s, 3H).

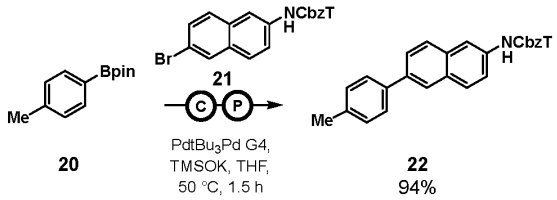
^{13}C NMR (151 MHz, $CDCl_3$) δ 143.53, 143.14, 142.83, 141.27, 138.44, 129.81, 128.76, 128.26, 128.08, 124.39, 121.32, 120.26, 118.12, 116.78, 21.69.

HRMS (ESI+) Calculated for $C_{19}H_{18}N$ $(M+H)^+$: 260.1439, found: 260.1439.

Synthesis of trimer 25



Preparation of (4-((((6-(p-tolyl)naphthalen-2-yl)carbamoyl)oxy)methyl)phenyl)boro-nic acid TIDA ester (22)



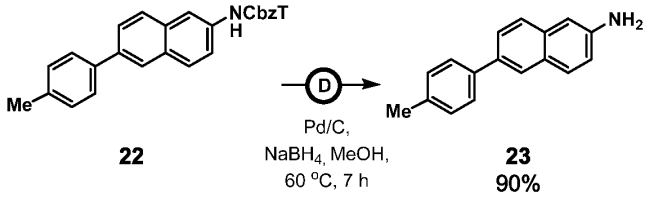
In an argon filled glovebox, an oven dried 40 mL vial equipped with a stir bar was charged with **21** (50 mg, 0.088 mmol, 1 equiv) **20** (29 mg, 0.13 mmol, 1.5 equiv.), TMSOK (17 mg, 0.13 mmol, 1.5 equiv) and Pd-P(tBu)$_3$-G4 precatalyst (5 mg, 0.009 mmol, 0.1 equiv). The vial was sealed with a PTFE septum cap, removed from the glovebox, and placed under positive argon pressure via a needle attached to a Schlenk line. Anhydrous, argon-sparged THF (4 mL) was added and the reaction was stirred at 50 °C for 1.5 hour. The reaction mixture was diluted with hexane (30 mL) and filtered through a silica plug. The silica plug was washed with Et_2O (40 mL) and the ether eluent was discarded. The silica plug was washed with EtOAc (40 mL) and then the solution was concentrated via rotary evaporation to yield **22** (48 mg, 94% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.95 (s, 1H), 7.83 (d, J = 8.5 Hz, 2H), 7.72 (d, J=8.5Hz, 1H), 7.60 (d, J=7.6Hz, 4H), 7.41-7.37 (m, 3H), 7.29 (d, J=7.77Hz, 2H), 6.84 (s, 1H), 5.26 (s,2H), 2.49 (s, 3H), 2.42 (s, 3H), 1.80 (s, 6H), 1.54 (s, 6H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 174.63, 138.10, 137.48, 137.13, 137.08, 135.12, 134.31, 132.98, 130.53, 129.59, 129.19, 127.87, 127.54, 127.10, 126.31, 125.11, 66.87, 37.38, 21.14.

HRMS (ESI+) Calculated for C34H35BN2O6 $(M+H)^+$: 578.4720, found: 578.2552.

Preparation of 6-(p-tolyl)naphthalen-2-amine (23)



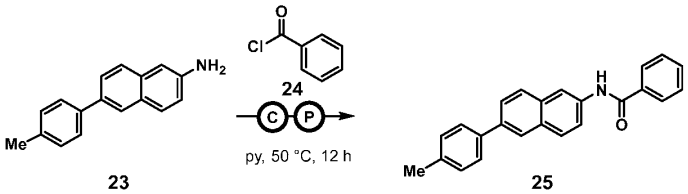
Following general deprotection procedure A, using **22** (48 mg, 0.083 mmol, 1 equiv), $NaBH_4$ (94 mg, 30.0 equiv, 2.48 mmol), 10% Pd/C (10 wt%, 5mg) afforded **23**, a white solid (17.50 mg, 90%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.71 (d, J=8.5Hz, 1H), 7.65 (s, 2H), 7.59 (d, J=8.2Hz, 2H), 7,28 (d, J=88Hz, 2H), 7.00 (s, 1H), 6.97 (dd, J_1= 2.3Hz, J_2=8.8Hz, 1H), 3.88 (s, 2H), 2.41 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 144.15, 138.52, 136.58, 135.16, 134.00, 129.51, 128.21, 126.94, 126.25, 126.01, 125.35, 118.60, 108.38, 21.11.

HRMS (ESI+) Calculated for $(M+H)^+$: 234.1283, found: 234.1285.

Preparation of N-(6-(p-tolyl)naphthalen-2-yl)benzamide (25)



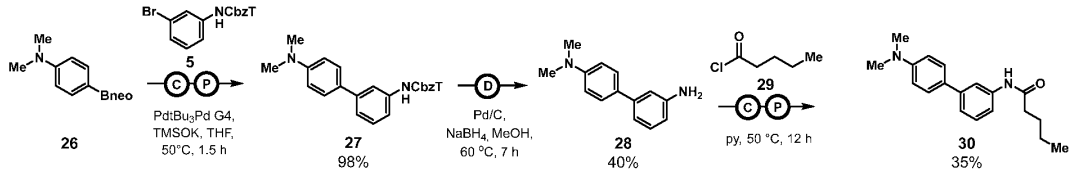
Compound **23** (7.7 mg, 0.033 mmol, 1 equiv) and benzoyl chloride (**24**, 5.6 mg, 0.043 mmol, 1.22 equiv) were added to an oven-dried 40 mL vial with a stir bar. The vial was sealed with a PTFE septum cap, and then evacuated and backfilled with nitrogen (3x) via a needle attached to a Schlenk line. Freshly distilled pyridine (2 mL) was added by syringe. The mixture was then placed in a pre-equilibrated 50° C heat block and stirred for 12 hours. The solvent was concentrated on a rotary evaporator using a water bath temperature of 70° C. Water (4 ml) was added, and then the solution was basified to pH 10 with 6 N NaOH, then acidified to pH=4 with 1N HCl and lastly neutralized pH=7 with 10% Sodium Bicarbonate. The aqueous solution was extracted with dichloromethane (2×10 mL), and the collected organic phase dried over anhydrous sodium sulfate. The crude reaction mixture was purified by silica gel column chromatography eluting with 0 to 25% EtOAc/hexanes to yield the title compound as a white solid (9.7mg, 0.028mmol, 88% yield).

^{1}H NMR (600 MHz,$CDCl_3$) δ 8.38 (d, J=2.2Hz, 1H), 7.98 (d, J=7.2Hz, 2H), 7.94 (d, J=8.0Hz, 2H), 7.90 (dd, J_1=2.6Hz, J_2= 8.4Hz, 2H), 7.75 (dd, J_1=1.8Hz, J_2= 8.4Hz, 1H), 7.63-7.57 (m, 4H), 7.53 (t, J= 7.1Hz, 2H), 7.30 (d, J=7.9Hz, 2H), 2.43 (s, 3H)

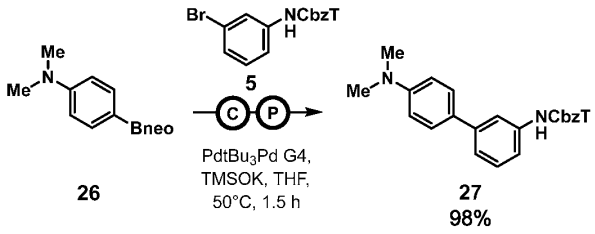
^{13}C NMR (151 MHz, $CDCl_3$) δ 165.78, 138.10, 137.85, 137.14, 135.32, 135.0, 132.94, 131.97, 131.08, 129.62, 129.14, 128.90, 128.21, 127.15, 127.04, 126.32, 125.13, 120.37, 116.73, 21.15

HRMS (ESI+) Calculated for C24H19NO $(M+H)^+$:338.1545, found:338.1543.

Synthesis of trimer 30



Preparation of (4-((((4'-(dimethylamino)-[1,1'-biphenyl]-3- yl)carbamoyl)oxy) methyl)phenyl)boronic acid, TIDA ester (27)



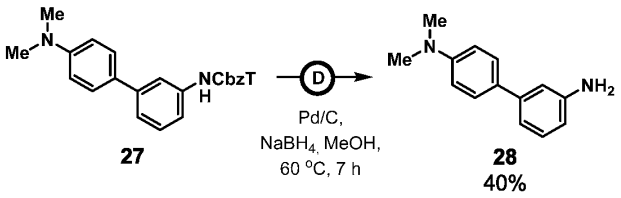
In an argon filled glovebox, an oven dried 40 mL vial equipped with a stir bar was charged with **5** (10 mg, 0.019 mmol, 1 equiv) **26** (6.76mg, 0.03 mmol, 1.5 equiv.), TMSOK (4 mg, 0.03 mmol, 1.5 equiv) and Pd-P(tBu)$_3$-G4 precatalyst (1.11 mg, 0.002 mmol, 0.1 equiv). The vial was sealed with a PTFE septum cap, removed from the glovebox, and placed under positive argon pressure via a needle attached to a Schlenk line. Anhydrous, argon-sparged THF (4 mL) was added and the reaction was stirred at 50 °C for 1.5 hour. The reaction mixture was diluted with hexane (30 mL) and filtered through a silica plug. The silica plug was washed with Et_2O (40 mL) and the ether eluent was discarded. The silica plug was washed with EtOAc (40 mL) and then the solution was concentrated via rotary evaporation to yield **27** (10 mg, 92% yield).

^{1}H NMR (600 MHz,$CDCl_3$) δ ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.6 (d, J = 8.0 Hz, 3H), 7.5 (d, J = 8.4 Hz, 2H), 7.4 (d, J = 7.7 Hz, 2H), 7.3 (d, J = 7.4 Hz, 2H), 7.3 (t, J = 2.3 Hz, 1H), 6.8 (d, J = 10.3 Hz, 3H), 5.2 (s, 2H), 3.0 (s, 6H), 2.5 (s, 3H), 1.8 (s, 6H), 1.5 (s, 6H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 174.7, 153.4, 142.1, 138.1, 137.2, 134.3, 129.4, 129.1, 127.5, 121.6, 116.5, 112.9, 71.8, 66.7, 37.4, 21.3.

HRMS (ESI+) Calculated for C24H19NO $(M+H)^+$:558.2775 , found:.558.2777.

Preparation of N4',N4'-dimethyl-[1,1'-biphenyl]-3,4'-diamine (28)



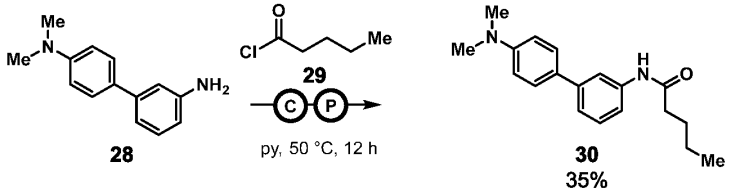
Following general deprotection procedure A, using **27** (14.10mg, 0.025 mmol, 1 equiv), $NaBH_4$ (28.71mg, 30.0 equiv, 0.79 mmol), 10% Pd/C (10 wt%, 1.5mg) afforded free amine **28** as a red solid (5mg, 93%).

^{1}H NMR (600 MHz,$CDCl_3$) 7.6 – 7.4 (m, 2H), 7.2 (t, J = 7.8 Hz, 1H), 7.0 (dt, J = 7.8, 1.3 Hz, 1H), 6.9 (t, J = 2.0 Hz, 1H), 6.8 (d, J = 8.4 Hz, 2H), 6.6 (dd, J = 8.0, 2.3 Hz, 1H), 3.0 (s, 6H).

^{13}C NMR δ 150.0, 146.6, 142.4, 129.5, 129.4, 127.6, 117.0, 113.1, 113.0, 112.7, 40.6.

HRMS (ESI+) Calculated for C24H19NO $(M+H)^+$: 213.1394, found: 213.1392.

Preparation of N-(4'- (dimethylamino)-[1,1'-biphenyl]-3-yl)p entanamide (30)



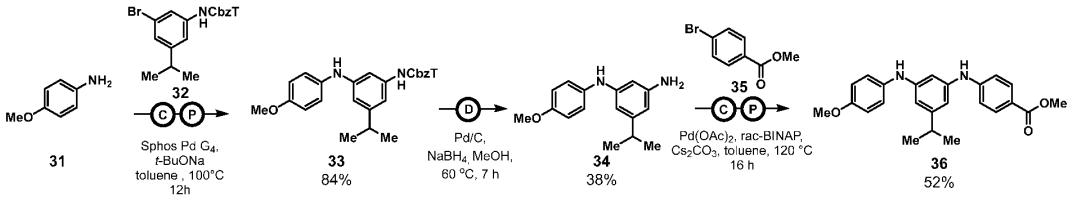
Compound **28** (31 mg, 0.146 mmol, 1 equiv) and pentanoyl chloride (**29**, 21.48 mg, 0.178 mmol, 1.22 equiv) were added to an oven-dried 40 mL vial with a stir bar. The vial was sealed with a PTFE septum cap, and then evacuated and backfilled with nitrogen (3x) via a needle attached to a Schlenk line. Freshly distilled pyridine (4 mL) was added by syringe. The mixture was then placed in a pre-equilibrated 50° C heat block and stirred for 12 hours. The solvent was concentrated on a rotary evaporator using a water bath temperature of 70° C. Water (4 ml) was added, and then the solution was basified to pH 10 with 6 N NaOH. The aqueous solution was extracted with dichloromethane (2×10 mL), and the collected organic phase dried over anhydrous sodium sulfate and obtained crude product (orange liquid). The orange liquid was purified by silica gel column chromatography eluting with 0 to 50% EtOAc/hexanes to yield the title compound as a white solid (15mg, 0.051mmol, 35% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.7 (s, 1H), 7.5 (d, J = 8.4 Hz, 2H), 7.4 (d, J = 7.8 Hz, 1H), 7.3 (dt, J = 15.8, 7.8 Hz, 2H), 7.2 (s, 1H), 6.8 (d, J = 8.2 Hz, 2H), 3.0 (s, 6H), 2.4 (t, J = 7.6 Hz, 2H), 1.4 (sextet, J = 7.4 Hz, 2H), 1.0 (t, J = 7.4 Hz, 3H).

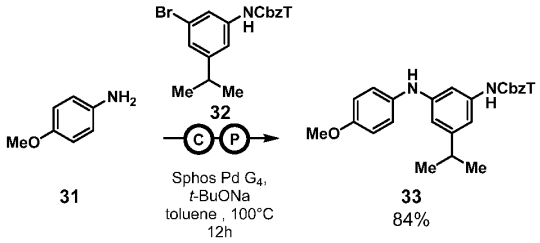
^{13}C NMR δ 170.4, 141.0, 137.3, 128.2, 126.8, 121.1, 116.6, 116.5, 111.9, 39.7, 36.6, 26.7, 21.4, 12.8.

HRMS (ESI+) Calculated for C19H24N2O $(M+H)^+$: 297.1967 , found: 297.1959.

Synthesis of trimer 34



Preparation of (4-((((3-isopropyl-5-((4-methoxyphenyl)amino) phenyl) carbamoyl) oxy)methyl)phenyl)boronic acid, TIDA ester (33)



In an argon filled glovebox, an oven dried 40 mL vial equipped with a stir bar was charged with **32** (100 mg, 0.178 mmol, 1 equiv), **31** (33.03 mg, 0.268 mmol, 1.5 equiv), SPhos G_4 (14.25 mg, 0.014 mmol, 0.1 equiv) and *t*-BuONa (25.78 mg, 0.268 mmol, 1.5 equiv). The vial was sealed with a PTFE septum cap, removed from the glovebox, and placed under positive pressure of argon via a needle attached to a Schlenk line. Anhydrous, argon-sparged toluene (4 mL) was added and then reaction was stirred at 100 °C for 12 hours. The reaction mixture was diluted with 5 mL of EtOAc and the organic phase washed with water (5 mL x 3) and then with brine (5 mL) directly in the vial, removing aqueous layers after each wash using a pipette. The organic layer was dried over anhydrous sodium sulfate, filtered through a cotton plug, and then concentrated via rotary

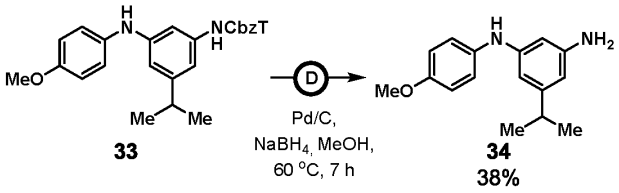
evaporation. The crude mixture was purified via silica gel column chromatography (0 to 100% hexanes/EtOAc) to yield the title compound as a white solid (91 mg, 0.151 mmol, 84% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.5 (d, J = 7.8 Hz, 2H), 7.3 (d, J = 7.8 Hz, 2H), 7.1 (d, J = 8.8 Hz, 2H), 6.8 (d, J = 8.9 Hz, 2H), 6.7 (s, 1H), 6.7 (s, 1H), 6.5 (s,1H), 5.2 (s, 2H), 3.8 (s, 3H), 2.8 (septet, J = 6.9 Hz, 1H), 1.8 (s, 7H), 1.5 (s, 7H), 1.2 (d, J = 6.9 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 174.7, 155.3, 153.2, 151.2, 145.9, 138.7, 137.3, 135.4, 134.2, 134.2, 127.4, 127.4, 122.4, 114.7, 109.0, 108.1, 103.3, 66.5, 55.6, 37.3, 34.3, 23.9, 23.8.

HRMS (ESI+) Calculated for C33H40BN3O7, $(M+H)^+$: 602.3038 , found: 602.3038.

Preparation of 5-isopropyl-N1-(4-methoxyphenyl)benzene-1,3-diamine (34)



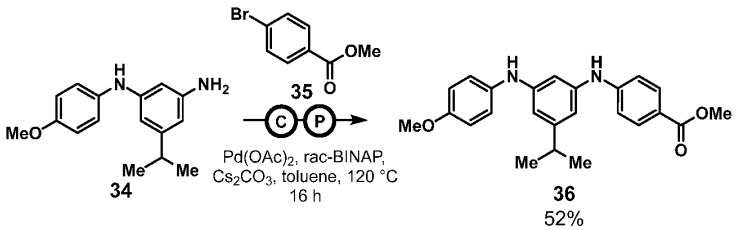
Following general deprotection procedure A, using **33** (91mg, 0.151 mmol, 1 equiv), $NaBH_4$ (171.7 mg, 30.0 equiv, 4.54 mmol), 10% Pd/C (10 wt%, 1.5mg) afforded a solid (15 mg, 38%).

^{1}H NMR (600 MHz,$CDCl_3$) δ 7.1 (d.1 (t, J = 1.8 Hz, 1H), 3.8 (s, 3H), 2.9 – 2.6 (septet, 1H), 1.2 (d, J = 6.9 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 155.1, 151.5, 147.4, 146.2, 135.9, 122.4, 114.6, 105.2, 105.1, 99.8, 55.6, 34.2, 23.9.

HRMS (ESI+) Calculated for C16H20N2O, $(M+H)^+$: 257.1654, found: 257.1650.

Preparation of methyl 3-((3-isopropyl-5-((4-methoxyphenyl)amino)phenyl)amino) benzoate (34)



In an argon filled glovebox, an oven dried 40 mL vial equipped with a stir bar was charged with **35** (11 mg, 0.052 mmol, 1 equiv), **34** (15.8 mg, 0.062 mmol, 1.5 equiv), $Pd(OAc)_2$(1.15 mg,

0.005 mmol, 0.1 equiv), Cs_2CO_3 (23.3 mg, 0.072 mmol, 1.4 equiv) and rac-BINAP (6.37 mg, 0.01 mmol, 0.2equiv). The vial was sealed with a PTFE septum cap, removed from the glovebox, and placed under positive pressure of argon via a needle attached to a Schlenk line. Anhydrous, argon-sparged toluene (4 mL) was added and then reaction was stirred at 120 °C for 16 hours. The reaction mixture was diluted with 5 mL of EtOAc and the organic phase washed with 2M HCL (2mL x 2) and then with brine (3 mL) directly in the vial, removing aqueous layers after each wash using a pipette. The organic layer was dried over anhydrous sodium sulfate, filtered through a cotton plug, and then concentrated via rotary evaporation. The crude mixture was purified via silica gel column chromatography (0 to 100% hexanes/EtOAc) to yield the title compound as a white solid (8 mg, 0.02 mmol, 52% yield).

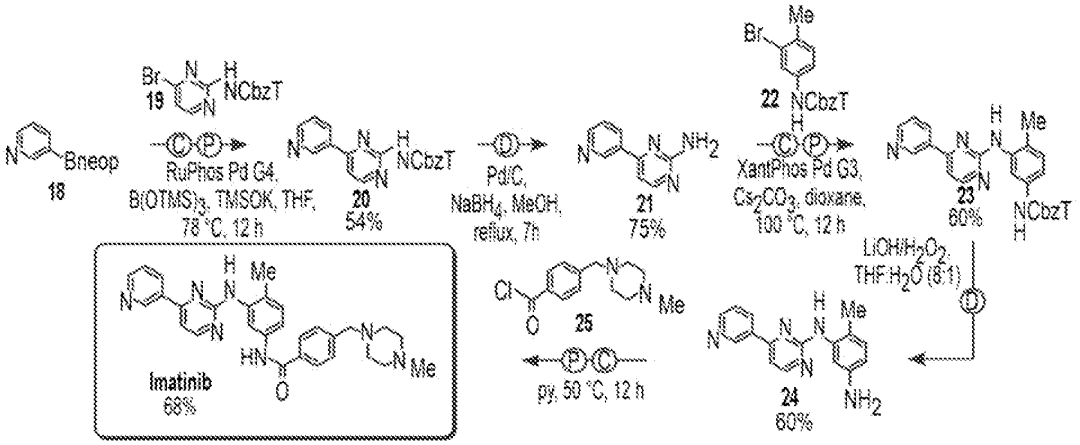
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.8 (d, *J* = 8.4 Hz, 2H), 7.0 (d, *J* = 8.8 Hz, 2H), 6.9 (d, *J* = 8.9 Hz, 2H), 6.8 (d, *J* = 8.8 Hz, 2H), 6.5 (s, 1H), 6.4 (s, 1H), 6.4 (s, 1H), 3.8 (s, 3H), 3.7 (s, 3H), 2.7 (septet, 1H), 1.1 (d, *J* = 6.9 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 167.0, 155.5, 151.7, 148.2, 146.4, 141.7, 135.3, 131.4, 128.2, 122.7, 120.8, 114.7, 109.8, 108.9, 104.5, 55.6, 51.7, 34.3, 23.9.

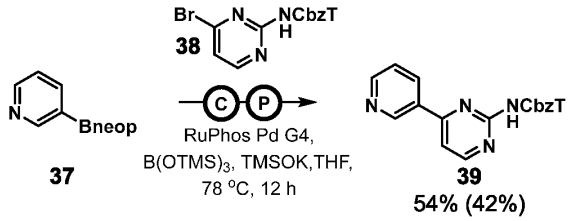
HRMS (ESI+) Calculated for C16H20N2O, $(M+H)^+$: 391.4910, found: 391.2014.

Example 4: Manual Synthesis of Imatinib

A schematic of the synthesis of imatinib is shown below.



Manual preparation of 4-(3,3,4,5,5-pentamethyl-2,6-dioxotetrahydro-2H-4λ⁴,8λ⁴-[1,3,2]oxazaborolo[2,3-b][1,3,2]oxazaborol-8-yl)benzyl (4-(pyridin-3-yl)pyrimidin-2-yl)carbamate (39)



In an argon filled glovebox, an oven dried 40 mL vial equipped with a stir bar was charged with **38** (100 mg, 0.19 mmol, 1 equiv) **37** (61 mg, 0.38 mmol, 2 equiv.), TMSOK (42 mg, 0.33 mmol, 1.7 equiv) and Pd-RuPhos-G4 precatalyst (16 mg, 0.019 mmol, 0.1 equiv). The vial was sealed with a PTFE septum cap, removed from the glovebox and $B(OTMS)_3$ (0.2 mL, 0.57 mmol, 3 equiv) followed by anhydrous THF (4 mL) were added via syringe. The vial was placed in a pre-equilibrated aluminum heating block set to 78 °C and stirred at 500 rpm overnight. The vial was removed from the heating block and allowed to cool to room temperature. The reaction mixture was diluted with hexane (30 mL) and filtered through a silica plug. The plug was washed with hexanes (100 mL), Et_2O (100 mL) and EtOAc (100 mL), and then the eluents were discarded. The silica plug was then washed with acetone (200 mL) to elute the product. The acetone eluent was concentrated via rotary evaporation to yield **39** as a white solid (54.2 mg, 54% yield).

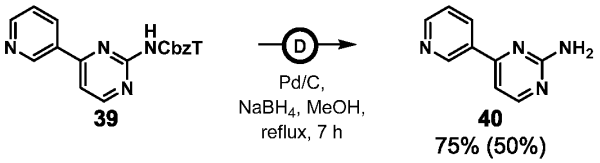
^{1}H NMR (600 MHz, $CDCl_3$) δ 9.29 (d, J = 2.4 Hz, 1H), 8.83 (s, 1H), 8.73 – 8.68 (m, 1H), 8.63 (dd, J = 5.5, 2.0 Hz, 1H), 8.39 (dd, J = 8.0, 2.3 Hz, 1H), 7.56 (dd, J = 7.9, 2.1 Hz, 2H), 7.43 – 7.38 (m, 4H), 5.27 (d, J = 2.0 Hz, 2H), 2.48 (d, J = 2.1 Hz, 3H), 1.85-1.70 (m, 6H), 1.59-1.45 (m, 6H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 174.78, 163.25, 159.48, 157.99, 152.01, 151.72, 148.58, 136.87, 134.98, 132.02, 127.91, 123.97, 111.76, 67.28, 37.50.

^{11}B NMR (161 MHz, $CDCl_3$) δ 8.73.

HRMS (ESI+) Calculated for $C_{26}H_{29}BN_5O_6$ $(M+H)^+$: 518.2211, found: 518.2232.

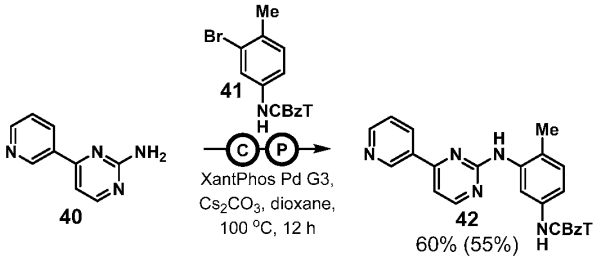
Manual deprotection of 39 to prepare 4-(pyridin-3-yl)pyrimidin-2-amine (40)



To a 40 mL vial with a stir bar was added **39** (50 mg, 0.096 mmol, 1.0 equiv), $NaBH_4$ (0.1 g, 2.90 mmol, 30.0 equiv,) and 10 wt % of 10% Pd/C (5 mg). Using a needle attached to a Schlenk line, the vial was evacuated and backfilled with nitrogen (3x) and then MeOH (3 mL) was added by syringe. An empty (deflated) balloon attached to a needle was placed through the septum to avoid loss of generated hydrogen without buildup of excess pressure and then the reaction was stirred at 68 °C for 2 hours. The reaction mixture was diluted with hexanes (30 mL) and filtered throug a silica plug. The plug was washed with hexanes (100 mL), Et_2O (100 mL) and EtOAc (100 mL) and then the eluent was discarded. The the silica plug was washed with acetone (250 mL) to release the product. The acetone eluent was then concentrated via rotary evaporation to yield **40** as a white solid (12.2 mg, 75% yield).

^{1}H NMR (400 MHz, CDCl3) δ 9.20 (d, J = 2.1 Hz, 1H), 8.70 (d, J = 4.9 Hz, 1H), 8.39 (d, J = 5.2 Hz, 1H), 8.34 – 8.27 (m, 1H), 7.41 (dd, J = 8.1, 4.8 Hz, 1H), 7.07 (d, J = 5.2 Hz, 1H). The data are in agreement with data from the literature: J. Kang, J.Y. Lee, J-H. Park, D-J. Chang, *J. Label Compd. Radiopharm.*, **2020**, 63:174–182.

Manual preparation of 4-(3,3,4,5,5-pentamethyl-2,6-dioxotetrahydro-2H-4λ^4,8λ^4-[1,3,2]oxazaborolo[2,3-b][1,3,2]oxazaborol-8-yl)benzyl (4-methyl-3-((4-(pyridin-3-yl)pyrimidin-2-yl)amino)phenyl)carbamate (42)



In an argon filled glovebox, an oven dried 40 mL vial equipped with a stir bar was charged with **40** (20 mg, 0.11 mmol, 1.0 equiv), **41** (185 mg, 0.35 mmol, 3.0 equiv), Cs_2CO_3 (75 mg, 0.232 mmol, 2.0 equiv), and XantPhos-Pd-G3 (22 mg, 0.023 mmol, 0.2 equiv). The vial was sealed with a PTFE septum cap, removed from the glovebox, and placed under positive pressure of argon via

needle attached to a Schlenk line. Anhydrous dioxane (3 mL) was added via syringe. The vial was placed in a pre-equilibrated aluminum heating block set to 100 °C and stirred at 600 rpm for 12 hours. The vial was removed from the heating block and allowed to cool to room temperature. The reaction mixture was diluted with hexane (30 mL) and filtered through a silica plug. The silica plug was washed with hexanes (100 mL), Et_2O (100 mL) and EtOAc (100 mL) then the eluents were discarded. The silica plug was washed with acetone (250 mL) to elute **42**. The acetone eluent was concentrated via rotary evaporation to **42** as a white solid (44 mg, 60% yield).

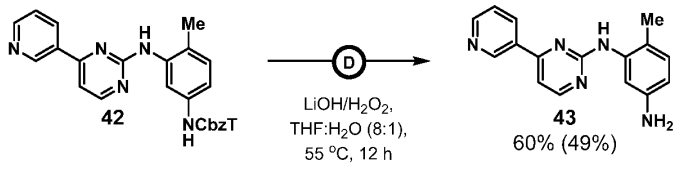
^{1}H NMR (600 MHz, $CDCl_3$) δ 9.25 (d, J = 2.2 Hz, 1H), 8.71 (dd, J = 5.0, 1.6 Hz, 1H), 8.50 (d, J = 5.1 Hz, 1H), 8.49 – 8.45 (m, 1H), 8.35 (s, 1H), 7.57 (d, J = 7.6 Hz, 2H), 7.43 – 7.35 (m, 3H), 7.18 (d, J = 5.1 Hz, 1H), 7.15 (d, J = 8.2 Hz, 1H), 7.05 (d, J = 8.3 Hz, 1H), 6.99 (s, 1H), 6.75 (s, 1H), 5.21 (s, 2H), 2.48 (s, 3H), 2.32 (s, 3H), 1.85-1.72 (m, 6H), 1.59-1.45 (m, 6H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 174.78, 162.89, 160.65, 159.19, 151.60, 148.65, 137.98, 137.43, 135.08, 134.38, 130.96, 127.61, 123.88, 108.59, 66.78, 37.51, 17.69.

^{11}B NMR (161 MHz, $CDCl_3$) δ 9.04.

HRMS (ESI+) Calculated for $C_{33}H_{36}BN_6O_6$ $(M+H)^+$: 623.2789, found: 623.2797.

Deprotection of 40 to prepare 6-methyl-N^1-(4-(pyridin-3-yl)pyrimidin-2-yl)benzene-1,3-diamine (43)



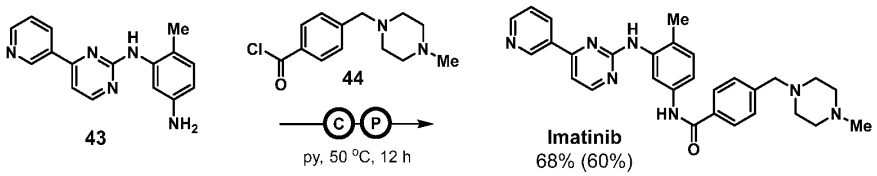
To a 40 mL vial with a stir bar was added **42** (44 mg, 0.064 mmol, 1 equiv) and then THF (5 mL) was added by syringe. The solution was vigorously stirred and then 3 M aqueous LiOH* (300 µL, 1.3 mmol, 15 equiv) was added by syringe. Aqueous 30% H_2O_2 (200 µL) was added by syringe, the vial was sealed tightly with a PTFE septum cap, the vial was placed in a pre-equilibrated 55 °C heating block, and then the reaction was stirred for 12 hours. The reaction mixture was diluted with hexane (30 mL) and filtered through a silica plug. Then silica plug was washed with hexanes (100 mL), Et_2O (100 mL) and EtOAc (100 mL) and then the eluents were

discarded. The silica plug was washed with acetone (250 mL) to elute the product. The acetone eluent was concentrated via rotary evaporation and to **43** as a white solid (11 mg, 60% yield).

*NaOH can be used as an alternative base. LiOH provides a milder option for deprotection.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.26 (s, 1H), 8.71 (d, J = 4.0 Hz, 1H), 8.50 (d, J = 5.2 Hz, 1H), 8.35 (d, J = 8.1 Hz, 1H), 7.61 (s, 1H), 7.43 (dd, J = 8.0, 4.8 Hz, 1H), 7.15 (d, J = 5.2 Hz, 1H), 7.00 (d, J = 8.0 Hz, 2H), 6.42 (dd, J = 8.0, 2.4 Hz, 1H), 2.25 (s, 3H).

Preparation of N-(4-methyl-3-((4-(pyridin-3-yl)pyrimidin-2-yl)amino)phenyl)-4-((4-methylpiperazin-1-yl)methyl)benzamide (Imatinib)



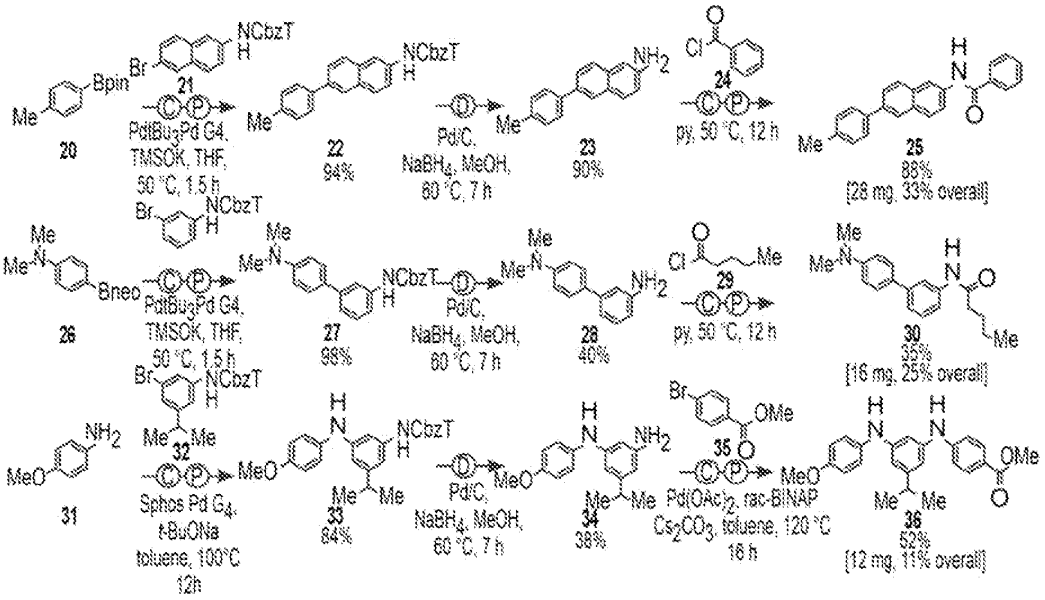
43 (10 mg, 0.036 mmol, 1 equiv) and 4-(4-methyl-piperazinomethyl)-benzoyl chloride (**44**, 11 mg, 0.043 mmol, 1.22 equiv) were added to an oven-dried 40 mL vial with a stir bar. The vial was sealed with a PTFE septum cap, and then evacuated and backfilled with nitrogen (3x) via a needle attached to a Schlenk line. Freshly distilled pyridine (2 mL) was added by syringe. The mixture was then placed in a pre-equilibrated 50° C heat block and stirred for 12 hours. The solvent was concentrated on a rotary evaporator using a water bath temperature of 70° C. Water (4 ml) was added, and then the solution was basified to pH 10 with 6 N NaOH. The aqueous solution was extracted with dichloromethane (2×10 mL), and the collected organic phase dried over anhydrous sodium sulfate. The crude reaction mixture was resuspended in 1:1 H_2O:ACN 0.1% Formic Acid for preparative HPLC purification with an Agilent 10 Prep-C18 250 x 50.0mm column. The final product imatinib was isolated as a white solid (12 mg, 68% yield).

^{1}H NMR (600 MHz, DMSO) δ 10.18 (s, 1H), 9.28 (s, 1H), 8.99 (s, 1H), 8.68 (dd, J = 4.8, 1.7 Hz, 1H), 8.51 (d, J = 5.1 Hz, 1H), 8.48 (dt, J = 8.0, 1.9 Hz, 1H), 8.11 (d, J = 2.2 Hz, 1H), 7.91 (d, J = 8.0 Hz, 2H), 7.53 – 7.47 (m, 2H), 7.45 – 7.40 (m, 3H), 7.20 (d, J = 8.3 Hz, 1H), 3.51 (s, 2H), 2.50-2.23 (m, 8H), 2.24 (s, 3H) 2.13 (s, 3H). Consistent with literature spectral data.

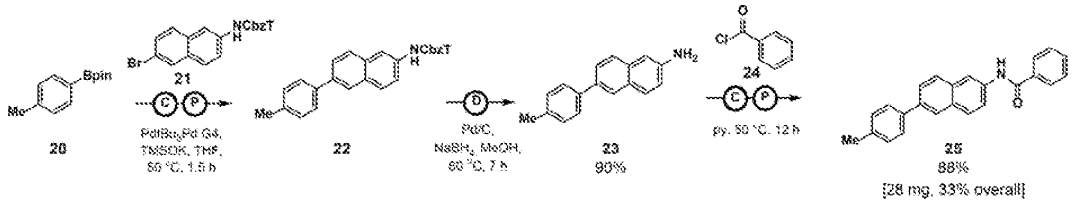
^{13}C NMR (151 MHz, DMSO) δ 165.27, 161.61, 161.20, 159.46, 151.38, 148.22, 142.11, 137.81, 137.24, 134.42, 133.78, 132.23, 130.04, 128.62, 127.60, 123.77, 117.20, 116.74, 107.51, 61.64, 54.70, 52.58, 45.74, 17.69.

HRMS (ESI+) Calculated for $C_{29}H_{32}N_7O$ $(M+H)^+$: 494.2668, found: 494.2671.

Example 5: Automated Synthesis of Trimers via Iterative N-C and C-C Bond Formation

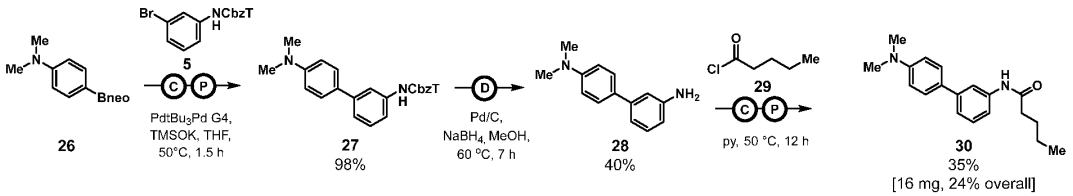


Automated synthesis of N-(6-(p-tolyl)naphthalen-2-yl)benzamide (25)



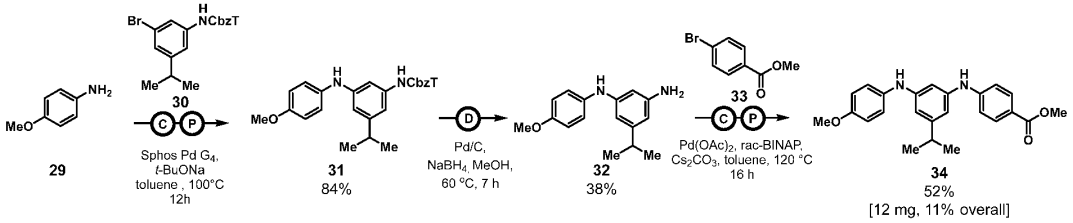
Following the general automated procedures as described in **Example 7** on 0.25 mmol scale of **21** (141.81 mg, 0.25 mmol, 1 equiv) and using the same reaction stoichiometries as described for the manual synthesis, **25** was isolated as a white solid (28 mg, 0.083 mmol, 33% overall yield). Yields and purities of intermediates were not checked. Characterization data for **23** match those reported in the manual synthesis section.

Automated synthesis of N-(4'-(dimethylamino)-[1,1'-biphenyl]-3-yl)pentanamide (30)



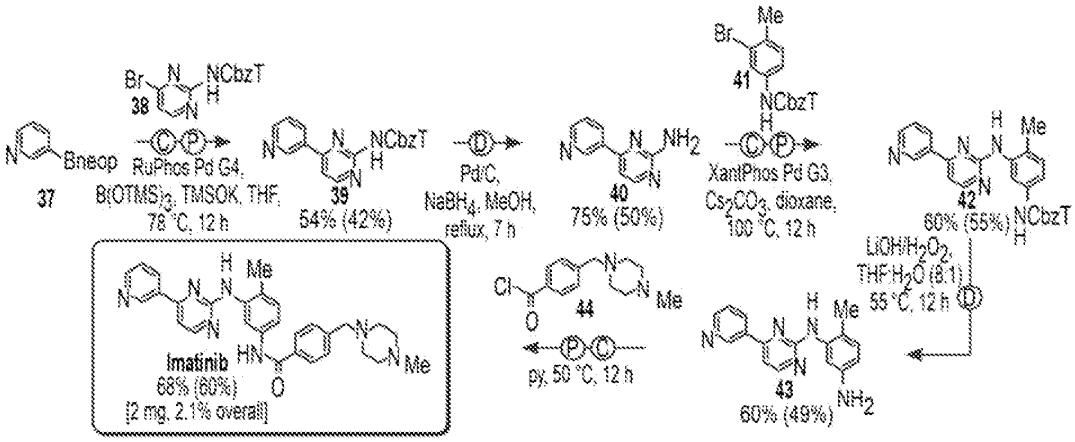
Following the general automated procedures as described in **Example 7** on 0.33 mmol scale of **5** (170 mg, 0.33 mmol, 1 equiv) and using the same reaction stoichiometries as described for the manual synthesis, **30** was isolated as a white solid (17 mg, 0.057 mmol, 17% overall yield). Yields and purities of intermediates were not checked. Characterization data for 30 match those reported in the manual synthesis section.

Automated synthesis of methyl 4-((3-isopropyl-5-((4-methoxyphenyl)amino)phenyl)amino)benzoate (34)



Following the general automated procedures as described in **Example 7** on 0.358 mmol scale of **30** (200 mg, 0.358 mmol, 1 equiv) and using the same reaction stoichiometries as described for the manual synthesis, **34** was isolated as a white solid (12 mg, 0.031 mmol, 11% overall yield). Yields and purities of intermediates were not checked. Characterization data for **34** match those reported in the manual synthesis section.

Example 6: Automated Synthesis of Imatinib



Following the general automated procedures as described in **Example 7** on 0.19 mmol scale of **38** (100 mg, 0.19 mmol, 1 equiv) and using the same reaction stoichiometries as described for the manual synthesis, Imatinib was isolated as a white solid (2.0 mg, 0.004 mmol, 2.1% overall yield). For the overall yield we are reporting of the fully automated sequence, yields and purities of intermediates were not checked. Characterization data for Imatinib match those reported in the manual synthesis section.

Example 7: Construction and Operation of the Automated Synthesis Platform

The automated synthesis machine was constructed using the same reconfigurable valves and syringe pumps as our prior reported iterative small molecule synthesizers in a unique configuration suited driven by custom LabVIEW software. Each reaction vial was connected to the solvent reservoirs via 18-gauge syringe needle, PEEK tubing, and Luer lock fittings, through four computer-controlled 9-port 4-valve modules and two computer-controlled syringe pumps (10 mL main pump and 10 mL wet pump). The synthesis machine uses many of the engineering controls optimized for reaction reproducibility from our now published studies of closed-loop optimization of general reaction conditions, notably symmetrically circular aluminium heating blocks, an automated Schlenk line driven by J-Kem valve modules, magnetic heating plates, rare earth stir bars, and Leur-lock cap solvent inert manifold, as well as our rapid automated iterative small molecule synthesizer, notably an automated rotary evaporator (see further improvements

below). The LabVIEW code was modified to account for the unique fluid path of this prototype configuration.

The solvents attached to the dry pump were stored in 250 mL to 1L Pyrex glass media bottles and connected via PEEK tubing, Luer lock fittings, and 3-port Cole-Parmer VapLock solvent delivery caps to both the argon manifold and the valve modules. One of the three ports on each solvent cap was connected to the argon manifold and one to PEEK tubing reaching the bottom of the solvent bottles (dip tube). The last port was capped. The full argon manifold was connected to a plugged passive 9-port valve (vent port). Solvents refilled on the system were degassed by argon purging for one hour. Degassing was accomplished by first depressurizing the manifold by uncapping the third port on the solvent cap and dipping the line connected to the argon manifold into the solvent (sparging begins). Following the degassing time, argon sparging is ceased by pulling the argon line out of the solvent and capping the open port. In this way, solvents could be refilled and degassed individually while pressure differences between solvents on the manifold cannot result in redistribution or mixing. Solvents attached to the wet pumps were added to 40 mL I-Chem vials and used immediately before any aqueous reaction. Automated rotary evaporation was accomplished as described in our prior report.

The automated Schlenk Process utilizes a Fisherbrand™ Maxima Rotary Vane Vacuum Pumps – 115 V, 60 Hz and autoSchlenk processes operated via alternating between 60 seconds of vacuum and 5 seconds of argon pressure cycles (valve module). The argon cylinder was maintained at ~4 PSI regulator setting throughout the study to ensure appropriate pressure at each position. A standard 10 cycles of autoschlenk (<15 min) was used to deoxygenize the system prior to executing automated synthesis procedures. AutoSchlenk is also useful for drying residual solvent vapours from the manifold in between automated runs or after automated cleaning procedures.

Vacuum draining during the automated purification used a KNF Neuberger Vacuum Diaphragm Pump connected to the headspace of a 3-port Cole-Parmer VapLock solvent delivery cap on a 1L Pyrex glass media bottle (the vacuum drained solvent is collected at the bottom of this bottle and is discarded between runs), and the pump is vented to laboratory exhaust in the same manner as the automated rotary evaporator. Buchi R-100 rotovap with Buchi V-100 vacuum pump and I-100 interface.

Modules description

Design of Anhydrous Suzuki Coupling Module

The anhydrous Suzuki coupling module consists of one 40 mL 9-Chem vial. The coupling module contains catalyst, halide, TMSOK, and neopentyl ester, and a 10 mm diameter rare earth Teflon coated stir bar. The main pump transfers reaction solvent into the coupling module. The coupling module is then stirred at the desired rpm until reaction completion. The reaction is then purified via catch-and-release. The release solvent is transferred to the anhydrous deprotection module and concentrated prior to deprotection.

Design of Anhydrous Deprotection Module

The anhydrous deprotection module consists of one 40 mL I-Chem vial. Upon concentration of solvent, the deprotection cartridge is loaded with $NaBH_4$ and Pd on Carbon (10% wt), and 10mm diameter rare earth Teflon coated stir bar. During addition of MeOH, a balloon is attached to prevent over pressurization while maintaining high H_2 atmosphere in the reaction vial. The main pump transfers solutions of TIDA boronates into the deprotection module. The deprotection cartridge is then stirred at the desired time, temperature, and rpm until reaction completion. The reaction is then purified via anhydrous catch-and-release. The release solvent is transferred through a polyethylene-fritted 12-gram Luknova cartridge containing approximately one cubic cm of celite. The celite in the filter cartridge is well packed onto the frit via wetting with hexanes followed by air drying.

Design of Buchwald-Hartwig Coupling Module

The Buchwald-Hartwig coupling module consists of two 40 mL I-Chem vials. The first vial is an isolation vial, where following anhydrous deprotection and filtration through a celite packed 12-gram Luknova column, the released solvent is concentrated off to dryness. Following concentration, the main pump adds reaction solvent to dissolve the deprotected amine and transfers it to the second 40 mL I-Chem vial containing halide, Cs_2CO_3, and catalyst. The reaction module is then stirred at the desired time, temperature, and rpm until reaction completion. The reaction is then purified via anhydrous catch-and-release. The release solvent is transferred back into the reaction vial and concentrated to a desired volume and transferred to the aqueous deprotection module via the main pump.

Design of Aqueous Deprotection Module

The deprotection module consists of one polyethylene-fritted 12-gram Luknova cartridge and 1 40 mL I-Chem vial containing 3 M solution of LiOH. One filter cartridge is situated on top of the deprotection cartridge and contains approximately one cubic cm of celite. The celite in the filter cartridges is well packed onto the frit via wetting with hexanes followed by air drying. The dry pump transfers solutions of TIDA boronates through the filter cartridge and into the deprotection cartridge. The wet pump adds an aqueous solution of H_2O_2. The deprotection cartridge is then stirred at the desired rpm until reaction completion. The reaction is then filtered through a 12-gram Luknova cartridge containing Na_2SO_4 into the amide coupling module.

Design of Amide Coupling Module

The amide coupling module consists of one 40-mL Ichem vial. Upon transferring from the aqueous deprotection module, the release solvent is concentrated to dryness. Prior to coupling, 2 40 mL I-Chem vials connected to the wet pump are filled with pyridine and a pyridine solution of carboxylic acid. The wet pump is prerinsed with pyridine by withdrawing 10 mL of pyridine and discarding it. The wet pump then withdraws the pyridine/carboxylic acid solution and adds it to the vial containing the purified deprotected amine. The deprotection cartridge is then stirred at the desired rpm until reaction completion.

Design of Anhydrous Reaction Module

The design of the anhydrous reaction module is shown in **FIG. 7**. The coupling module consists of up to 4 40 mL I-Chem vials (reaction cartridges) each with septa cap and equipped with rare earth Teflon coated stir bar (10 mm diameter). Each reaction cartridge is connected to the argon manifold and the valve modules via 16- and 18-gauge needles, respectively. The reaction cartridges are all simultaneously deoxygenated via an automated Schlenk process as described previously. Sensitive reagents are loaded prior to reaction. Otherwise, the reaction cartridges are preloaded with required chemicals. For reactions requiring higher temperatures, the heating block is set to the desired reaction temperature at the start of the automated reaction time. The 16-gauge needle connecting each reaction cartridge to the valve modules is connected internally to 0.125" PEEK tubing fitted on the bottom with a 20 μm end line filter (Biolytic Lab Performance Inc).

This dip tube enables transfer from the bottom of the reaction cartridge to any other component of the module. The reaction cartridge is also connected to the automated rotary evaporator to allow for concentration of purified reaction mixtures.

Design of Aqueous Reaction Module

The design of the aqueous reaction module is shown in **FIG. 8**. The coupling module consists of two 40 mL I-Chem vials (reaction cartridges) each with septa cap and equipped with rare earth Teflon coated stir bar (10 mm diameter). Sensitive reagents are loaded prior to reaction. Otherwise, the reaction cartridges are preloaded with required chemicals, or chemicals are transferred from elsewhere on the module. For reactions requiring higher temperatures, the heating block is set to the desired reaction temperature at the start of the automated reaction time. The 16-gauge needle connecting each reaction cartridge to the valve modules is connected internally to 0.125" PEEK tubing fitted on the bottom with a 20 μm end line filter (Biolytic Lab Performance Inc). This dip tube enables transfer from the bottom of the reaction cartridge to any other component of the module. The reaction cartridge is also connected to the automated rotary evaporator to allow for concentration of purified reaction mixtures.

Design of Purification Modules

The design of the purification module is shown in **FIG. 9**. The purification module consists of one 10 gram Biotage column. The purification cartridge is made by first adding a packed bed of silica (0.75 in.) to the bottom frit. Glass beads (4 mm) are then loaded on top of the silica bed, and a 1:1 silica:sand is added to fill the dead volume. The top frit, cap, and insert are then fitted together to complete the purification cartridge. The filtration cartridge is fitted directly into the purification cartridge inline on the valve module and standing upside down. During purification, the pump adds hexane/Et_2O/EtOAc directly to the reaction cartridge. This reaction solution is then vacuum filtered through the endline filter and through the filtration cartridge followed by the purification cartridge. Then, the dry/wet pump reverse elutes the two cartridges with acetone/THF into the reaction cartridge and the reaction cartridge is concentrated via automated rotary evaporation.

Automated Synthesis Procedures

Automated Suzuki-Miyaura Coupling Procedure

To a 40 mL I-Chem vial was loaded TIDA bifunctional, neopentyl ester and catalyst. The vial was placed in the coupling module aluminum heating block. An automated Schlenk-line procedure[2] was performed followed by addition of 4 mL desired solvent via dry pump. The reaction was heated and stirred for the given reaction time.

Automated Anhydrous Purification Procedure

To the crude reaction mixture was added hexane or ether (20 mL) via the dry pump to precipitate the TIDA boronate. The hexane/ether was then purged through the filter and purification cartridge via a diaphragm vacuum pump (20 minutes). Ether (if precipitation solvent was hexane) or Ethyl acetate (if precipitation solvent was ether) (20 mL) solution was then added to the reaction vial and purged through the filter and purification cartridge (20 minutes). This process was repeated twice. Acetone/THF was then reverse eluted (2x10 mL) and concentrated via automated rotary evaporation either to completion or a desired volume (~30 min).

Automated Anhydrous Deprotection Procedure

Immediately following purification of the Suzuki coupling, the THF is evacuated to dryness. The TIDA boronate is redissolved in MeOH. To the reaction cartridge containing 1 equiv. TIDA boronate is added 10 wt% Pd/C and 30 equiv $NaBH_4$. The reaction is stirred at the desired temperature for 7 hours.

Automated Buchwald-Hartwig Coupling Procedure

To a 40 mL I-Chem vial was loaded TIDA bifunctional, amine, base, and catalyst. The vial was placed in the coupling module aluminum heating block. An automated Schlenk-line procedure was performed followed by addition of 4 mL desired solvent via dry pump. The reaction was heated and stirred for the given reaction time.

Automated Aqueous Deprotection Procedure

Following the *Automated Anhydrous Purification Procedure*, the THF solution of purified TIDA is then transferred to a vial containing LiOH. The wet pump then adds an aqueous solution of H_2O_2 to the vial. The reaction is then stirred at the desired time and temperature.

Automated Aqueous Purification Procedure

Following the *Automated Aqueous Deprotection Procedure*, the THF:H_2O:H_2O_2 solution is filtered through a cartridge containing Na_2SO_4. The deprotected product is used without any further purification.

Automated Amide Coupling Procedure

Following the *Automated Aqueous Deprotection Procedure*, the dried THF solution of amine is concentrated to dryness. A solution of carboxylic acid dissolved in 4 mL pyridine is added to dissolve the concentrated amine. The reaction is then heated to the desired temperature and stirred for the desired time.

Example 8: Single-Crystal X-Ray Diffraction Data

Crystal data and structure refinement for chloroformate **1** (10632ds), CCDC Number: 2291420 are provided below.

Table 1. Crystal data and structure refinement for 10632ds.

Identification code	10632ds
Empirical formula	$C_{16.86}H_{21.04}BCl_{0.95}NO_{5.76}$
Formula weight	374.32
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	$P2_1/c$
Unit cell dimensions	a = 15.4683(6) Å a= 90°. B = 7.8079(3) Å b= 95.7730(13)°. C = 15.0685(6) Å g = 90°.
Volume	1810.67(12) $Å^3$

Z	4
Density (calculated)	1.373 mg/m^3
Absorption coefficient	0.235 mm^{-1}
F(000)	786
Crystal size	0.404 x 0.161 x 0.034 mm^3
Theta range for data collection	2.647 to 27.540°
Index ranges	-20<=h<=20, -10<=k<=10, -19<=l<=19
Reflections collected	**66612**
Independent reflections	4176 [R(int) = 0.0425]
Completeness to theta = 25.242°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7456 and 0.7051
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4176 / 39 / 256
Goodness-of-fit on F^2	**1.097**
Final R indices [I>2sigma(I)]	R1 = 0.0376, wR2 = 0.0930
R indices (all data)	R1 = 0.0418, wR2 = 0.0959
Extinction coefficient	n/a
Largest diff. peak and hole	0.345 and -0.275 e.$Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for 10632ds.

U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	7075(1)	4838(1)	2890(1)	21(1)
O(2)	7498(1)	6752(2)	1906(1)	30(1)
O(3)	4593(1)	4981(1)	4008(1)	25(1)
O(4)	5941(1)	4066(1)	3863(1)	20(1)

N(1)	6683(1)	6826(1)	4000(1)	17(1)
C(1)	7292(1)	6413(2)	2637(1)	22(1)
C(2)	7309(1)	7678(2)	3413(1)	21(1)
C(3)	5699(1)	7035(2)	3697(1)	20(1)
C(4)	5342(1)	5269(2)	3905(1)	19(1)
C(5)	8248(1)	7617(2)	3868(1)	26(1)
C(6)	7113(1)	9541(2)	3152(1)	29(1)
C(7)	5260(1)	8482(2)	4163(1)	29(1)
C(8)	5455(1)	7149(2)	2674(1)	27(1)
C(9)	6872(1)	7300(2)	4967(1)	21(1)
C(10)	7485(1)	3679(2)	4482(1)	19(1)
C(11)	7229(1)	3142(2)	5305(1)	21(1)
C(12)	7763(1)	2138(2)	5892(1)	23(1)
C(13)	8575(1)	1625(2)	5668(1)	22(1)
C(14)	8839(1)	2124(2)	4850(1)	25(1)
C(15)	8302(1)	3131(2)	4266(1)	23(1)
C(16)	9157(1)	559(2)	6305(1)	26(1)
B(1)	6826(1)	4756(2)	3816(1)	18(1)
Cl(1)	9258(1)	-4390(1)	6103(1)	33(1)
O(5)	9093(2)	-1182(2)	5963(1)	19(1)
O(6)	9750(1)	-2104(2)	7288(1)	36(1)
C(17)	9410(1)	-2351(2)	6563(1)	21(1)
Cl(2)	9137(6)	-1738(10)	6163(6)	39(2)
O(7)	9627(17)	1130(30)	7154(13)	36(1)

Table 3. Bond lengths [Å] and angles [°] for 10632ds.

O(1)-C(1)	1.3404(17)
O(1)-B(1)	1.4856(16)
O(2)-C(1)	1.2056(17)
O(3)-C(4)	1.2055(17)
O(4)-C(4)	1.3252(16)

O(4)-B(1)	1.4793(17)
N(1)-C(9)	1.5029(16)
N(1)-C(2)	1.5280(16)
N(1)-C(3)	1.5522(17)
N(1)-B(1)	1.6589(18)
C(1)-C(2)	1.5296(19)
C(2)-C(6)	1.5293(19)
C(2)-C(5)	1.544(2)
C(3)-C(7)	1.5258(19)
C(3)-C(4)	1.5296(19)
C(3)-C(8)	1.5531(19)
C(5)-H(5A)	0.9800
C(5)-H(5B)	0.9800
C(5)-H(5C)	0.9800
C(6)-H(6A)	0.9800
C(6)-H(6B)	0.9800
C(6)-H(6C)	0.9800
C(7)-H(7A)	0.9800
C(7)-H(7B)	0.9800
C(7)-H(7C)	0.9800
C(8)-H(8A)	0.9800
C(8)-H(8B)	0.9800
C(8)-H(8C)	0.9800
C(9)-H(9A)	0.9800
C(9)-H(9B)	0.9800
C(9)-H(9C)	0.9800
C(10)-C(15)	1.4027(18)
C(10)-C(11)	1.4044(18)
C(10)-B(1)	1.5958(19)
C(11)-C(12)	1.3904(19)
C(11)-H(11)	0.9500

C(12)-C(13)	1.393(2)	
C(12)-H(12)	0.9500	
C(13)-C(14)	1.392(2)	
C(13)-C(16)	1.5002(19)	
C(14)-C(15)	1.392(2)	
C(14)-H(14)	0.9500	
C(15)-H(15)	0.9500	
C(16)-O(5)	1.454(2)	
C(16)-O(7)	1.476(15)	
C(16)-Cl(2)	1.806(8)	
C(16)-H(16A)	0.9900	
C(16)-H(16B)	0.9900	
C(16)-H(16C)	0.9900	
C(16)-H(16D)	0.9900	
C(16)-H(16E)	0.9900	
C(16)-H(16F)	0.9900	
Cl(1)-C(17)	1.7429(17)	
O(5)-C(17)	1.342(2)	
O(6)-C(17)	1.178(2)	
O(7)-H(7)	0.8400	
C(1)-O(1)-B(1)		113.76(10)
C(4)-O(4)-B(1)		113.54(10)
C(9)-N(1)-C(2)		112.40(10)
C(9)-N(1)-C(3)		110.41(10)
C(2)-N(1)-C(3)		116.30(10)
C(9)-N(1)-B(1)		112.72(10)
C(2)-N(1)-B(1)		102.93(9)
C(3)-N(1)-B(1)		101.36(9)
O(2)-C(1)-O(1)		123.91(13)
O(2)-C(1)-C(2)		124.84(13)
O(1)-C(1)-C(2)		111.10(11)

N(1)-C(2)-C(6)	116.26(11)
N(1)-C(2)-C(1)	101.48(10)
C(6)-C(2)-C(1)	115.42(11)
N(1)-C(2)-C(5)	110.67(11)
C(6)-C(2)-C(5)	107.29(12)
C(1)-C(2)-C(5)	105.18(11)
C(7)-C(3)-C(4)	112.76(11)
C(7)-C(3)-N(1)	114.30(11)
C(4)-C(3)-N(1)	102.02(10)
C(7)-C(3)-C(8)	109.82(12)
C(4)-C(3)-C(8)	101.42(11)
N(1)-C(3)-C(8)	115.58(11)
O(3)-C(4)-O(4)	124.04(13)
O(3)-C(4)-C(3)	124.48(13)
O(4)-C(4)-C(3)	111.13(11)
C(2)-C(5)-H(5A)	109.5
C(2)-C(5)-H(5B)	109.5
H(5A)-C(5)-H(5B)	109.5
C(2)-C(5)-H(5C)	109.5
H(5A)-C(5)-H(5C)	109.5
H(5B)-C(5)-H(5C)	109.5
C(2)-C(6)-H(6A)	109.5
C(2)-C(6)-H(6B)	109.5
H(6A)-C(6)-H(6B)	109.5
C(2)-C(6)-H(6C)	109.5
H(6A)-C(6)-H(6C)	109.5
H(6B)-C(6)-H(6C)	109.5
C(3)-C(7)-H(7A)	109.5
C(3)-C(7)-H(7B)	109.5
H(7A)-C(7)-H(7B)	109.5
C(3)-C(7)-H(7C)	109.5

H(7A)-C(7)-H(7C)	109.5
H(7B)-C(7)-H(7C)	109.5
C(3)-C(8)-H(8A)	109.5
C(3)-C(8)-H(8B)	109.5
H(8A)-C(8)-H(8B)	109.5
C(3)-C(8)-H(8C)	109.5
H(8A)-C(8)-H(8C)	109.5
H(8B)-C(8)-H(8C)	109.5
N(1)-C(9)-H(9A)	109.5
N(1)-C(9)-H(9B)	109.5
H(9A)-C(9)-H(9B)	109.5
N(1)-C(9)-H(9C)	109.5
H(9A)-C(9)-H(9C)	109.5
H(9B)-C(9)-H(9C)	109.5
C(15)-C(10)-C(11)	117.07(12)
C(15)-C(10)-B(1)	123.26(12)
C(11)-C(10)-B(1)	119.54(11)
C(12)-C(11)-C(10)	121.88(12)
C(12)-C(11)-H(11)	119.1
C(10)-C(11)-H(11)	119.1
C(11)-C(12)-C(13)	120.02(13)
C(11)-C(12)-H(12)	120.0
C(13)-C(12)-H(12)	120.0
C(14)-C(13)-C(12)	119.12(13)
C(14)-C(13)-C(16)	120.74(13)
C(12)-C(13)-C(16)	120.14(13)
C(15)-C(14)-C(13)	120.59(13)
C(15)-C(14)-H(14)	119.7
C(13)-C(14)-H(14)	119.7
C(14)-C(15)-C(10)	121.31(13)
C(14)-C(15)-H(15)	119.3

C(10)-C(15)-H(15)	119.3
O(5)-C(16)-C(13)	106.07(13)
O(7)-C(16)-C(13)	126.7(10)
C(13)-C(16)-Cl(2)	118.2(3)
O(5)-C(16)-H(16A)	110.5
C(13)-C(16)-H(16A)	110.5
O(5)-C(16)-H(16B)	110.5
C(13)-C(16)-H(16B)	110.5
H(16A)-C(16)-H(16B)	108.7
C(13)-C(16)-H(16C)	107.8
Cl(2)-C(16)-H(16C)	107.8
C(13)-C(16)-H(16D)	107.8
Cl(2)-C(16)-H(16D)	107.8
H(16C)-C(16)-H(16D)	107.1
O(7)-C(16)-H(16E)	105.6
C(13)-C(16)-H(16E)	105.6
O(7)-C(16)-H(16F)	105.6
C(13)-C(16)-H(16F)	105.6
H(16E)-C(16)-H(16F)	106.1
O(4)-B(1)-O(1)	112.89(11)
O(4)-B(1)-C(10)	108.30(11)
O(1)-B(1)-C(10)	113.83(11)
O(4)-B(1)-N(1)	101.91(10)
O(1)-B(1)-N(1)	99.61(10)
C(10)-B(1)-N(1)	119.70(11)
C(17)-O(5)-C(16)	112.93(17)
O(6)-C(17)-O(5)	127.70(19)
O(6)-C(17)-Cl(1)	123.18(16)
O(5)-C(17)-Cl(1)	109.12(15)
C(16)-O(7)-H(7)	109.5

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x 10^3$) for 10632ds.

The anisotropic displacement factor exponent takes the form: $-2p^2[h^2 a^{*2} U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	28(1)	20(1)	15(1)	-3(1)	4(1)	0(1)
O(2)	38(1)	34(1)	17(1)	1(1)	7(1)	-1(1)
O(3)	21(1)	33(1)	22(1)	-2(1)	3(1)	-2(1)
O(4)	20(1)	19(1)	20(1)	-1(1)	1(1)	-1(1)
N(1)	21(1)	17(1)	13(1)	-2(1)	2(1)	-1(1)
C(1)	24(1)	24(1)	17(1)	0(1)	2(1)	0(1)
C(2)	26(1)	19(1)	16(1)	0(1)	4(1)	-4(1)
C(3)	21(1)	21(1)	18(1)	0(1)	1(1)	2(1)
C(4)	21(1)	23(1)	13(1)	-3(1)	0(1)	0(1)
C(5)	26(1)	30(1)	23(1)	1(1)	3(1)	-8(1)
C(6)	40(1)	20(1)	27(1)	2(1)	4(1)	-4(1)
C(7)	31(1)	24(1)	33(1)	-3(1)	6(1)	7(1)
C(8)	27(1)	31(1)	21(1)	5(1)	-4(1)	1(1)
C(9)	29(1)	21(1)	14(1)	-4(1)	2(1)	-2(1)
C(10)	20(1)	16(1)	20(1)	-1(1)	3(1)	-1(1)
C(11)	21(1)	21(1)	23(1)	2(1)	6(1)	1(1)
C(12)	26(1)	21(1)	22(1)	3(1)	4(1)	0(1)
C(13)	24(1)	18(1)	25(1)	-1(1)	-2(1)	0(1)
C(14)	20(1)	25(1)	29(1)	-2(1)	5(1)	3(1)
C(15)	24(1)	24(1)	21(1)	0(1)	6(1)	0(1)
C(16)	28(1)	21(1)	28(1)	-2(1)	-5(1)	1(1)
B(1)	22(1)	16(1)	15(1)	-2(1)	3(1)	-1(1)
Cl(1)	40(1)	17(1)	40(1)	2(1)	-10(1)	1(1)

O(5)	22(1)	15(1)	19(1)	6(1)	-2(1)	4(1)
O(6)	50(1)	27(1)	28(1)	4(1)	-17(1)	3(1)
C(17)	22(1)	17(1)	22(1)	5(1)	-2(1)	1(1)
Cl(2)	37(3)	43(4)	39(4)	-13(3)	7(3)	-1(3)
O(7)	50(1)	27(1)	28(1)	4(1)	-17(1)	3(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for 10632d__

	x	y	z	U(e__	
H(5A)	8376	6461	4099	39	
H(5B)	8312	8441	4361	39	
H(5C)	8654	7909	3432	39	
H(6A)	7568	9976	2804	43	
H(6B)	7095	10235	3692	43	
H(6C)	6549	9605	2792	43	
H(7A)	5539	9573	4043	44	
H(7B)	5314	8272	4807	44	
H(7C)	4643	8532	3938	44	
H(8A)	5690	8210	2447	40	
H(8B)	4821	7146	2546	40	
H(8C)	5699	6164	2382	40	
H(9A)	7453	6893	5189	32	
H(9B)	6439	6768	5312	32	
H(9C)	6846	8547	5030	32	
H(11)	6674	3475	5465	26	
H(12)	7573	1801	6447	28	
H(14)	9391	1775	4690	30	
H(15)	8493	3454	3710	27	
H(16A)		9764	974	6332	31
H(16B)		8964	612	6911	31
H(16C)		9010	812	6916	31

H(16D)	9762	950	6271	31
H(16E)	8800	-428	6460	31
H(16F)	9607	88	5950	31
H(7)	9630	340	7532	54

Table 6. Torsion angles [°] for 10632ds.

B(1)-O(1)-C(1)-O(2)	-178.63(13)
B(1)-O(1)-C(1)-C(2)	5.53(15)
C(9)-N(1)-C(2)-C(6)	-80.37(14)
C(3)-N(1)-C(2)-C(6)	48.28(15)
B(1)-N(1)-C(2)-C(6)	158.09(11)
C(9)-N(1)-C(2)-C(1)	153.57(11)
C(3)-N(1)-C(2)-C(1)	-77.78(13)
B(1)-N(1)-C(2)-C(1)	32.02(12)
C(9)-N(1)-C(2)-C(5)	42.34(15)
C(3)-N(1)-C(2)-C(5)	170.98(11)
B(1)-N(1)-C(2)-C(5)	-79.21(12)
O(2)-C(1)-C(2)-N(1)	159.05(14)
O(1)-C(1)-C(2)-N(1)	-25.15(14)
O(2)-C(1)-C(2)-C(6)	32.4(2)
O(1)-C(1)-C(2)-C(6)	-151.76(12)
O(2)-C(1)-C(2)-C(5)	-85.59(17)
O(1)-C(1)-C(2)-C(5)	90.21(13)
C(9)-N(1)-C(3)-C(7)	32.63(15)
C(2)-N(1)-C(3)-C(7)	-96.97(13)
B(1)-N(1)-C(3)-C(7)	152.30(11)
C(9)-N(1)-C(3)-C(4)	-89.39(12)
C(2)-N(1)-C(3)-C(4)	141.01(10)
B(1)-N(1)-C(3)-C(4)	30.28(11)
C(9)-N(1)-C(3)-C(8)	161.56(11)

C(2)-N(1)-C(3)-C(8)	31.96(16)
B(1)-N(1)-C(3)-C(8)	-78.77(13)
B(1)-O(4)-C(4)-O(3)	-174.69(12)
B(1)-O(4)-C(4)-C(3)	11.86(14)
C(7)-C(3)-C(4)-O(3)	35.45(18)
N(1)-C(3)-C(4)-O(3)	158.52(12)
C(8)-C(3)-C(4)-O(3)	-81.92(15)
C(7)-C(3)-C(4)-O(4)	-151.13(11)
N(1)-C(3)-C(4)-O(4)	-28.07(13)
C(8)-C(3)-C(4)-O(4)	91.49(12)
C(15)-C(10)-C(11)-C(12)	1.2(2)
B(1)-C(10)-C(11)-C(12)	177.10(13)
C(10)-C(11)-C(12)-C(13)	-0.5(2)
C(11)-C(12)-C(13)-C(14)	-0.3(2)
C(11)-C(12)-C(13)-C(16)	179.26(13)
C(12)-C(13)-C(14)-C(15)	0.4(2)
C(16)-C(13)-C(14)-C(15)	-179.18(13)
C(13)-C(14)-C(15)-C(10)	0.4(2)
C(11)-C(10)-C(15)-C(14)	-1.1(2)
B(1)-C(10)-C(15)-C(14)	-176.86(13)
C(14)-C(13)-C(16)-O(5)	-77.58(18)
C(12)-C(13)-C(16)-O(5)	102.89(17)
C(14)-C(13)-C(16)-O(7)	108.1(14)
C(12)-C(13)-C(16)-O(7)	-71.5(14)
C(14)-C(13)-C(16)-Cl(2)	-85.1(3)
C(12)-C(13)-C(16)-Cl(2)	95.4(3)
C(4)-O(4)-B(1)-O(1)	-97.26(13)
C(4)-O(4)-B(1)-C(10)	135.76(11)
C(4)-O(4)-B(1)-N(1)	8.66(13)
C(1)-O(1)-B(1)-O(4)	122.32(12)
C(1)-O(1)-B(1)-C(10)	-113.68(13)

C(1)-O(1)-B(1)-N(1)	14.94(13)
C(15)-C(10)-B(1)-O(4)	137.71(13)
C(11)-C(10)-B(1)-O(4)	-37.95(16)
C(15)-C(10)-B(1)-O(1)	11.28(18)
C(11)-C(10)-B(1)-O(1)	-164.39(12)
C(15)-C(10)-B(1)-N(1)	-106.25(15)
C(11)-C(10)-B(1)-N(1)	78.09(16)
C(9)-N(1)-B(1)-O(4)	93.43(12)
C(2)-N(1)-B(1)-O(4)	-145.23(10)
C(3)-N(1)-B(1)-O(4)	-24.58(11)
C(9)-N(1)-B(1)-O(1)	-150.54(10)
C(2)-N(1)-B(1)-O(1)	-29.20(12)
C(3)-N(1)-B(1)-O(1)	91.45(10)
C(9)-N(1)-B(1)-C(10)	-25.90(16)
C(2)-N(1)-B(1)-C(10)	95.44(13)
C(3)-N(1)-B(1)-C(10)	-143.91(11)
C(13)-C(16)-O(5)-C(17)	-165.15(17)
C(16)-O(5)-C(17)-O(6)	-3.3(3)
C(16)-O(5)-C(17)-Cl(1)	177.34(13)

Symmetry transformations used to generate equivalent atoms

Crystal data and structure refinement for **5** (10631ds), CCDC Number: 2290142 are provided below.

Table 7. Crystal data and structure refinement for 10631ds.

Identification code	10631ds
Empirical formula	$C_{23}H_{26}BBrN_2O_6$
Formula weight	517.18
Temperature	100(2) K
Wavelength	0.71073 Å

Crystal system	Monoclinic
Space group	C2/c
Unit cell dimensions	a = 26.2043(8) Å a= 90°. B = 7.1829(2) Å b= 98.2121(11)°. C = 29.9444(8) Å g = 90°.
Volume	4647.0(2) $Å^3$
Z	8
Density (calculated)	1.478 mg/m^3
Absorption coefficient	1.811 mm^{-1}
F(000)	2128
Crystal size	0.426 x 0.329 x 0.080 mm^3
Theta range for data collection	2.109 to 26.470°
Index ranges	-32<=h<=32, -8<=k<=8, -31<=l<=31
Reflections collected	46785
Independent reflections	4770 [R(int) = 0.0646]
Completeness to theta = 25.242°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7454 and 0.6073
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4770 / 1166 / 558
Goodness-of-fit on F^2	1.111
Final R indices [I>2sigma(I)]	R1 = 0.0861, wR2 = 0.2478
R indices (all data)	R1 = 0.0960, wR2 = 0.2555
Extinction coefficient	n/a
Largest diff. peak and hole	1.310 and -0.794 $e.Å^{-3}$

Table 8. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x10^3) for 10631ds. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Br(1)	7291(2)	-4827(6)	5651(2)	78(1)
O(1)	4135(3)	6803(10)	2550(3)	42(1)
O(2)	4408(4)	8547(13)	1912(4)	60(2)
O(3)	2599(3)	7852(11)	3124(4)	46(2)
O(4)	3359(3)	6564(10)	3025(5)	39(1)
O(5)	5422(3)	944(12)	4309(4)	58(2)
O(6)	5853(4)	-248(15)	5052(4)	76(2)
N(1)	3862(3)	9356(11)	3071(3)	40(1)
N(2)	5956(5)	-1376(19)	4215(5)	57(2)
C(1)	4173(5)	8419(13)	2294(4)	46(1)
C(2)	3818(4)	9843(12)	2470(4)	47(1)
C(3)	3374(3)	9620(11)	3334(3)	40(1)
C(4)	3057(3)	7997(13)	3131(4)	40(1)
C(5)	3983(5)	11837(15)	2356(6)	63(2)
C(6)	3291(5)	9443(17)	2120(5)	61(2)
C(7)	3493(4)	9469(12)	3947(3)	41(2)
C(8)	3096(4)	11503(13)	3201(4)	48(2)
C(9)	4323(4)	10236(13)	3385(4)	49(2)
C(10)	4283(3)	5975(10)	3541(3)	40(1)
C(11)	4074(2)	5073(11)	3952(3)	41(1)
C(12)	4383(3)	3952(10)	4318(3)	46(1)
C(13)	4903(2)	3732(10)	4274(3)	52(1)
C(14)	5112(2)	4634(11)	3863(3)	52(1)
C(15)	4802(3)	5755(10)	3496(3)	49(1)
C(16)	5252(5)	2436(15)	4647(4)	57(2)
C(17)	5758(5)	-231(16)	4567(4)	59(2)
C(18)	6353(7)	-2700(20)	4331(4)	55(1)
C(19)	6617(7)	-3000(20)	4848(4)	57(2)
C(20)	6977(6)	-4431(19)	4938(3)	56(2)
C(21)	7074(5)	-5559(17)	4511(3)	56(2)

	C(22)	6810(5)	-5260(18)	3994(3)	57(2)
	C(23)	6450(6)	-3830(20)	3904(3)	55(2)
	B(1)	3910(4)	7050(14)	3063(4)	39(1)
	Br(1A)	7368(2)	-4660(7)	5758(2)	54(1)
	O(1A)	4035(5)	7131(15)	2499(5)	41(1)
	O(2A)	4298(5)	9237(16)	1947(5)	51(2)
	O(3A)	2577(4)	7069(18)	3164(6)	52(2)
	O(4A)	3378(5)	6159(15)	3055(7)	39(1)
	O(5A)	5591(5)	1278(16)	4252(5)	56(2)
	O(6A)	6118(5)	479(17)	5017(5)	63(3)
	N(1A)	3744(4)	9251(15)	3148(4)	41(1)
	N(2A)	6059(7)	-1270(30)	4240(7)	57(2)
	C(1A)	4127(7)	8915(17)	2367(5)	45(1)
	C(2A)	4086(5)	10223(14)	2809(5)	45(1)
	C(3A)	3157(4)	9242(15)	2905(5)	43(1)
	C(4A)	3007(5)	7411(18)	3098(6)	41(1)
	C(5A)	4628(5)	10417(19)	3147(6)	53(3)
	C(6A)	3936(7)	12194(18)	2614(7)	54(3)
	C(7A)	2872(7)	10850(20)	3119(7)	56(3)
	C(8A)	3039(7)	9170(20)	2270(5)	57(3)
	C(9A)	3796(5)	9711(18)	3730(5)	47(2)
	C(10A)	4305(4)	5887(15)	3461(4)	41(1)
	C(11A)	4196(3)	5287(16)	3962(4)	42(1)
	C(12A)	4567(4)	4323(15)	4309(3)	45(1)
	C(13A)	5046(3)	3959(15)	4155(3)	49(1)
	C(14A)	5155(3)	4559(15)	3654(4)	49(2)
	C(15A)	4784(4)	5523(15)	3307(3)	44(2)
	C(16A)	5457(6)	2950(20)	4547(5)	53(2)
	C(17A)	5945(7)	190(20)	4548(6)	59(2)
	C(18A)	6398(9)	-2770(30)	4413(6)	56(1)
	C(19A)	6649(10)	-2970(30)	4940(5)	57(2)
	C(20A)	7029(8)	-4320(30)	5057(4)	57(2)
	C(21A)	7157(7)	-5470(20)	4648(5)	56(2)
	C(22A)	6906(7)	-5270(30)	4122(5)	57(2)
	C(23A)	6527(8)	-3910(30)	4004(5)	56(2)

B(1A)	3887(5)	7033(18)	3053(6)	40(1)

Table 9. Bond lengths [Å] and angles [°] for 10631ds.

Br(1)-C(20)	1.870(6)
O(1)-C(1)	1.335(10)
O(1)-B(1)	1.492(10)
O(2)-C(1)	1.209(10)
O(3)-C(4)	1.203(10)
O(4)-C(4)	1.346(10)
O(4)-B(1)	1.477(10)
O(5)-C(17)	1.320(11)
O(5)-C(16)	1.472(10)
O(6)-C(17)	1.199(11)
N(1)-C(9)	1.484(11)
N(1)-C(2)	1.529(11)
N(1)-C(3)	1.529(10)
N(1)-B(1)	1.661(10)
N(2)-C(17)	1.357(11)
N(2)-C(18)	1.412(9)
N(2)-H(2)	0.8800
C(1)-C(2)	1.491(12)
C(2)-C(5)	1.534(13)
C(2)-C(6)	1.551(14)
C(3)-C(4)	1.477(12)
C(3)-C(7)	1.522(11)
C(3)-C(8)	1.549(11)
C(5)-H(5A)	0.9800
C(5)-H(5B)	0.9800
C(5)-H(5C)	0.9800
C(6)-H(6A)	0.9800
C(6)-H(6B)	0.9800
C(6)-H(6C)	0.9800
C(7)-H(7A)	0.9800
C(7)-H(7B)	0.9800

C(7)-H(7C)	0.9800
C(8)-H(8A)	0.9800
C(8)-H(8B)	0.9800
C(8)-H(8C)	0.9800
C(9)-H(9A)	0.9800
C(9)-H(9B)	0.9800
C(9)-H(9C)	0.9800
C(10)-C(11)	1.3900
C(10)-C(15)	1.3900
C(10)-B(1)	1.625(9)
C(11)-C(12)	1.3900
C(11)-H(11)	0.9500
C(12)-C(13)	1.3900
C(12)-H(12)	0.9500
C(13)-C(14)	1.3900
C(13)-C(16)	1.527(9)
C(14)-C(15)	1.3900
C(14)-H(14)	0.9500
C(15)-H(15)	0.9500
C(16)-H(16A)	0.9900
C(16)-H(16B)	0.9900
C(18)-C(19)	1.3900
C(18)-C(23)	1.3900
C(19)-C(20)	1.3900
C(19)-H(19)	0.9500
C(20)-C(21)	1.3900
C(21)-C(22)	1.3900
C(21)-H(21)	0.9500
C(22)-C(23)	1.3900
C(22)-H(22)	0.9500
C(23)-H(23)	0.9500
Br(1A)-C(20A)	1.862(9)
O(1A)-C(1A)	1.353(13)
O(1A)-B(1A)	1.488(12)
O(2A)-C(1A)	1.220(13)
O(3A)-C(4A)	1.189(12)

O(4A)-C(4A)	1.339(13)
O(4A)-B(1A)	1.477(13)
O(5A)-C(17A)	1.348(13)
O(5A)-C(16A)	1.476(13)
O(6A)-C(17A)	1.209(14)
N(1A)-C(9A)	1.476(13)
N(1A)-C(2A)	1.491(13)
N(1A)-C(3A)	1.569(14)
N(1A)-B(1A)	1.662(12)
N(2A)-C(17A)	1.362(14)
N(2A)-C(18A)	1.421(12)
N(2A)-H(2A)	0.8800
C(1A)-C(2A)	1.465(15)
C(2A)-C(6A)	1.530(15)
C(2A)-C(5A)	1.552(16)
C(3A)-C(4A)	1.474(14)
C(3A)-C(7A)	1.515(15)
C(3A)-C(8A)	1.569(15)
C(5A)-H(5D)	0.9800
C(5A)-H(5E)	0.9800
C(5A)-H(5F)	0.9800
C(6A)-H(6D)	0.9800
C(6A)-H(6E)	0.9800
C(6A)-H(6F)	0.9800
C(7A)-H(7D)	0.9800
C(7A)-H(7E)	0.9800
C(7A)-H(7F)	0.9800
C(8A)-H(8D)	0.9800
C(8A)-H(8E)	0.9800
C(8A)-H(8F)	0.9800
C(9A)-H(9D)	0.9800
C(9A)-H(9E)	0.9800
C(9A)-H(9F)	0.9800
C(10A)-C(11A)	1.3900
C(10A)-C(15A)	1.3900
C(10A)-B(1A)	1.611(11)

C(11A)-C(12A)	1.3900
C(11A)-H(11A)	0.9500
C(12A)-C(13A)	1.3900
C(12A)-H(12A)	0.9500
C(13A)-C(14A)	1.3900
C(13A)-C(16A)	1.530(11)
C(14A)-C(15A)	1.3900
C(14A)-H(14A)	0.9500
C(15A)-H(15A)	0.9500
C(16A)-H(16C)	0.9900
C(16A)-H(16D)	0.9900
C(18A)-C(19A)	1.3900
C(18A)-C(23A)	1.3900
C(19A)-C(20A)	1.3900
C(19A)-H(19A)	0.9500
C(20A)-C(21A)	1.3900
C(21A)-C(22A)	1.3900
C(21A)-H(21A)	0.9500
C(22A)-C(23A)	1.3900
C(22A)-H(22A)	0.9500
C(23A)-H(23A)	0.9500
C(1)-O(1)-B(1)	111.9(7)
C(4)-O(4)-B(1)	113.7(7)
C(17)-O(5)-C(16)	114.9(8)
C(9)-N(1)-C(2)	111.1(7)
C(9)-N(1)-C(3)	112.9(7)
C(2)-N(1)-C(3)	116.2(7)
C(9)-N(1)-B(1)	111.9(7)
C(2)-N(1)-B(1)	102.1(6)
C(3)-N(1)-B(1)	101.5(6)
C(17)-N(2)-C(18)	128.0(10)
C(17)-N(2)-H(2)	116.0
C(18)-N(2)-H(2)	116.0
O(2)-C(1)-O(1)	121.6(9)
O(2)-C(1)-C(2)	126.1(9)
O(1)-C(1)-C(2)	111.2(7)

C(1)-C(2)-N(1)	99.8(7)
C(1)-C(2)-C(5)	112.4(8)
N(1)-C(2)-C(5)	114.4(8)
C(1)-C(2)-C(6)	104.5(9)
N(1)-C(2)-C(6)	116.5(8)
C(5)-C(2)-C(6)	108.6(9)
C(4)-C(3)-C(7)	108.2(7)
C(4)-C(3)-N(1)	102.6(6)
C(7)-C(3)-N(1)	110.9(7)
C(4)-C(3)-C(8)	113.1(8)
C(7)-C(3)-C(8)	107.5(7)
N(1)-C(3)-C(8)	114.4(7)
O(3)-C(4)-O(4)	122.9(9)
O(3)-C(4)-C(3)	125.7(8)
O(4)-C(4)-C(3)	110.8(7)
C(2)-C(5)-H(5A)	109.5
C(2)-C(5)-H(5B)	109.5
H(5A)-C(5)-H(5B)	109.5
C(2)-C(5)-H(5C)	109.5
H(5A)-C(5)-H(5C)	109.5
H(5B)-C(5)-H(5C)	109.5
C(2)-C(6)-H(6A)	109.5
C(2)-C(6)-H(6B)	109.5
H(6A)-C(6)-H(6B)	109.5
C(2)-C(6)-H(6C)	109.5
H(6A)-C(6)-H(6C)	109.5
H(6B)-C(6)-H(6C)	109.5
C(3)-C(7)-H(7A)	109.5
C(3)-C(7)-H(7B)	109.5
H(7A)-C(7)-H(7B)	109.5
C(3)-C(7)-H(7C)	109.5
H(7A)-C(7)-H(7C)	109.5
H(7B)-C(7)-H(7C)	109.5
C(3)-C(8)-H(8A)	109.5
C(3)-C(8)-H(8B)	109.5
H(8A)-C(8)-H(8B)	109.5

C(3)-C(8)-H(8C)	109.5
H(8A)-C(8)-H(8C)	109.5
H(8B)-C(8)-H(8C)	109.5
N(1)-C(9)-H(9A)	109.5
N(1)-C(9)-H(9B)	109.5
H(9A)-C(9)-H(9B)	109.5
N(1)-C(9)-H(9C)	109.5
H(9A)-C(9)-H(9C)	109.5
H(9B)-C(9)-H(9C)	109.5
C(11)-C(10)-C(15)	120.0
C(11)-C(10)-B(1)	120.2(5)
C(15)-C(10)-B(1)	119.2(5)
C(12)-C(11)-C(10)	120.0
C(12)-C(11)-H(11)	120.0
C(10)-C(11)-H(11)	120.0
C(13)-C(12)-C(11)	120.0
C(13)-C(12)-H(12)	120.0
C(11)-C(12)-H(12)	120.0
C(12)-C(13)-C(14)	120.0
C(12)-C(13)-C(16)	122.0(6)
C(14)-C(13)-C(16)	117.9(6)
C(15)-C(14)-C(13)	120.0
C(15)-C(14)-H(14)	120.0
C(13)-C(14)-H(14)	120.0
C(14)-C(15)-C(10)	120.0
C(14)-C(15)-H(15)	120.0
C(10)-C(15)-H(15)	120.0
O(5)-C(16)-C(13)	107.3(7)
O(5)-C(16)-H(16A)	110.3
C(13)-C(16)-H(16A)	110.3
O(5)-C(16)-H(16B)	110.3
C(13)-C(16)-H(16B)	110.3
H(16A)-C(16)-H(16B)	108.5
O(6)-C(17)-O(5)	121.7(9)
O(6)-C(17)-N(2)	127.0(10)
O(5)-C(17)-N(2)	111.2(9)

C(19)-C(18)-C(23)	120.0
C(19)-C(18)-N(2)	123.2(7)
C(23)-C(18)-N(2)	116.6(7)
C(18)-C(19)-C(20)	120.0
C(18)-C(19)-H(19)	120.0
C(20)-C(19)-H(19)	120.0
C(21)-C(20)-C(19)	120.0
C(21)-C(20)-Br(1)	122.4(5)
C(19)-C(20)-Br(1)	117.6(5)
C(20)-C(21)-C(22)	120.0
C(20)-C(21)-H(21)	120.0
C(22)-C(21)-H(21)	120.0
C(23)-C(22)-C(21)	120.0
C(23)-C(22)-H(22)	120.0
C(21)-C(22)-H(22)	120.0
C(22)-C(23)-C(18)	120.0
C(22)-C(23)-H(23)	120.0
C(18)-C(23)-H(23)	120.0
O(4)-B(1)-O(1)	114.8(9)
O(4)-B(1)-C(10)	114.5(7)
O(1)-B(1)-C(10)	107.6(7)
O(4)-B(1)-N(1)	99.2(6)
O(1)-B(1)-N(1)	99.8(6)
C(10)-B(1)-N(1)	120.2(8)
C(1A)-O(1A)-B(1A)	110.5(10)
C(4A)-O(4A)-B(1A)	112.4(10)
C(17A)-O(5A)-C(16A)	113.0(10)
C(9A)-N(1A)-C(2A)	118.3(10)
C(9A)-N(1A)-C(3A)	109.3(9)
C(2A)-N(1A)-C(3A)	114.6(9)
C(9A)-N(1A)-B(1A)	111.4(9)
C(2A)-N(1A)-B(1A)	101.6(8)
C(3A)-N(1A)-B(1A)	99.8(8)
C(17A)-N(2A)-C(18A)	126.2(13)
C(17A)-N(2A)-H(2A)	116.9
C(18A)-N(2A)-H(2A)	116.9

O(2A)-C(1A)-O(1A)	119.3(12)
O(2A)-C(1A)-C(2A)	127.0(11)
O(1A)-C(1A)-C(2A)	112.9(10)
C(1A)-C(2A)-N(1A)	104.0(9)
C(1A)-C(2A)-C(6A)	113.3(11)
N(1A)-C(2A)-C(6A)	117.8(11)
C(1A)-C(2A)-C(5A)	107.8(11)
N(1A)-C(2A)-C(5A)	108.2(10)
C(6A)-C(2A)-C(5A)	105.2(10)
C(4A)-C(3A)-C(7A)	113.3(11)
C(4A)-C(3A)-N(1A)	99.7(9)
C(7A)-C(3A)-N(1A)	111.5(10)
C(4A)-C(3A)-C(8A)	106.0(11)
C(7A)-C(3A)-C(8A)	110.3(11)
N(1A)-C(3A)-C(8A)	115.6(10)
O(3A)-C(4A)-O(4A)	125.9(12)
O(3A)-C(4A)-C(3A)	122.2(12)
O(4A)-C(4A)-C(3A)	110.0(9)
C(2A)-C(5A)-H(5D)	109.5
C(2A)-C(5A)-H(5E)	109.5
H(5D)-C(5A)-H(5E)	109.5
C(2A)-C(5A)-H(5F)	109.5
H(5D)-C(5A)-H(5F)	109.5
H(5E)-C(5A)-H(5F)	109.5
C(2A)-C(6A)-H(6D)	109.5
C(2A)-C(6A)-H(6E)	109.5
H(6D)-C(6A)-H(6E)	109.5
C(2A)-C(6A)-H(6F)	109.5
H(6D)-C(6A)-H(6F)	109.5
H(6E)-C(6A)-H(6F)	109.5
C(3A)-C(7A)-H(7D)	109.5
C(3A)-C(7A)-H(7E)	109.5
H(7D)-C(7A)-H(7E)	109.5
C(3A)-C(7A)-H(7F)	109.5
H(7D)-C(7A)-H(7F)	109.5
H(7E)-C(7A)-H(7F)	109.5

C(3A)-C(8A)-H(8D)	109.5
C(3A)-C(8A)-H(8E)	109.5
H(8D)-C(8A)-H(8E)	109.5
C(3A)-C(8A)-H(8F)	109.5
H(8D)-C(8A)-H(8F)	109.5
H(8E)-C(8A)-H(8F)	109.5
N(1A)-C(9A)-H(9D)	109.5
N(1A)-C(9A)-H(9E)	109.5
H(9D)-C(9A)-H(9E)	109.5
N(1A)-C(9A)-H(9F)	109.5
H(9D)-C(9A)-H(9F)	109.5
H(9E)-C(9A)-H(9F)	109.5
C(11A)-C(10A)-C(15A)	120.0
C(11A)-C(10A)-B(1A)	121.3(7)
C(15A)-C(10A)-B(1A)	118.7(7)
C(10A)-C(11A)-C(12A)	120.0
C(10A)-C(11A)-H(11A)	120.0
C(12A)-C(11A)-H(11A)	120.0
C(13A)-C(12A)-C(11A)	120.0
C(13A)-C(12A)-H(12A)	120.0
C(11A)-C(12A)-H(12A)	120.0
C(12A)-C(13A)-C(14A)	120.0
C(12A)-C(13A)-C(16A)	119.5(8)
C(14A)-C(13A)-C(16A)	120.4(8)
C(15A)-C(14A)-C(13A)	120.0
C(15A)-C(14A)-H(14A)	120.0
C(13A)-C(14A)-H(14A)	120.0
C(14A)-C(15A)-C(10A)	120.0
C(14A)-C(15A)-H(15A)	120.0
C(10A)-C(15A)-H(15A)	120.0
O(5A)-C(16A)-C(13A)	105.2(9)
O(5A)-C(16A)-H(16C)	110.7
C(13A)-C(16A)-H(16C)	110.7
O(5A)-C(16A)-H(16D)	110.7
C(13A)-C(16A)-H(16D)	110.7
H(16C)-C(16A)-H(16D)	108.8

O(6A)-C(17A)-O(5A)	124.4(12)
O(6A)-C(17A)-N(2A)	126.5(12)
O(5A)-C(17A)-N(2A)	109.1(11)
C(19A)-C(18A)-C(23A)	120.0
C(19A)-C(18A)-N(2A)	123.9(9)
C(23A)-C(18A)-N(2A)	115.6(9)
C(20A)-C(19A)-C(18A)	120.0
C(20A)-C(19A)-H(19A)	120.0
C(18A)-C(19A)-H(19A)	120.0
C(21A)-C(20A)-C(19A)	120.0
C(21A)-C(20A)-Br(1A)	118.6(7)
C(19A)-C(20A)-Br(1A)	121.4(7)
C(22A)-C(21A)-C(20A)	120.0
C(22A)-C(21A)-H(21A)	120.0
C(20A)-C(21A)-H(21A)	120.0
C(21A)-C(22A)-C(23A)	120.0
C(21A)-C(22A)-H(22A)	120.0
C(23A)-C(22A)-H(22A)	120.0
C(22A)-C(23A)-C(18A)	120.0
C(22A)-C(23A)-H(23A)	120.0
C(18A)-C(23A)-H(23A)	120.0
O(4A)-B(1A)-O(1A)	112.3(12)
O(4A)-B(1A)-C(10A)	108.3(9)
O(1A)-B(1A)-C(10A)	111.6(9)
O(4A)-B(1A)-N(1A)	100.6(8)
O(1A)-B(1A)-N(1A)	100.5(8)
C(10A)-B(1A)-N(1A)	123.1(10)

Symmetry transformations used to generate equivalent atoms

Table 10. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for 10631ds.

The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2\ a^{*2}U^{11} + \ldots + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$.

U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}

Br(1)	93(2)	84(2)	55(1)	3(1)	-1(1)	50(2)
O(1)	55(3)	29(2)	46(2)	3(2)	20(2)	4(2)
O(2)	81(4)	46(4)	63(4)	16(4)	39(3)	19(4)
O(3)	45(3)	34(3)	60(3)	-3(3)	6(3)	-5(3)
O(4)	47(2)	26(2)	43(2)	-5(2)	8(2)	-6(2)
O(5)	67(3)	53(3)	53(2)	-10(2)	3(3)	22(3)
O(6)	91(5)	76(5)	57(4)	-4(4)	1(4)	42(4)
N(1)	48(2)	27(2)	48(2)	0(2)	16(2)	0(2)
N(2)	67(3)	53(2)	52(2)	-3(2)	7(3)	22(3)
C(1)	59(3)	32(3)	51(2)	6(2)	20(2)	7(2)
C(2)	61(2)	32(2)	50(2)	5(2)	19(2)	3(2)
C(3)	46(2)	29(2)	46(2)	-2(2)	12(2)	-1(2)
C(4)	46(2)	29(3)	46(2)	-2(2)	10(2)	-2(2)
C(5)	85(5)	39(4)	70(5)	7(4)	33(5)	6(4)
C(6)	74(6)	58(5)	53(5)	9(4)	13(4)	16(5)
C(7)	47(4)	31(4)	47(4)	-5(3)	10(3)	-4(3)
C(8)	55(4)	29(4)	62(4)	-3(4)	13(4)	2(3)
C(9)	51(4)	33(3)	66(4)	-5(3)	16(3)	-7(3)
C(10)	48(2)	30(2)	44(2)	-6(2)	10(2)	4(2)
C(11)	50(3)	32(2)	41(2)	-6(2)	7(2)	7(2)
C(12)	55(3)	39(3)	43(2)	-6(2)	6(2)	11(2)
C(13)	60(3)	46(2)	49(2)	-5(2)	5(2)	15(2)
C(14)	57(3)	47(2)	52(3)	-3(2)	9(3)	11(2)
C(15)	54(2)	41(2)	51(3)	-3(3)	10(3)	6(2)
C(16)	64(3)	51(3)	53(3)	-7(2)	3(3)	22(3)
C(17)	70(3)	56(3)	51(2)	-4(2)	5(3)	22(3)
C(18)	65(3)	52(2)	50(3)	2(2)	11(3)	18(2)
C(19)	67(3)	53(2)	52(3)	3(3)	13(3)	21(2)
C(20)	66(3)	54(3)	50(3)	7(3)	12(3)	20(3)
C(21)	66(3)	52(3)	51(4)	6(3)	14(3)	20(3)
C(22)	67(4)	54(3)	51(3)	4(3)	13(3)	21(3)
C(23)	65(4)	53(3)	50(3)	3(3)	12(3)	18(3)
B(1)	48(2)	27(2)	44(2)	-1(2)	13(2)	0(2)
Br(1A)	50(1)	55(1)	57(2)	13(1)	11(1)	10(1)
O(1A)	54(3)	28(3)	44(2)	2(2)	15(2)	4(2)

O(2A)	72(5)	36(4)	51(4)	1(4)	22(4)	1(4)
O(3A)	45(4)	54(5)	56(4)	6(5)	5(3)	-7(5)
O(4A)	46(2)	28(3)	43(2)	-1(2)	9(2)	-4(2)
O(5A)	65(3)	51(3)	50(3)	-8(2)	5(3)	21(3)
O(6A)	80(6)	54(5)	52(4)	-10(4)	-5(5)	24(4)
N(1A)	51(2)	28(2)	46(2)	0(2)	13(2)	0(2)
N(2A)	67(3)	53(3)	52(3)	-2(2)	7(3)	20(3)
C(1A)	60(3)	31(3)	49(2)	4(2)	19(2)	4(2)
C(2A)	58(2)	30(2)	51(2)	3(2)	17(2)	1(2)
C(3A)	50(2)	32(2)	49(2)	-2(2)	11(2)	0(2)
C(4A)	47(2)	31(3)	46(2)	1(3)	9(2)	-3(2)
C(5A)	63(6)	39(5)	59(6)	-5(5)	12(5)	-6(5)
C(6A)	78(5)	32(5)	53(5)	1(5)	17(5)	0(5)
C(7A)	63(6)	48(5)	58(5)	-2(5)	12(5)	10(5)
C(8A)	64(6)	49(6)	55(6)	4(5)	2(5)	4(6)
C(9A)	56(4)	36(4)	50(4)	-5(4)	11(4)	3(4)
C(10A)	50(2)	31(2)	43(2)	-4(2)	10(2)	3(2)
C(11A)	51(3)	34(3)	42(2)	-6(2)	8(3)	8(2)
C(12A)	54(3)	39(3)	43(2)	-5(2)	9(3)	11(2)
C(13A)	57(3)	45(2)	45(3)	-6(2)	8(3)	15(2)
C(14A)	57(3)	46(3)	45(3)	-7(3)	10(3)	11(2)
C(15A)	52(3)	38(3)	44(3)	-7(3)	10(3)	8(2)
C(16A)	62(3)	48(3)	49(3)	-7(3)	5(3)	18(3)
C(17A)	68(3)	54(3)	52(2)	-4(2)	4(3)	21(3)
C(18A)	65(3)	52(2)	51(3)	2(3)	11(3)	19(2)
C(19A)	67(3)	53(3)	52(3)	3(3)	13(3)	20(3)
C(20A)	65(3)	54(3)	53(3)	6(3)	14(3)	20(3)
C(21A)	65(4)	53(3)	51(4)	7(3)	12(3)	19(3)
C(22A)	66(4)	53(3)	52(4)	3(3)	12(3)	20(3)
C(23A)	65(4)	53(3)	51(3)	3(3)	11(3)	18(3)
B(1A)	49(2)	28(2)	44(2)	-1(2)	13(2)	0(2)

Table 11. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x10^3) for 10631ds.

	x	y	z	U(eq)
H(2)	5819	-1278	3873	86
H(5A)	4005	11971	1969	94
H(5B)	4320	12095	2567	94
H(5C)	3728	12717	2459	94
H(6A)	3330	9523	1735	92
H(6B)	3037	10363	2202	92
H(6C)	3174	8192	2201	92
H(7A)	3689	8325	4044	62
H(7B)	3170	9435	4102	62
H(7C)	3697	10548	4091	62
H(8A)	2951	11535	2817	72
H(8B)	3343	12524	3281	72
H(8C)	2817	11640	3422	72
H(9A)	4625	9990	3206	74
H(9B)	4379	9717	3752	74
H(9C)	4268	11583	3404	74
H(11)	3719	5224	3982	50
H(12)	4240	3336	4599	55
H(14)	5467	4483	3833	62
H(15)	4945	6371	3215	58
H(16A)	5554	3129	4832	68
H(16B)	5062	1903	4927	68
H(19)	6551	-2232	5140	68
H(21)	7320	-6535	4573	67
H(22)	6876	-6032	3703	68
H(23)	6270	-3628	3551	66
H(2A)	5909	-1296	3901	86
H(5D)	4726	9237	3331	80
H(5E)	4622	11404	3417	80
H(5F)	4880	10733	2907	80
H(6D)	4224	12765	2463	81
H(6E)	3855	12942	2919	81
H(6F)	3633	12137	2334	81
H(7D)	3038	12025	3044	84

H(7E)	2880	10710	3511	84
H(7F)	2513	10854	2942	84
H(8D)	3127	7932	2144	85
H(8E)	3244	10114	2115	85
H(8F)	2671	9407	2155	85
H(9D)	3760	11059	3774	71
H(9E)	4136	9312	3909	71
H(9F)	3527	9069	3894	71
H(11A)	3869	5536	4068	51
H(12A)	4493	3913	4652	54
H(14A)	5482	4311	3548	59
H(15A)	4858	5934	2964	53
H(16C)	5764	3751	4644	64
H(16D)	5319	2596	4882	64
H(19A)	6561	-2186	5219	68
H(21A)	7416	-6391	4729	67
H(22A)	6994	-6050	3842	68
H(23A)	6356	-3776	3644	67

Table 12. Torsion angles [°] for 10631ds.

B(1)-O(1)-C(1)-O(2)	169.8(11)
B(1)-O(1)-C(1)-C(2)	-20.9(13)
O(2)-C(1)-C(2)-N(1)	-153.9(12)
O(1)-C(1)-C(2)-N(1)	37.4(11)
O(2)-C(1)-C(2)-C(5)	-32.3(17)
O(1)-C(1)-C(2)-C(5)	159.0(10)
O(2)-C(1)-C(2)-C(6)	85.3(14)
O(1)-C(1)-C(2)-C(6)	-83.4(11)
C(9)-N(1)-C(2)-C(1)	83.2(9)
C(3)-N(1)-C(2)-C(1)	-145.9(8)
B(1)-N(1)-C(2)-C(1)	-36.4(8)
C(9)-N(1)-C(2)-C(5)	-37.0(11)
C(3)-N(1)-C(2)-C(5)	94.0(10)
B(1)-N(1)-C(2)-C(5)	-156.5(8)

C(9)-N(1)-C(2)-C(6)	-165.2(8)
C(3)-N(1)-C(2)-C(6)	-34.2(10)
B(1)-N(1)-C(2)-C(6)	75.3(9)
C(9)-N(1)-C(3)-C(4)	-153.8(8)
C(2)-N(1)-C(3)-C(4)	76.0(9)
B(1)-N(1)-C(3)-C(4)	-33.8(8)
C(9)-N(1)-C(3)-C(7)	-38.5(9)
C(2)-N(1)-C(3)-C(7)	-168.6(7)
B(1)-N(1)-C(3)-C(7)	81.6(8)
C(9)-N(1)-C(3)-C(8)	83.3(9)
C(2)-N(1)-C(3)-C(8)	-46.8(10)
B(1)-N(1)-C(3)-C(8)	-156.7(8)
B(1)-O(4)-C(4)-O(3)	-179.3(11)
B(1)-O(4)-C(4)-C(3)	-8.1(13)
C(7)-C(3)-C(4)-O(3)	81.6(12)
N(1)-C(3)-C(4)-O(3)	-161.1(11)
C(8)-C(3)-C(4)-O(3)	-37.3(14)
C(7)-C(3)-C(4)-O(4)	-89.3(10)
N(1)-C(3)-C(4)-O(4)	27.9(10)
C(8)-C(3)-C(4)-O(4)	151.7(9)
C(15)-C(10)-C(11)-C(12)	0.0
B(1)-C(10)-C(11)-C(12)	171.5(7)
C(10)-C(11)-C(12)-C(13)	0.0
C(11)-C(12)-C(13)-C(14)	0.0
C(11)-C(12)-C(13)-C(16)	-176.7(8)
C(12)-C(13)-C(14)-C(15)	0.0
C(16)-C(13)-C(14)-C(15)	176.8(7)
C(13)-C(14)-C(15)-C(10)	0.0
C(11)-C(10)-C(15)-C(14)	0.0
B(1)-C(10)-C(15)-C(14)	-171.6(7)
C(17)-O(5)-C(16)-C(13)	175.5(10)
C(12)-C(13)-C(16)-O(5)	115.6(8)
C(14)-C(13)-C(16)-O(5)	-61.2(10)
C(16)-O(5)-C(17)-O(6)	11.3(19)
C(16)-O(5)-C(17)-N(2)	-170.3(12)
C(18)-N(2)-C(17)-O(6)	-7(3)

C(18)-N(2)-C(17)-O(5)	174.4(16)
C(17)-N(2)-C(18)-C(19)	-1(2)
C(17)-N(2)-C(18)-C(23)	173.8(14)
C(23)-C(18)-C(19)-C(20)	0.0
N(2)-C(18)-C(19)-C(20)	175.1(17)
C(18)-C(19)-C(20)-C(21)	0.0
C(18)-C(19)-C(20)-Br(1)	-176.9(11)
C(19)-C(20)-C(21)-C(22)	0.0
Br(1)-C(20)-C(21)-C(22)	176.7(11)
C(20)-C(21)-C(22)-C(23)	0.0
C(21)-C(22)-C(23)-C(18)	0.0
C(19)-C(18)-C(23)-C(22)	0.0
N(2)-C(18)-C(23)-C(22)	-175.5(16)
C(4)-O(4)-B(1)-O(1)	-119.1(10)
C(4)-O(4)-B(1)-C(10)	115.6(10)
C(4)-O(4)-B(1)-N(1)	-13.8(11)
C(1)-O(1)-B(1)-O(4)	100.9(10)
C(1)-O(1)-B(1)-C(10)	-130.4(9)
C(1)-O(1)-B(1)-N(1)	-4.2(10)
C(11)-C(10)-B(1)-O(4)	-15.5(10)
C(15)-C(10)-B(1)-O(4)	156.1(7)
C(11)-C(10)-B(1)-O(1)	-144.4(6)
C(15)-C(10)-B(1)-O(1)	27.2(9)
C(11)-C(10)-B(1)-N(1)	102.5(8)
C(15)-C(10)-B(1)-N(1)	-85.9(8)
C(9)-N(1)-B(1)-O(4)	149.7(8)
C(2)-N(1)-B(1)-O(4)	-91.3(8)
C(3)-N(1)-B(1)-O(4)	29.0(9)
C(9)-N(1)-B(1)-O(1)	-93.0(8)
C(2)-N(1)-B(1)-O(1)	26.0(8)
C(3)-N(1)-B(1)-O(1)	146.3(7)
C(9)-N(1)-B(1)-C(10)	24.2(11)
C(2)-N(1)-B(1)-C(10)	143.2(8)
C(3)-N(1)-B(1)-C(10)	-96.5(8)
B(1A)-O(1A)-C(1A)-O(2A)	173.4(15)
B(1A)-O(1A)-C(1A)-C(2A)	3.4(17)

O(2A)-C(1A)-C(2A)-N(1A)	167.1(16)
O(1A)-C(1A)-C(2A)-N(1A)	-23.8(16)
O(2A)-C(1A)-C(2A)-C(6A)	38(2)
O(1A)-C(1A)-C(2A)-C(6A)	-153.0(13)
O(2A)-C(1A)-C(2A)-C(5A)	-78(2)
O(1A)-C(1A)-C(2A)-C(5A)	90.9(14)
C(9A)-N(1A)-C(2A)-C(1A)	153.3(11)
C(3A)-N(1A)-C(2A)-C(1A)	-75.5(12)
B(1A)-N(1A)-C(2A)-C(1A)	31.1(12)
C(9A)-N(1A)-C(2A)-C(6A)	-80.3(14)
C(3A)-N(1A)-C(2A)-C(6A)	50.9(14)
B(1A)-N(1A)-C(2A)-C(6A)	157.5(11)
C(9A)-N(1A)-C(2A)-C(5A)	38.8(13)
C(3A)-N(1A)-C(2A)-C(5A)	170.1(9)
B(1A)-N(1A)-C(2A)-C(5A)	-83.4(10)
C(9A)-N(1A)-C(3A)-C(4A)	-78.5(11)
C(2A)-N(1A)-C(3A)-C(4A)	146.1(10)
B(1A)-N(1A)-C(3A)-C(4A)	38.4(10)
C(9A)-N(1A)-C(3A)-C(7A)	41.5(13)
C(2A)-N(1A)-C(3A)-C(7A)	-94.0(12)
B(1A)-N(1A)-C(3A)-C(7A)	158.4(10)
C(9A)-N(1A)-C(3A)-C(8A)	168.4(11)
C(2A)-N(1A)-C(3A)-C(8A)	33.0(13)
B(1A)-N(1A)-C(3A)-C(8A)	-74.6(11)
B(1A)-O(4A)-C(4A)-O(3A)	-171.8(16)
B(1A)-O(4A)-C(4A)-C(3A)	23.7(17)
C(7A)-C(3A)-C(4A)-O(3A)	36(2)
N(1A)-C(3A)-C(4A)-O(3A)	154.4(14)
C(8A)-C(3A)-C(4A)-O(3A)	-85.2(17)
C(7A)-C(3A)-C(4A)-O(4A)	-159.0(13)
N(1A)-C(3A)-C(4A)-O(4A)	-40.4(14)
C(8A)-C(3A)-C(4A)-O(4A)	80.0(14)
C(15A)-C(10A)-C(11A)-C(12A)	0.0
B(1A)-C(10A)-C(11A)-C(12A)	-179.1(11)
C(10A)-C(11A)-C(12A)-C(13A)	0.0
C(11A)-C(12A)-C(13A)-C(14A)	0.0

C(11A)-C(12A)-C(13A)-C(16A)	178.2(11)
C(12A)-C(13A)-C(14A)-C(15A)	0.0
C(16A)-C(13A)-C(14A)-C(15A)	-178.1(11)
C(13A)-C(14A)-C(15A)-C(10A)	0.0
C(11A)-C(10A)-C(15A)-C(14A)	0.0
B(1A)-C(10A)-C(15A)-C(14A)	179.1(10)
C(17A)-O(5A)-C(16A)-C(13A)	-178.6(13)
C(12A)-C(13A)-C(16A)-O(5A)	122.4(10)
C(14A)-C(13A)-C(16A)-O(5A)	-59.5(14)
C(16A)-O(5A)-C(17A)-O(6A)	4(3)
C(16A)-O(5A)-C(17A)-N(2A)	-177.7(16)
C(18A)-N(2A)-C(17A)-O(6A)	1(4)
C(18A)-N(2A)-C(17A)-O(5A)	-177(2)
C(17A)-N(2A)-C(18A)-C(19A)	3(3)
C(17A)-N(2A)-C(18A)-C(23A)	-168.7(19)
C(23A)-C(18A)-C(19A)-C(20A)	0.0
N(2A)-C(18A)-C(19A)-C(20A)	-171(2)
C(18A)-C(19A)-C(20A)-C(21A)	0.0
C(18A)-C(19A)-C(20A)-Br(1A)	-179.2(16)
C(19A)-C(20A)-C(21A)-C(22A)	0.0
Br(1A)-C(20A)-C(21A)-C(22A)	179.2(16)
C(20A)-C(21A)-C(22A)-C(23A)	0.0
C(21A)-C(22A)-C(23A)-C(18A)	0.0
C(19A)-C(18A)-C(23A)-C(22A)	0.0
N(2A)-C(18A)-C(23A)-C(22A)	172(2)
C(4A)-O(4A)-B(1A)-O(1A)	-102.6(14)
C(4A)-O(4A)-B(1A)-C(10A)	133.8(13)
C(4A)-O(4A)-B(1A)-N(1A)	3.5(15)
C(1A)-O(1A)-B(1A)-O(4A)	122.3(12)
C(1A)-O(1A)-B(1A)-C(10A)	-116.0(13)
C(1A)-O(1A)-B(1A)-N(1A)	16.2(14)
C(11A)-C(10A)-B(1A)-O(4A)	-42.4(13)
C(15A)-C(10A)-B(1A)-O(4A)	138.5(9)
C(11A)-C(10A)-B(1A)-O(1A)	-166.4(9)
C(15A)-C(10A)-B(1A)-O(1A)	14.5(13)
C(11A)-C(10A)-B(1A)-N(1A)	74.1(12)

C(15A)-C(10A)-B(1A)-N(1A)	-105.0(11)
C(9A)-N(1A)-B(1A)-O(4A)	88.9(12)
C(2A)-N(1A)-B(1A)-O(4A)	-144.3(11)
C(3A)-N(1A)-B(1A)-O(4A)	-26.5(11)
C(9A)-N(1A)-B(1A)-O(1A)	-155.9(10)
C(2A)-N(1A)-B(1A)-O(1A)	-29.0(11)
C(3A)-N(1A)-B(1A)-O(1A)	88.8(10)
C(9A)-N(1A)-B(1A)-C(10A)	-31.3(14)
C(2A)-N(1A)-B(1A)-C(10A)	95.6(12)
C(3A)-N(1A)-B(1A)-C(10A)	-146.6(10)

Symmetry transformations used to generate equivalent atoms

Table 13. Hydrogen bonds for 10631ds [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)	
N(2^a)-H(2^a)...O(2^a)#1	0.88	1.97	2.839(16)	169.6	
N(2A^b)-H(2A^b)...O(2A^b)#1	0.88	2.14	3.00(2)	163.9	

Symmetry transformations used to generate equivalent atoms:
#1 -x+1,y-1,-z+1/2

Crystal data and structure refinement for **8** (10957ds), CCDC Number: 2293444 are provided below.

Table 14. Crystal data and structure refinement for 10957ds.

Identification code	10631ds
Empirical formula	$C_{29}H_{31}BN_2O_6$
Formula weight	514.37
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	I2/a

Unit cell dimensions	a = 17.8628(7) Å a= 90°. b = 10.6229(4) Å b= 95.8404(12)°. c = 27.5698(14) Å g = 90°.
Volume	5204.3(4) $Å^3$
Z	8
Density (calculated)	1.313 mg/m^3
Absorption coefficient	0.091 mm^{-1}
F(000)	2176
Crystal size	0.346 x 0.166 x 0.044 mm^3
Theta range for data collection	2.234 to 26.461°
Index ranges	-22<=h<=22, -13<=k<=13, -34<=l<=34
Reflections collected	70939
Independent reflections	5366 [R(int) = 0.0669]
Completeness to theta = 25.242°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7454 and 0.6636
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5366 / 0 / 351
Goodness-of-fit on F^2	1.075
Final R indices [I>2sigma(I)]	R1 = 0.0435, wR2 = 0.0988
R indices (all data)	R1 = 0.0532, wR2 = 0.1035
Extinction coefficient	n/a
Largest diff. peak and hole	0.309 and -0.211 $e.Å^{-3}$

Table 15. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x10^3) for 10957d1s. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	8655(1)	1015(1)	6824(1)	24(1)
O(2)	9641(1)	1372(1)	7375(1)	34(1)
O(3)	8946(1)	581(1)	5219(1)	26(1)
O(4)	8472(1)	578(1)	5937(1)	20(1)
O(5)	4604(1)	2009(1)	6009(1)	22(1)
O(6)	4454(1)	3957(1)	5672(1)	31(1)
N(1)	8936(1)	2584(1)	6232(1)	18(1)
N(2)	3921(1)	2195(1)	5302(1)	22(1)
C(1)	9326(1)	1501(2)	6972(1)	24(1)
C(2)	9663(1)	2152(2)	6550(1)	23(1)
C(3)	8953(1)	2524(2)	5683(1)	20(1)
C(4)	8805(1)	1122(2)	5584(1)	20(1)
C(5)	10197(1)	3228(2)	6715(1)	32(1)
C(6)	10121(1)	1083(2)	6336(1)	28(1)
C(7)	8281(1)	3236(2)	5421(1)	24(1)
C(8)	9661(1)	3021(2)	5484(1)	24(1)
C(9)	8695(1)	3838(2)	6406(1)	24(1)
C(10)	7462(1)	1772(1)	6344(1)	18(1)
C(11)	6931(1)	1473(2)	5954(1)	20(1)
C(12)	6164(1)	1699(2)	5966(1)	21(1)
C(13)	5906(1)	2237(2)	6376(1)	20(1)
C(14)	6423(1)	2533(2)	6772(1)	22(1)
C(15)	7184(1)	2303(2)	6756(1)	22(1)
C(16)	5082(1)	2508(2)	6416(1)	24(1)
C(17)	4334(1)	2836(2)	5656(1)	21(1)
C(18)	3561(1)	2650(2)	4857(1)	20(1)
C(19)	3622(1)	3872(2)	4684(1)	21(1)
C(20)	3278(1)	4186(2)	4224(1)	22(1)
C(21)	2867(1)	3310(2)	3929(1)	20(1)
C(22)	2799(1)	2097(2)	4113(1)	24(1)
C(23)	3139(1)	1772(2)	4568(1)	25(1)
C(24)	2519(1)	3624(2)	3430(1)	21(1)
C(25)	2893(1)	4389(2)	3121(1)	24(1)
C(26)	2576(1)	4655(2)	2651(1)	30(1)

C(27)	1877(1)	4181(2)	2485(1)	32(1)
C(28)	1495(1)	3428(2)	2788(1)	32(1)
C(29)	1815(1)	3145(2)	3255(1)	27(1)
B(1)	8337(1)	1450(2)	6340(1)	19(1)

Table 16. Bond lengths [Å] and angles [°] for 10957d1s.

O(1)-C(1)	1.330(2)
O(1)-B(1)	1.469(2)
O(2)-C(1)	1.201(2)
O(3)-C(4)	1.2076(19)
O(4)-C(4)	1.3228(19)
O(4)-B(1)	1.486(2)
O(5)-C(17)	1.3617(19)
O(5)-C(16)	1.4404(19)
O(6)-C(17)	1.210(2)
N(1)-C(9)	1.495(2)
N(1)-C(3)	1.5205(19)
N(1)-C(2)	1.5590(19)
N(1)-B(1)	1.658(2)
N(2)-C(17)	1.347(2)
N(2)-C(18)	1.412(2)
N(2)-H(2)	0.84(2)
C(1)-C(2)	1.529(2)
C(2)-C(5)	1.527(2)
C(2)-C(6)	1.550(2)
C(3)-C(8)	1.523(2)
C(3)-C(4)	1.532(2)
C(3)-C(7)	1.536(2)
C(5)-H(5A)	0.9800
C(5)-H(5B)	0.9800
C(5)-H(5C)	0.9800
C(6)-H(6A)	0.9800
C(6)-H(6B)	0.9800
C(6)-H(6C)	0.9800
C(7)-H(7A)	0.9800
C(7)-H(7B)	0.9800
C(7)-H(7C)	0.9800
C(8)-H(8A)	0.9800
C(8)-H(8B)	0.9800
C(8)-H(8C)	0.9800

C(9)-H(9A)	0.9800
C(9)-H(9B)	0.9800
C(9)-H(9C)	0.9800
C(10)-C(11)	1.396(2)
C(10)-C(15)	1.404(2)
C(10)-B(1)	1.601(2)
C(11)-C(12)	1.395(2)
C(11)-H(11)	0.9500
C(12)-C(13)	1.386(2)
C(12)-H(12)	0.9500
C(13)-C(14)	1.394(2)
C(13)-C(16)	1.516(2)
C(14)-C(15)	1.386(2)
C(14)-H(14)	0.9500
C(15)-H(15)	0.9500
C(16)-H(16A)	0.9900
C(16)-H(16B)	0.9900
C(18)-C(19)	1.392(2)
C(18)-C(23)	1.397(2)
C(19)-C(20)	1.391(2)
C(19)-H(19)	0.9500
C(20)-C(21)	1.395(2)
C(20)-H(20)	0.9500
C(21)-C(22)	1.395(2)
C(21)-C(24)	1.487(2)
C(22)-C(23)	1.380(2)
C(22)-H(22)	0.9500
C(23)-H(23)	0.9500
C(24)-C(29)	1.396(2)
C(24)-C(25)	1.397(2)
C(25)-C(26)	1.387(2)
C(25)-H(25)	0.9500
C(26)-C(27)	1.381(3)
C(26)-H(26)	0.9500
C(27)-C(28)	1.386(3)
C(27)-H(27)	0.9500

C(28)-C(29)	1.387(2)
C(28)-H(28)	0.9500
C(29)-H(29)	0.9500
C(1)-O(1)-B(1)	114.13(13)
C(4)-O(4)-B(1)	113.37(12)
C(17)-O(5)-C(16)	117.25(13)
C(9)-N(1)-C(3)	113.16(12)
C(9)-N(1)-C(2)	109.45(12)
C(3)-N(1)-C(2)	116.57(11)
C(9)-N(1)-B(1)	112.15(11)
C(3)-N(1)-B(1)	103.12(11)
C(2)-N(1)-B(1)	101.65(11)
C(17)-N(2)-C(18)	128.63(14)
C(17)-N(2)-H(2)	115.1(14)
C(18)-N(2)-H(2)	116.1(14)
O(2)-C(1)-O(1)	124.25(16)
O(2)-C(1)-C(2)	124.80(15)
O(1)-C(1)-C(2)	110.79(13)
C(5)-C(2)-C(1)	113.27(14)
C(5)-C(2)-C(6)	108.90(14)
C(1)-C(2)-C(6)	102.77(14)
C(5)-C(2)-N(1)	113.96(14)
C(1)-C(2)-N(1)	100.93(12)
C(6)-C(2)-N(1)	116.33(13)
N(1)-C(3)-C(8)	116.44(13)
N(1)-C(3)-C(4)	101.33(12)
C(8)-C(3)-C(4)	114.13(13)
N(1)-C(3)-C(7)	110.68(12)
C(8)-C(3)-C(7)	107.39(13)
C(4)-C(3)-C(7)	106.44(13)
O(3)-C(4)-O(4)	123.51(15)
O(3)-C(4)-C(3)	124.26(14)
O(4)-C(4)-C(3)	112.16(13)
C(2)-C(5)-H(5A)	109.5
C(2)-C(5)-H(5B)	109.5
H(5A)-C(5)-H(5B)	109.5

C(2)-C(5)-H(5C)	109.5
H(5A)-C(5)-H(5C)	109.5
H(5B)-C(5)-H(5C)	109.5
C(2)-C(6)-H(6A)	109.5
C(2)-C(6)-H(6B)	109.5
H(6A)-C(6)-H(6B)	109.5
C(2)-C(6)-H(6C)	109.5
H(6A)-C(6)-H(6C)	109.5
H(6B)-C(6)-H(6C)	109.5
C(3)-C(7)-H(7A)	109.5
C(3)-C(7)-H(7B)	109.5
H(7A)-C(7)-H(7B)	109.5
C(3)-C(7)-H(7C)	109.5
H(7A)-C(7)-H(7C)	109.5
H(7B)-C(7)-H(7C)	109.5
C(3)-C(8)-H(8A)	109.5
C(3)-C(8)-H(8B)	109.5
H(8A)-C(8)-H(8B)	109.5
C(3)-C(8)-H(8C)	109.5
H(8A)-C(8)-H(8C)	109.5
H(8B)-C(8)-H(8C)	109.5
N(1)-C(9)-H(9A)	109.5
N(1)-C(9)-H(9B)	109.5
H(9A)-C(9)-H(9B)	109.5
N(1)-C(9)-H(9C)	109.5
H(9A)-C(9)-H(9C)	109.5
H(9B)-C(9)-H(9C)	109.5
C(11)-C(10)-C(15)	116.46(14)
C(11)-C(10)-B(1)	122.24(14)
C(15)-C(10)-B(1)	121.18(14)
C(12)-C(11)-C(10)	122.39(14)
C(12)-C(11)-H(11)	118.8
C(10)-C(11)-H(11)	118.8
C(13)-C(12)-C(11)	119.87(14)
C(13)-C(12)-H(12)	120.1
C(11)-C(12)-H(12)	120.1

C(12)-C(13)-C(14)	118.97(14)
C(12)-C(13)-C(16)	122.95(14)
C(14)-C(13)-C(16)	118.07(14)
C(15)-C(14)-C(13)	120.57(15)
C(15)-C(14)-H(14)	119.7
C(13)-C(14)-H(14)	119.7
C(14)-C(15)-C(10)	121.73(14)
C(14)-C(15)-H(15)	119.1
C(10)-C(15)-H(15)	119.1
O(5)-C(16)-C(13)	112.11(13)
O(5)-C(16)-H(16A)	109.2
C(13)-C(16)-H(16A)	109.2
O(5)-C(16)-H(16B)	109.2
C(13)-C(16)-H(16B)	109.2
H(16A)-C(16)-H(16B)	107.9
O(6)-C(17)-N(2)	127.30(16)
O(6)-C(17)-O(5)	124.08(15)
N(2)-C(17)-O(5)	108.62(14)
C(19)-C(18)-C(23)	118.90(15)
C(19)-C(18)-N(2)	124.97(15)
C(23)-C(18)-N(2)	116.07(14)
C(20)-C(19)-C(18)	119.57(15)
C(20)-C(19)-H(19)	120.2
C(18)-C(19)-H(19)	120.2
C(19)-C(20)-C(21)	121.94(15)
C(19)-C(20)-H(20)	119.0
C(21)-C(20)-H(20)	119.0
C(20)-C(21)-C(22)	117.62(15)
C(20)-C(21)-C(24)	122.35(14)
C(22)-C(21)-C(24)	120.02(14)
C(23)-C(22)-C(21)	121.03(15)
C(23)-C(22)-H(22)	119.5
C(21)-C(22)-H(22)	119.5
C(22)-C(23)-C(18)	120.92(15)
C(22)-C(23)-H(23)	119.5
C(18)-C(23)-H(23)	119.5

C(29)-C(24)-C(25)	118.01(15)
C(29)-C(24)-C(21)	121.02(15)
C(25)-C(24)-C(21)	120.96(14)
C(26)-C(25)-C(24)	120.93(15)
C(26)-C(25)-H(25)	119.5
C(24)-C(25)-H(25)	119.5
C(27)-C(26)-C(25)	120.27(16)
C(27)-C(26)-H(26)	119.9
C(25)-C(26)-H(26)	119.9
C(26)-C(27)-C(28)	119.68(16)
C(26)-C(27)-H(27)	120.2
C(28)-C(27)-H(27)	120.2
C(27)-C(28)-C(29)	120.14(16)
C(27)-C(28)-H(28)	119.9
C(29)-C(28)-H(28)	119.9
C(28)-C(29)-C(24)	120.96(16)
C(28)-C(29)-H(29)	119.5
C(24)-C(29)-H(29)	119.5
O(1)-B(1)-O(4)	113.97(13)
O(1)-B(1)-C(10)	110.37(13)
O(4)-B(1)-C(10)	111.75(13)
O(1)-B(1)-N(1)	101.22(12)
O(4)-B(1)-N(1)	99.34(11)
C(10)-B(1)-N(1)	119.63(13)

Symmetry transformations used to generate equivalent atoms:

Table 17. Anisotropic displacement parameters ($Å^2 x 10^3$) for 10957d1s.

The anisotropic displacement factor exponent takes the form: $-2p^2[h^2 a^{*2} U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	15(1)	31(1)	25(1)	6(1)	3(1)	-1(1)
O(2)	21(1)	56(1)	23(1)	4(1)	0(1)	3(1)
O(3)	31(1)	23(1)	25(1)	-5(1)	5(1)	1(1)

O(4)	18(1)	16(1)	26(1)	0(1)	6(1)	-1(1)
O(5)	16(1)	24(1)	26(1)	1(1)	-1(1)	0(1)
O(6)	39(1)	20(1)	31(1)	-3(1)	-3(1)	-2(1)
N(1)	13(1)	20(1)	21(1)	-2(1)	3(1)	-1(1)
N(2)	20(1)	18(1)	28(1)	2(1)	1(1)	-1(1)
C(1)	16(1)	32(1)	25(1)	-1(1)	4(1)	2(1)
C(2)	14(1)	32(1)	22(1)	-1(1)	1(1)	-2(1)
C(3)	20(1)	20(1)	19(1)	-1(1)	5(1)	-1(1)
C(4)	14(1)	21(1)	23(1)	1(1)	0(1)	1(1)
C(5)	22(1)	41(1)	32(1)	-4(1)	0(1)	-11(1)
C(6)	18(1)	38(1)	29(1)	2(1)	4(1)	5(1)
C(7)	23(1)	23(1)	25(1)	4(1)	3(1)	0(1)
C(8)	22(1)	24(1)	27(1)	1(1)	9(1)	-2(1)
C(9)	22(1)	21(1)	30(1)	-4(1)	8(1)	-3(1)
C(10)	14(1)	18(1)	24(1)	2(1)	4(1)	-2(1)
C(11)	18(1)	19(1)	23(1)	-2(1)	5(1)	-2(1)
C(12)	16(1)	23(1)	23(1)	-2(1)	0(1)	-2(1)
C(13)	15(1)	19(1)	25(1)	3(1)	3(1)	-2(1)
C(14)	19(1)	26(1)	21(1)	-1(1)	5(1)	-1(1)
C(15)	17(1)	28(1)	20(1)	0(1)	1(1)	-3(1)
C(16)	17(1)	31(1)	24(1)	-3(1)	1(1)	1(1)
C(17)	14(1)	23(1)	25(1)	-1(1)	5(1)	2(1)
C(18)	14(1)	23(1)	24(1)	0(1)	4(1)	2(1)
C(19)	17(1)	19(1)	28(1)	-4(1)	3(1)	0(1)
C(20)	19(1)	17(1)	30(1)	1(1)	4(1)	1(1)
C(21)	12(1)	22(1)	26(1)	-1(1)	5(1)	2(1)
C(22)	23(1)	20(1)	28(1)	-2(1)	1(1)	-4(1)
C(23)	25(1)	19(1)	30(1)	1(1)	1(1)	-3(1)
C(24)	18(1)	21(1)	26(1)	-1(1)	4(1)	3(1)
C(25)	17(1)	23(1)	31(1)	1(1)	4(1)	1(1)
C(26)	28(1)	33(1)	29(1)	6(1)	7(1)	1(1)
C(27)	30(1)	42(1)	24(1)	3(1)	-2(1)	2(1)
C(28)	22(1)	43(1)	31(1)	-2(1)	-2(1)	-5(1)
C(29)	21(1)	32(1)	28(1)	0(1)	4(1)	-4(1)
B(1)	17(1)	18(1)	24(1)	2(1)	4(1)	-2(1)

Table 18. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x10^3) for 10957d1s.

	x	y	z	U(eq)
H(2)	3909(11)	1410(20)	5343(7)	33
H(5A)	10340	3680	6428	48
H(5B)	10649	2885	6899	48
H(5C)	9945	3807	6922	48
H(6A)	9775	445	6186	43
H(6B)	10455	696	6598	43
H(6C)	10421	1431	6090	43
H(7A)	8234	3029	5073	35
H(7B)	8360	4144	5463	35
H(7C)	7819	2990	5561	35
H(8A)	9602	2973	5127	36
H(8B)	10095	2512	5612	36
H(8C)	9743	3899	5585	36
H(9A)	9030	4493	6302	36
H(9B)	8718	3833	6763	36
H(9C)	8177	4010	6269	36
H(11)	7098	1103	5671	24
H(12)	5819	1485	5693	25
H(14)	6252	2895	7056	26
H(15)	7526	2510	7031	26
H(16A)	4935	2134	6721	29
H(16B)	5007	3429	6433	29
H(19)	3896	4489	4878	26
H(20)	3324	5022	4108	26
H(22)	2513	1485	3923	29
H(23)	3086	939	4685	30
H(25)	3370	4732	3233	29
H(26)	2842	5166	2444	35
H(27)	1659	4370	2165	39
H(28)	1012	3106	2676	39

H(29)	1552	2617	3458	33

Table 19. Torsion angles [°] for 10957d1s.

B(1)-O(1)-C(1)-O(2)	171.59(16)
B(1)-O(1)-C(1)-C(2)	-12.81(19)
O(2)-C(1)-C(2)-C(5)	-32.6(2)
O(1)-C(1)-C(2)-C(5)	151.81(15)
O(2)-C(1)-C(2)-C(6)	84.7(2)
O(1)-C(1)-C(2)-C(6)	-90.88(15)
O(2)-C(1)-C(2)-N(1)	-154.85(17)
O(1)-C(1)-C(2)-N(1)	29.58(17)
C(9)-N(1)-C(2)-C(5)	-35.03(17)
C(3)-N(1)-C(2)-C(5)	94.98(16)
B(1)-N(1)-C(2)-C(5)	-153.79(13)
C(9)-N(1)-C(2)-C(1)	86.70(14)
C(3)-N(1)-C(2)-C(1)	-143.28(13)
B(1)-N(1)-C(2)-C(1)	-32.05(14)
C(9)-N(1)-C(2)-C(6)	-163.01(13)
C(3)-N(1)-C(2)-C(6)	-33.00(19)
B(1)-N(1)-C(2)-C(6)	78.23(15)
C(9)-N(1)-C(3)-C(8)	83.63(16)
C(2)-N(1)-C(3)-C(8)	-44.61(18)
B(1)-N(1)-C(3)-C(8)	-154.99(13)
C(9)-N(1)-C(3)-C(4)	-151.95(12)
C(2)-N(1)-C(3)-C(4)	79.81(14)
B(1)-N(1)-C(3)-C(4)	-30.57(14)
C(9)-N(1)-C(3)-C(7)	-39.36(16)
C(2)-N(1)-C(3)-C(7)	-167.60(13)
B(1)-N(1)-C(3)-C(7)	82.02(14)
B(1)-O(4)-C(4)-O(3)	-178.09(15)
B(1)-O(4)-C(4)-C(3)	-0.96(17)
N(1)-C(3)-C(4)-O(3)	-161.27(14)
C(8)-C(3)-C(4)-O(3)	-35.3(2)
C(7)-C(3)-C(4)-O(3)	82.96(18)

N(1)-C(3)-C(4)-O(4)	21.63(15)
C(8)-C(3)-C(4)-O(4)	147.59(13)
C(7)-C(3)-C(4)-O(4)	-94.14(14)
C(15)-C(10)-C(11)-C(12)	0.8(2)
B(1)-C(10)-C(11)-C(12)	176.92(15)
C(10)-C(11)-C(12)-C(13)	-0.1(2)
C(11)-C(12)-C(13)-C(14)	-0.6(2)
C(11)-C(12)-C(13)-C(16)	-179.86(15)
C(12)-C(13)-C(14)-C(15)	0.5(2)
C(16)-C(13)-C(14)-C(15)	179.87(15)
C(13)-C(14)-C(15)-C(10)	0.2(2)
C(11)-C(10)-C(15)-C(14)	-0.8(2)
B(1)-C(10)-C(15)-C(14)	-176.98(15)
C(17)-O(5)-C(16)-C(13)	-102.20(16)
C(12)-C(13)-C(16)-O(5)	6.9(2)
C(14)-C(13)-C(16)-O(5)	-172.42(14)
C(18)-N(2)-C(17)-O(6)	3.3(3)
C(18)-N(2)-C(17)-O(5)	-177.01(14)
C(16)-O(5)-C(17)-O(6)	-2.1(2)
C(16)-O(5)-C(17)-N(2)	178.16(12)
C(17)-N(2)-C(18)-C(19)	5.5(3)
C(17)-N(2)-C(18)-C(23)	-177.18(15)
C(23)-C(18)-C(19)-C(20)	-1.4(2)
N(2)-C(18)-C(19)-C(20)	175.84(15)
C(18)-C(19)-C(20)-C(21)	0.2(2)
C(19)-C(20)-C(21)-C(22)	1.2(2)
C(19)-C(20)-C(21)-C(24)	-177.90(14)
C(20)-C(21)-C(22)-C(23)	-1.4(2)
C(24)-C(21)-C(22)-C(23)	177.69(15)
C(21)-C(22)-C(23)-C(18)	0.2(3)
C(19)-C(18)-C(23)-C(22)	1.2(2)
N(2)-C(18)-C(23)-C(22)	-176.31(15)
C(20)-C(21)-C(24)-C(29)	-142.02(16)
C(22)-C(21)-C(24)-C(29)	38.9(2)
C(20)-C(21)-C(24)-C(25)	39.1(2)
C(22)-C(21)-C(24)-C(25)	-139.93(16)

C(29)-C(24)-C(25)-C(26)	-0.6(2)
C(21)-C(24)-C(25)-C(26)	178.34(15)
C(24)-C(25)-C(26)-C(27)	1.1(3)
C(25)-C(26)-C(27)-C(28)	-0.5(3)
C(26)-C(27)-C(28)-C(29)	-0.5(3)
C(27)-C(28)-C(29)-C(24)	1.0(3)
C(25)-C(24)-C(29)-C(28)	-0.5(3)
C(21)-C(24)-C(29)-C(28)	-179.36(16)
C(1)-O(1)-B(1)-O(4)	96.64(16)
C(1)-O(1)-B(1)-C(10)	-136.66(14)
C(1)-O(1)-B(1)-N(1)	-8.98(17)
C(4)-O(4)-B(1)-O(1)	-125.04(14)
C(4)-O(4)-B(1)-C(10)	108.98(14)
C(4)-O(4)-B(1)-N(1)	-18.25(15)
C(11)-C(10)-B(1)-O(1)	-140.37(15)
C(15)-C(10)-B(1)-O(1)	35.6(2)
C(11)-C(10)-B(1)-O(4)	-12.4(2)
C(15)-C(10)-B(1)-O(4)	163.49(14)
C(11)-C(10)-B(1)-N(1)	102.89(18)
C(15)-C(10)-B(1)-N(1)	-81.18(19)
C(9)-N(1)-B(1)-O(1)	-90.83(14)
C(3)-N(1)-B(1)-O(1)	147.11(12)
C(2)-N(1)-B(1)-O(1)	25.98(14)
C(9)-N(1)-B(1)-O(4)	152.28(12)
C(3)-N(1)-B(1)-O(4)	30.21(13)
C(2)-N(1)-B(1)-O(4)	-90.91(12)
C(9)-N(1)-B(1)-C(10)	30.57(19)
C(3)-N(1)-B(1)-C(10)	-91.49(15)
C(2)-N(1)-B(1)-C(10)	147.38(14)

Symmetry transformations used to generate equivalent atoms

Table 20. Hydrogen bonds for 10957d1s [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(2)-H(2)...O(3)#1	0.84(2)	2.14(2)	2.9581(19)	162.4(19)

Symmetry transformations used to generate equivalent atoms:
#1 x-1/2,-y,z

Crystal data and structure refinement for **19** (10941ds), CCDC Number: 2291892 are provided below.

Table 21. Crystal data and structure refinement for 10941ds.

Identification code	10941ds
Empirical formula	$C_{21}H_{24}BBrN_4O_6$
Formula weight	519.16
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P-1
Unit cell dimensions	a = 6.9360(2) Å a= 97.7552(12)°. b = 12.7875(4) Å b= 98.0562(12)°. c = 13.1096(4) Å g = 102.3547(11)°.
Volume	1108.14(6) $Å^3$
Z	2
Density (calculated)	1.556 mg/m^3
Absorption coefficient	1.902 mm^{-1}
F(000)	532
Crystal size	0.293 x 0.216 x 0.065 mm^3
Theta range for data collection	2.092 to 28.351°
Index ranges	-9<=h<=9, -17<=k<=17, -17<=l<=17
Reflections collected	25869

Independent reflections	5504 [R(int) = 0.0266]
Completeness to theta = 25.242°	99.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7457 and 0.6220
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5504 / 0 / 306
Goodness-of-fit on F^2	1.096
Final R indices [I>2sigma(I)]	R1 = 0.0267, wR2 = 0.0640
R indices (all data)	R1 = 0.0285, wR2 = 0.0647
Extinction coefficient	n/a
Largest diff. peak and hole	0.391 and -0.459 e.$Å^{-3}$

Table 22. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x10^3) for 10941ds. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Br(1)	-7470(1)	344(1)	3562(1)	18(1)
O(1)	8842(2)	8321(1)	8846(1)	15(1)
O(2)	10821(2)	9859(1)	8572(1)	21(1)
O(3)	10355(2)	6351(1)	11225(1)	21(1)
O(4)	8568(2)	6798(1)	9859(1)	16(1)
O(5)	636(2)	3925(1)	6248(1)	23(1)
O(6)	-583(2)	2322(1)	5144(1)	25(1)
N(1)	11246(2)	7220(1)	8864(1)	12(1)
N(2)	-2219(2)	2878(1)	6457(1)	20(1)
N(3)	-4719(2)	1701(1)	5178(1)	16(1)
N(4)	-4912(2)	1858(1)	6998(1)	18(1)
C(1)	10518(2)	8902(1)	8613(1)	15(1)
C(2)	11922(2)	8175(1)	8318(1)	14(1)

C(3)	12068(2)	7400(1)	10058(1)	14(1)
C(4)	10273(2)	6766(1)	10447(1)	16(1)
C(5)	11377(2)	7834(1)	7122(1)	17(1)
C(6)	14155(2)	8719(1)	8565(1)	18(1)
C(7)	13988(2)	7024(1)	10333(1)	19(1)
C(8)	12298(3)	8562(1)	10658(1)	19(1)
C(9)	11591(2)	6175(1)	8343(1)	16(1)
C(10)	7190(2)	6352(1)	7944(1)	14(1)
C(11)	6303(2)	6678(1)	7052(1)	15(1)
C(12)	4762(2)	5967(1)	6320(1)	17(1)
C(13)	4042(2)	4907(1)	6469(1)	18(1)
C(14)	4900(3)	4570(1)	7354(1)	20(1)
C(15)	6442(2)	5276(1)	8073(1)	18(1)
C(16)	2349(3)	4131(2)	5711(1)	23(1)
C(17)	-714(2)	2976(1)	5864(1)	18(1)
C(18)	-4020(2)	2093(1)	6191(1)	16(1)
C(19)	-6388(2)	921(1)	4991(1)	16(1)
C(20)	-7397(2)	528(1)	5755(1)	19(1)
C(21)	-6609(2)	1070(1)	6762(1)	19(1)
B(1)	8844(3)	7161(1)	8851(1)	14(1)

Table 23. Bond lengths [Å] and angles [°] for 10941ds.

Br(1)-C(19)	1.9012(16)
O(1)-C(1)	1.3369(19)
O(1)-B(1)	1.485(2)
O(2)-C(1)	1.206(2)
O(3)-C(4)	1.211(2)
O(4)-C(4)	1.3295(19)
O(4)-B(1)	1.483(2)
O(5)-C(17)	1.350(2)
O(5)-C(16)	1.458(2)
O(6)-C(17)	1.201(2)
N(1)-C(9)	1.4986(19)
N(1)-C(2)	1.5193(19)

N(1)-C(3)	1.5569(19)
N(1)-B(1)	1.649(2)
N(2)-C(17)	1.381(2)
N(2)-C(18)	1.392(2)
N(2)-H(2)	0.83(2)
N(3)-C(19)	1.325(2)
N(3)-C(18)	1.337(2)
N(4)-C(18)	1.335(2)
N(4)-C(21)	1.343(2)
C(1)-C(2)	1.536(2)
C(2)-C(6)	1.525(2)
C(2)-C(5)	1.539(2)
C(3)-C(7)	1.524(2)
C(3)-C(4)	1.525(2)
C(3)-C(8)	1.549(2)
C(5)-H(5A)	0.9800
C(5)-H(5B)	0.9800
C(5)-H(5C)	0.9800
C(6)-H(6A)	0.9800
C(6)-H(6B)	0.9800
C(6)-H(6C)	0.9800
C(7)-H(7A)	0.9800
C(7)-H(7B)	0.9800
C(7)-H(7C)	0.9800
C(8)-H(8A)	0.9800
C(8)-H(8B)	0.9800
C(8)-H(8C)	0.9800
C(9)-H(9A)	0.9800
C(9)-H(9B)	0.9800
C(9)-H(9C)	0.9800
C(10)-C(11)	1.400(2)
C(10)-C(15)	1.405(2)
C(10)-B(1)	1.605(2)
C(11)-C(12)	1.397(2)
C(11)-H(11)	0.9500
C(12)-C(13)	1.390(2)

C(12)-H(12)	0.9500
C(13)-C(14)	1.392(2)
C(13)-C(16)	1.503(2)
C(14)-C(15)	1.387(2)
C(14)-H(14)	0.9500
C(15)-H(15)	0.9500
C(16)-H(16A)	0.9900
C(16)-H(16B)	0.9900
C(19)-C(20)	1.389(2)
C(20)-C(21)	1.381(2)
C(20)-H(20)	0.9500
C(21)-H(21)	0.9500
C(1)-O(1)-B(1)	113.67(12)
C(4)-O(4)-B(1)	113.47(12)
C(17)-O(5)-C(16)	114.68(13)
C(9)-N(1)-C(2)	113.47(12)
C(9)-N(1)-C(3)	109.61(12)
C(2)-N(1)-C(3)	115.70(12)
C(9)-N(1)-B(1)	112.04(12)
C(2)-N(1)-B(1)	103.59(11)
C(3)-N(1)-B(1)	101.67(11)
C(17)-N(2)-C(18)	124.39(15)
C(17)-N(2)-H(2)	116.8(17)
C(18)-N(2)-H(2)	117.5(17)
C(19)-N(3)-C(18)	114.35(14)
C(18)-N(4)-C(21)	115.52(14)
O(2)-C(1)-O(1)	124.15(15)
O(2)-C(1)-C(2)	124.53(15)
O(1)-C(1)-C(2)	111.15(13)
N(1)-C(2)-C(6)	116.02(13)
N(1)-C(2)-C(1)	101.52(12)
C(6)-C(2)-C(1)	115.68(13)
N(1)-C(2)-C(5)	111.00(12)
C(6)-C(2)-C(5)	106.66(13)
C(1)-C(2)-C(5)	105.53(12)
C(7)-C(3)-C(4)	113.87(13)

C(7)-C(3)-C(8)	109.83(13)
C(4)-C(3)-C(8)	101.44(12)
C(7)-C(3)-N(1)	114.28(13)
C(4)-C(3)-N(1)	100.94(12)
C(8)-C(3)-N(1)	115.56(12)
O(3)-C(4)-O(4)	123.79(15)
O(3)-C(4)-C(3)	125.42(15)
O(4)-C(4)-C(3)	110.61(13)
C(2)-C(5)-H(5A)	109.5
C(2)-C(5)-H(5B)	109.5
H(5A)-C(5)-H(5B)	109.5
C(2)-C(5)-H(5C)	109.5
H(5A)-C(5)-H(5C)	109.5
H(5B)-C(5)-H(5C)	109.5
C(2)-C(6)-H(6A)	109.5
C(2)-C(6)-H(6B)	109.5
H(6A)-C(6)-H(6B)	109.5
C(2)-C(6)-H(6C)	109.5
H(6A)-C(6)-H(6C)	109.5
H(6B)-C(6)-H(6C)	109.5
C(3)-C(7)-H(7A)	109.5
C(3)-C(7)-H(7B)	109.5
H(7A)-C(7)-H(7B)	109.5
C(3)-C(7)-H(7C)	109.5
H(7A)-C(7)-H(7C)	109.5
H(7B)-C(7)-H(7C)	109.5
C(3)-C(8)-H(8A)	109.5
C(3)-C(8)-H(8B)	109.5
H(8A)-C(8)-H(8B)	109.5
C(3)-C(8)-H(8C)	109.5
H(8A)-C(8)-H(8C)	109.5
H(8B)-C(8)-H(8C)	109.5
N(1)-C(9)-H(9A)	109.5
N(1)-C(9)-H(9B)	109.5
H(9A)-C(9)-H(9B)	109.5
N(1)-C(9)-H(9C)	109.5

H(9A)-C(9)-H(9C)	109.5
H(9B)-C(9)-H(9C)	109.5
C(11)-C(10)-C(15)	116.76(14)
C(11)-C(10)-B(1)	123.62(14)
C(15)-C(10)-B(1)	119.41(14)
C(12)-C(11)-C(10)	121.72(15)
C(12)-C(11)-H(11)	119.1
C(10)-C(11)-H(11)	119.1
C(13)-C(12)-C(11)	120.40(15)
C(13)-C(12)-H(12)	119.8
C(11)-C(12)-H(12)	119.8
C(12)-C(13)-C(14)	118.69(15)
C(12)-C(13)-C(16)	121.70(16)
C(14)-C(13)-C(16)	119.61(15)
C(15)-C(14)-C(13)	120.69(15)
C(15)-C(14)-H(14)	119.7
C(13)-C(14)-H(14)	119.7
C(14)-C(15)-C(10)	121.74(15)
C(14)-C(15)-H(15)	119.1
C(10)-C(15)-H(15)	119.1
O(5)-C(16)-C(13)	107.17(13)
O(5)-C(16)-H(16A)	110.3
C(13)-C(16)-H(16A)	110.3
O(5)-C(16)-H(16B)	110.3
C(13)-C(16)-H(16B)	110.3
H(16A)-C(16)-H(16B)	108.5
O(6)-C(17)-O(5)	125.13(15)
O(6)-C(17)-N(2)	126.43(15)
O(5)-C(17)-N(2)	108.42(14)
N(4)-C(18)-N(3)	127.20(15)
N(4)-C(18)-N(2)	114.73(15)
N(3)-C(18)-N(2)	117.97(14)
N(3)-C(19)-C(20)	124.79(15)
N(3)-C(19)-Br(1)	116.26(12)
C(20)-C(19)-Br(1)	118.93(12)
C(21)-C(20)-C(19)	114.71(15)

C(21)-C(20)-H(20)	122.6
C(19)-C(20)-H(20)	122.6
N(4)-C(21)-C(20)	122.94(15)
N(4)-C(21)-H(21)	118.5
C(20)-C(21)-H(21)	118.5
O(4)-B(1)-O(1)	114.19(13)
O(4)-B(1)-C(10)	108.05(13)
O(1)-B(1)-C(10)	112.85(13)
O(4)-B(1)-N(1)	101.38(12)
O(1)-B(1)-N(1)	99.88(11)
C(10)-B(1)-N(1)	120.12(13)

Symmetry transformations used to generate equivalent atoms

Table 24. Anisotropic displacement parameters ($Å^2$x 10^3) for 10941ds.

The anisotropic displacement factor exponent takes the form: $-2p^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	16(1)	20(1)	18(1)	4(1)	1(1)	2(1)
O(1)	12(1)	14(1)	19(1)	2(1)	4(1)	4(1)
O(2)	25(1)	14(1)	24(1)	4(1)	6(1)	6(1)
O(3)	21(1)	22(1)	18(1)	7(1)	4(1)	3(1)
O(4)	12(1)	22(1)	16(1)	5(1)	5(1)	4(1)
O(5)	17(1)	21(1)	25(1)	-6(1)	9(1)	-5(1)
O(6)	21(1)	27(1)	22(1)	-5(1)	6(1)	-2(1)
N(1)	11(1)	12(1)	14(1)	2(1)	4(1)	3(1)
N(2)	17(1)	22(1)	17(1)	-3(1)	5(1)	-3(1)
N(3)	15(1)	16(1)	18(1)	3(1)	4(1)	3(1)
N(4)	17(1)	18(1)	19(1)	4(1)	5(1)	2(1)
C(1)	15(1)	16(1)	14(1)	2(1)	1(1)	3(1)
C(2)	13(1)	12(1)	17(1)	4(1)	4(1)	2(1)
C(3)	13(1)	17(1)	13(1)	3(1)	3(1)	3(1)
C(4)	15(1)	15(1)	16(1)	2(1)	4(1)	3(1)
C(5)	16(1)	19(1)	16(1)	4(1)	5(1)	4(1)

C(6)	14(1)	18(1)	22(1)	4(1)	5(1)	0(1)
C(7)	15(1)	23(1)	21(1)	6(1)	2(1)	7(1)
C(8)	20(1)	18(1)	17(1)	0(1)	3(1)	3(1)
C(9)	16(1)	12(1)	20(1)	1(1)	5(1)	4(1)
C(10)	10(1)	15(1)	19(1)	2(1)	5(1)	3(1)
C(11)	13(1)	15(1)	18(1)	3(1)	6(1)	2(1)
C(12)	13(1)	22(1)	16(1)	2(1)	5(1)	3(1)
C(13)	13(1)	18(1)	20(1)	-3(1)	6(1)	0(1)
C(14)	17(1)	13(1)	28(1)	2(1)	6(1)	2(1)
C(15)	15(1)	16(1)	24(1)	6(1)	3(1)	4(1)
C(16)	16(1)	26(1)	22(1)	-4(1)	8(1)	-4(1)
C(17)	15(1)	19(1)	16(1)	1(1)	1(1)	-1(1)
C(18)	14(1)	14(1)	21(1)	2(1)	4(1)	2(1)
C(19)	14(1)	17(1)	16(1)	3(1)	0(1)	4(1)
C(20)	14(1)	20(1)	23(1)	7(1)	2(1)	1(1)
C(21)	16(1)	22(1)	21(1)	8(1)	6(1)	3(1)
B(1)	11(1)	15(1)	16(1)	3(1)	4(1)	3(1)

Table 25. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for 10941ds.

	x	y	z	U(eq)
H(2)	-1930(40)	3220(20)	7065(19)	30
H(5A)	11543	8484	6792	25
H(5B)	9981	7416	6931	25
H(5C)	12260	7386	6880	25
H(6A)	14921	8189	8358	27
H(6B)	14550	8994	9317	27
H(6C)	14428	9324	8179	27
H(7A)	13771	6255	10033	29
H(7B)	14362	7120	11095	29
H(7C)	15067	7456	10049	29
H(8A)	13352	9069	10427	28

H(8B)	12659	8571	11410	28
H(8C)	11027	8779	10518	28
H(9A)	10788	5970	7639	24
H(9B)	11197	5603	8753	24
H(9C)	13015	6269	8297	24
H(11)	6762	7402	6941	18
H(12)	4202	6209	5717	20
H(14)	4423	3848	7467	23
H(15)	7008	5025	8669	22
H(16A)	2011	4452	5083	27
H(16B)	2733	3444	5489	27
H(20)	-8539	-66	5598	23
H(21)	-7299	877	7311	23

Table 26. Torsion angles [°] for 10941ds.

B(1)-O(1)-C(1)-O(2)	-179.65(15)
B(1)-O(1)-C(1)-C(2)	4.98(18)
C(9)-N(1)-C(2)-C(6)	-81.29(16)
C(3)-N(1)-C(2)-C(6)	46.67(18)
B(1)-N(1)-C(2)-C(6)	156.99(13)
C(9)-N(1)-C(2)-C(1)	152.44(12)
C(3)-N(1)-C(2)-C(1)	-79.61(14)
B(1)-N(1)-C(2)-C(1)	30.72(14)
C(9)-N(1)-C(2)-C(5)	40.67(17)
C(3)-N(1)-C(2)-C(5)	168.62(12)
B(1)-N(1)-C(2)-C(5)	-81.05(14)
O(2)-C(1)-C(2)-N(1)	160.80(15)
O(1)-C(1)-C(2)-N(1)	-23.86(16)
O(2)-C(1)-C(2)-C(6)	34.3(2)
O(1)-C(1)-C(2)-C(6)	-150.36(13)
O(2)-C(1)-C(2)-C(5)	-83.34(19)
O(1)-C(1)-C(2)-C(5)	92.01(15)
C(9)-N(1)-C(3)-C(7)	36.72(17)
C(2)-N(1)-C(3)-C(7)	-93.13(15)

B(1)-N(1)-C(3)-C(7)	155.42(13)
C(9)-N(1)-C(3)-C(4)	-85.93(13)
C(2)-N(1)-C(3)-C(4)	144.23(12)
B(1)-N(1)-C(3)-C(4)	32.78(13)
C(9)-N(1)-C(3)-C(8)	165.63(13)
C(2)-N(1)-C(3)-C(8)	35.79(17)
B(1)-N(1)-C(3)-C(8)	-75.66(15)
B(1)-O(4)-C(4)-O(3)	-169.24(15)
B(1)-O(4)-C(4)-C(3)	15.52(18)
C(7)-C(3)-C(4)-O(3)	30.3(2)
C(8)-C(3)-C(4)-O(3)	-87.61(19)
N(1)-C(3)-C(4)-O(3)	153.22(16)
C(7)-C(3)-C(4)-O(4)	-154.55(14)
C(8)-C(3)-C(4)-O(4)	87.54(15)
N(1)-C(3)-C(4)-O(4)	-31.63(16)
C(15)-C(10)-C(11)-C(12)	-0.5(2)
B(1)-C(10)-C(11)-C(12)	-175.13(14)
C(10)-C(11)-C(12)-C(13)	0.9(2)
C(11)-C(12)-C(13)-C(14)	-0.6(2)
C(11)-C(12)-C(13)-C(16)	178.35(15)
C(12)-C(13)-C(14)-C(15)	-0.1(2)
C(16)-C(13)-C(14)-C(15)	-178.99(15)
C(13)-C(14)-C(15)-C(10)	0.4(3)
C(11)-C(10)-C(15)-C(14)	-0.1(2)
B(1)-C(10)-C(15)-C(14)	174.75(15)
C(17)-O(5)-C(16)-C(13)	-155.89(15)
C(12)-C(13)-C(16)-O(5)	-111.96(17)
C(14)-C(13)-C(16)-O(5)	66.9(2)
C(16)-O(5)-C(17)-O(6)	0.3(3)
C(16)-O(5)-C(17)-N(2)	178.73(14)
C(18)-N(2)-C(17)-O(6)	-12.4(3)
C(18)-N(2)-C(17)-O(5)	169.22(16)
C(21)-N(4)-C(18)-N(3)	6.4(2)
C(21)-N(4)-C(18)-N(2)	-177.39(15)
C(19)-N(3)-C(18)-N(4)	-6.9(2)
C(19)-N(3)-C(18)-N(2)	176.97(15)

C(17)-N(2)-C(18)-N(4)	155.51(16)
C(17)-N(2)-C(18)-N(3)	-27.9(2)
C(18)-N(3)-C(19)-C(20)	1.0(2)
C(18)-N(3)-C(19)-Br(1)	179.29(11)
N(3)-C(19)-C(20)-C(21)	4.5(3)
Br(1)-C(19)-C(20)-C(21)	-173.81(12)
C(18)-N(4)-C(21)-C(20)	0.2(2)
C(19)-C(20)-C(21)-N(4)	-5.0(3)
C(4)-O(4)-B(1)-O(1)	-99.51(15)
C(4)-O(4)-B(1)-C(10)	134.04(13)
C(4)-O(4)-B(1)-N(1)	6.88(16)
C(1)-O(1)-B(1)-O(4)	121.87(14)
C(1)-O(1)-B(1)-C(10)	-114.22(14)
C(1)-O(1)-B(1)-N(1)	14.55(16)
C(11)-C(10)-B(1)-O(4)	146.82(14)
C(15)-C(10)-B(1)-O(4)	-27.64(19)
C(11)-C(10)-B(1)-O(1)	19.6(2)
C(15)-C(10)-B(1)-O(1)	-154.86(14)
C(11)-C(10)-B(1)-N(1)	-97.78(18)
C(15)-C(10)-B(1)-N(1)	87.77(18)
C(9)-N(1)-B(1)-O(4)	91.72(14)
C(2)-N(1)-B(1)-O(4)	-145.61(12)
C(3)-N(1)-B(1)-O(4)	-25.24(14)
C(9)-N(1)-B(1)-O(1)	-150.94(12)
C(2)-N(1)-B(1)-O(1)	-28.27(14)
C(3)-N(1)-B(1)-O(1)	92.10(12)
C(9)-N(1)-B(1)-C(10)	-27.11(18)
C(2)-N(1)-B(1)-C(10)	95.56(15)
C(3)-N(1)-B(1)-C(10)	-144.07(14)

Symmetry transformations used to generate equivalent atoms:

Table 27. Hydrogen bonds for 10941ds [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(2)-H(2)...O(3)#1	0.83(2)	2.29(2)	3.0700(19)	156(2)

Symmetry transformations used to generate equivalent atoms:
#1 -x+1,-y+1,-z+2

INCORPORATION BY REFERENCE

All US patents and US and PCT patent application publications mentioned herein are hereby incorporated by reference in their entirety as if each individual publication or patent was specifically and individually indicated to be incorporated by reference. In case of conflict, the present application, including any definitions herein, will control.

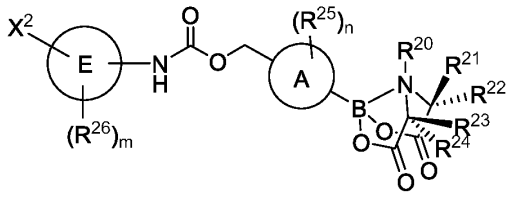
EQUIVALENTS

While specific embodiments of the subject invention have been discussed, the above specification is illustrative and not restrictive. Many variations of the invention will become apparent to those skilled in the art upon review of this specification and the claims below. The full scope of the invention should be determined by reference to the claims, along with their full scope of equivalents, and the specification, along with such variations.

CLAIMS

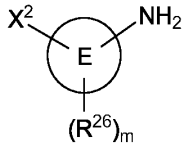
We claim:

1. A method of making a compound of formula (I):



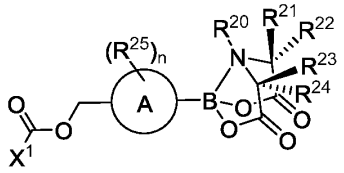
(**I**);

comprising combining a compound of formula (II):



(**II**);

and a compound of formula (III):



(**III**);

thereby forming the compound of Formula I;

wherein:

A is aryl or heteroaryl;

E is aryl or heteroaryl;

B is a boron having sp^3 hybridization;

n is an integer selected from 1, 2, 3, or 4;

m is an integer selected from 0, 1, 2, 3, or 4;

X^1 is halogen or $-OR^j$;

X^2 is halogen;

R^j is selected from the group consisting of alkyl, nitrophenyl, pentafluorophenyl, and $-N(C(O)CH_2)_2$;

R^{20} is selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, and aryl;

R^{21} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, and heteroaralkyl;

R^{22} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, and heteroaralkyl;

R^{23} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, and heteroaralkyl;

R^{24} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, and heteroaralkyl;

R^{25} is, independently for each occurrence, selected from the group consisting of H, alkyl, cycloalkyl, alkoxy, hydroxyl, halogen, acyl, aryl, heteroaryl, heterocyclyl, cyano, nitro, and sulfonyl; and

R^{26} is, independently for each occurrence, selected from the group consisting of H, alkyl, cycloalkyl, alkoxy, hydroxyl, acyl, aryl, heteroaryl, heterocyclyl, cyano, nitro, and sulfonyl.

2. The method of claim 1, further comprising a base selected from the group consisting of triethylamine, pyridine, 2,6-lutidine, 1,8-diazabicyclo[5.4.0]undec-7-ene, 2,2,6,6-tetramethylpiperidine, $NaHCO_3$, K_2CO_3, $CsCO_3$, and K_3PO_4.

3. The method of claim 1 or 2, wherein A is phenyl.

4. The method of any one of claims 1-3, wherein each of R^{20}, R^{21}, R^{22}, R^{23}, and R^{24} is methyl; or each of R^{21}, R^{22}, R^{23}, and R^{24} is methyl.

5. The method of any one of claims 1-4, wherein R^{25} is H.

6. The method of any one of claims 1-5, wherein X^1 is chloro or fluoro.

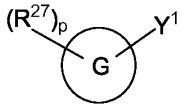
7. The method of claim 6, wherein X^1 is chloro.

8. The method of any one of claims 1-5, wherein X^1 is OR^j.

9. The method of claim 8, wherein R^j is selected from the group consisting of methyl, ethyl, nitrophenyl, pentafluorophenyl, and $-N(C(O)CH_2)_2$.

10. The method of any one of claims 1-9, wherein X^2 is bromo or iodo.

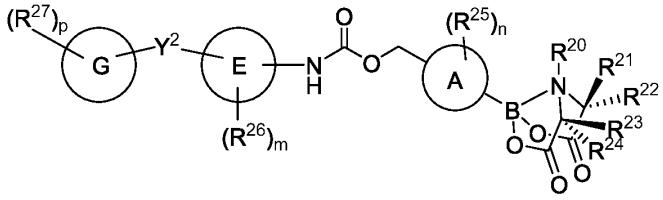
11. The method of any one of claims 1-10, wherein the method further comprises combining the compound of Formula (I), a compound of Formula (V):



(**V**);

a palladium catalyst, and a base;

thereby forming a compound of Formula (IV):



(**IV**);

wherein:

G is aryl or heteroaryl;

p is an integer selected from 0, 1, 2, 3, and 4;

R^{27} is, independently for each occurrence, selected from the group consisting of H, alkyl, cycloalkyl, alkoxy, hydroxyl, halogen, acyl, aryl, heteroaryl, heterocyclyl, cyano, nitro, and sulfonyl;

Y^1 is selected from the group consisting of $-NH_2$, -B(pin), -B(neop), -B(dan), -B(MIDA), and $-B(OH)_2$; and

Y^2 is -NH- or is a bond.

12. The method of claim 11, wherein Y^1 is $-NH_2$.

13. The method of claim 11, wherein Y^1 is $-B(OH)_2$.

14. The method of claim 12, wherein Y^2 is -NH-.

15. The method of claim 13, wherein Y^2 is a bond.

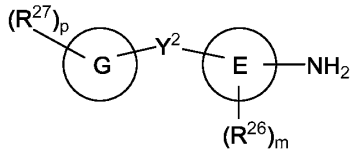
16. The method of any one of claims 11-15, wherein the palladium catalyst is selected from the group consisting of (t-Bu-XPhos)Pd G3, (t-Bu-XPhos)Pd G4, (XPhos)Pd G3, (XPhos)Pd G4, $Pd(PPh_3)4$, (RuPhos)Pd G3, (RuPhos)Pd G4, (XantPhos)Pd G3, (XantPhos)Pd G4, $(t\text{-}Bu\text{-}P)_3Pd$ G3, $(t\text{-}Bu\text{-}P)_3Pd$ G4, (SPhos)Pd G3, (Sphos)Pd G4, $Pd(Oac)_2$, $(Pd)_2(DBA)_3$, and $Pd(PPh_3)_2(Cl)_2$.

17. The method of claim 16, wherein the palladium catalyst is (t-Bu-XPhos)Pd G3 or $(t\text{-}Bu\text{-}P)_3Pd$ G4.

18. The method of any one of claims 11-17, wherein the base is selected from the group consisting of potassium trimethylsilanolate, triethylamine, pyridine, 2,6-lutidine, 1,8-diazabicyclo[5.4.0]undec-7-ene, 2,2,6,6-tetramethylpiperidine, $NaHCO_3$, K_2CO_3, $CsCO_3$, and K_3PO_4.

19. The method of claim 18, wherein the base is potassium trimethylsilanolate.

20. The method of any one of claims 11-19, wherein the method further comprises combining the compound of Formula (IV) and a reducing agent, thereby forming a compound of Formula (VI):

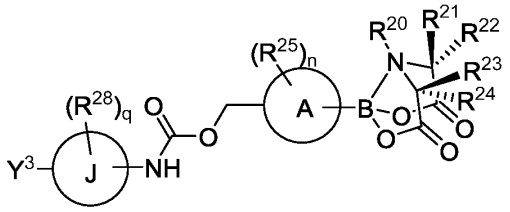


(VI).

21. The method of claim 20, wherein the reducing agent is selected from the group consisting of $BF_3{\bullet}Oet_2$, EtSH, TBAF, TMSI, Pd/C, H_2, and $NaBH_4$, or a combination of any of them.

22. The method of claim 21, wherein the reducing agent is the combination of Pd/C, $NaBH_4$ and H_2.

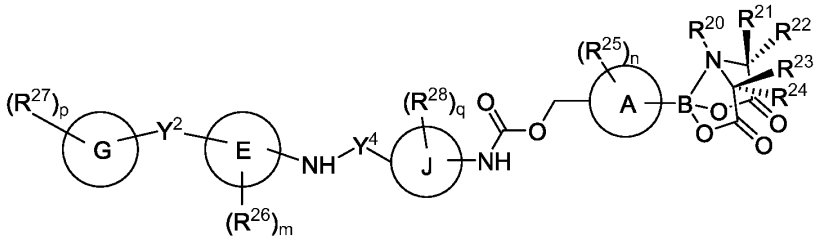
23. The method of any one of claims 20-22, further comprising combining the compound of Formula (VI), a compound of Formula (VIII):



(**VIII**);

an activating agent, and a base;

thereby forming a compound of Formula (VII):



(**VII**);

wherein:

J is aryl or heteroaryl;

q is an integer selected from 0, 1, 2, 3, or 4;

R^{28} is, independently for each occurrence, selected from the group consisting of H, alkyl, cycloalkyl, alkoxy, hydroxyl, halogen, acyl, aryl, heteroaryl, heterocyclyl, cyano, nitro, and sulfonyl;

Y^3 is $-C(O)_2H$ or a carboxylate salt, and Y^4 is –C(O)-; or Y^3 is halogen, and Y^4 is a bond;

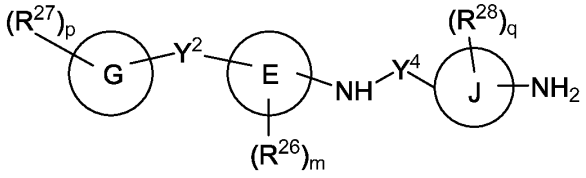
when Y^3 is $-CO_2H$ or a carboxylate salt, the activating agent is selected from the group consisting of propylphosphonic anhydride, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide, benzotriazole-1-yl-oxy-tris-(dimethylamino)-phosphonium hexafluorophosphate, 1-[(1-(cyano-2-ethoxy-2-oxoethylideneaminooxy) dimethylaminomorpholino)] uronium hexafluorophosphate, hexafluorophosphate azabenzotriazole tetramethyluronium, hexafluorophosphate benzotriazole tetramethyluronium, benzotriazol-1-yloxytripyrrolidinophosphonium hexafluorophosphate, and benzotriazol-1-yloxytris(dimethylamino)phosphonium hexafluorophosphate; and

when Y^3 is halogen, the activating agent is selected from the group consisting of $Pd(OAc)_2$, (SPhos)$Pd(OAc)_2$, (SPhos)Pd G3, and (SPhos)Pd G4.

24. The method of claim 23, wherein Y^3 is CO_2H or a carboxylate salt, and the activating agent is propylphosphonic anhydride; or wherein Y^3 is halogen, and the activating agent is (SPhos)$Pd(OAc)_2$.

25. The method of claim 23 or 24, wherein the base is pyridine or Cs_2CO_3.

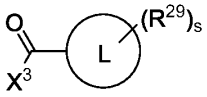
26. The method of any one of claims 23-25, wherein the method further comprises combining the compound of Formula (VII) and an oxidizing agent, thereby forming a compound of Formula (IX):



(**IX**).

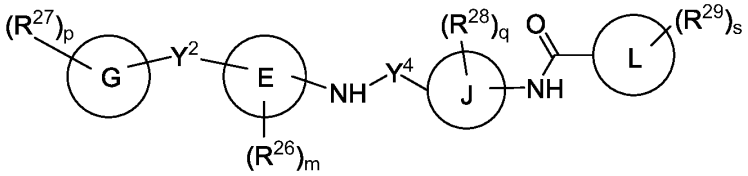
27. The method of claim 26, wherein the oxidizing agent is the combination of LiOH and H_2O_2.

28. The method of claim 26 or 27, wherein the method further comprises combining the compound of Formula (IX), a compound of Formula (XI):



(**XI**),

and a base; thereby forming a compound of Formula (X):



(**X**);

wherein:

L is aryl or heteroaryl;

X^3 is halogen;

s is an integer selected from 0, 1, 2, 3, 4, or 5; and

R^{29} is, independently for each occurrence, selected from the group consisting of H, alkyl, cycloalkyl, heterocyclyl, heterocyclylalkyl, aryl, and heteroaryl.

29. The method of claim 28, wherein the base is pyridine.

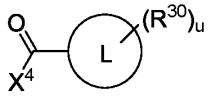
30. The method of claim 28 or 29, wherein X^3 is chloro.

31. The method of any one of claims 28-30, wherein L is phenyl.

32. The method of any one of claims 28-31, wherein R^{29} is N-methylpiperazinylmethylene.

33. The method of any one of claims 28-32, wherein s is 1.

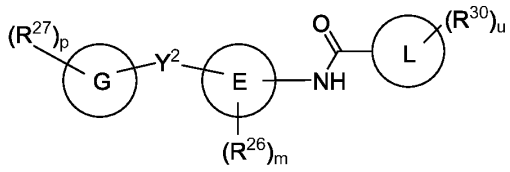
34. The method of any one of claims 20-22, further comprising combining the compound of Formula (VI), a compound of Formula (XII):



(**XII**);

and a base;

thereby forming a compound of Formula (XIII):



(**XIII**);

wherein:

L is aryl or heteroaryl;

X^4 is halogen;

u is an integer selected from 0, 1, 2, 3, 4, or 5; and

R^{30} is, independently for each occurrence, selected from the group consisting of H, alkyl, cycloalkyl, heterocyclyl, heterocyclylalkyl, aryl, and heteroaryl.

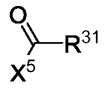
35. The method of claim 34, wherein L is aryl.

36. The method of claim 35, wherein L is phenyl.

37. The method of any one of claims 34-36, wherein X^4 is chloro.

38. The method of any one of claims 34-37, wherein the base is pyridine.

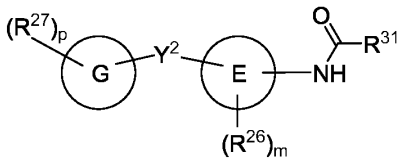
39. The method of any one of claims 20-22, further comprising combining the compound of Formula (VI), a compound of Formula (XIV):



(**XIV**);

and a base;

thereby forming a compound of Formula (XV):



(**XV**);

wherein:

X^5 is halogen;

R^{31} is selected from the group consisting of H, alkyl, cycloalkyl, heterocyclyl, and heterocyclylalkyl.

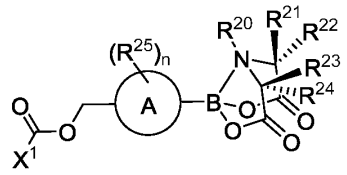
40. The method of claim 39, wherein X^5 is chloro.

41. The method of claim 39 or 40, wherein R^{31} is alkyl.

42. The method of claim 41, wherein R^{31} is butyl.

43. The method of any one of claims 40-42, wherein the base is pyridine.

44. A compound of Formula (I):



(I)

or a salt thereof;

wherein:

A is aryl or heteroaryl;

B is a boron having sp^3 hybridization;

n is an integer selected from 1, 2, 3, or 4;

X^1 is halogen or OR^j;

R^j is selected from the group consisting of alkyl, nitrophenyl, pentafluorophenyl, and $-N(C(O)CH_2)_2$;

R^{20} is selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, and aryl;

R^{21} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, and heteroaryl;

R^{22} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, and heteroaryl;

R^{23} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, and heteroaryl;

R^{24} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, and heteroaryl; and

R^{25} is, independently for each occurrence, selected from the group consisting of H, alkyl, cycloalkyl, alkoxy, hydroxyl, halogen, acyl, aryl, heteroaryl, heterocyclyl, cyano, nitro, and sulfonyl.

45. The compound of claim 44, wherein A is phenyl.

46. The compound of claim 44 or 45, wherein R^{25} is H.

47. The compound of any one of claims 44-46, wherein at least one of R^{21}, R^{22}, R^{23}, or R^{24} is not H.

48. The compound of claim 47, wherein at least two of R^{21}, R^{22}, R^{23}, or R^{24} are not H.

49. The compound of claim 48, wherein at least three of R^{21}, R^{22}, R^{23}, or R^{24} are not H.

50. The compound of claim 49, wherein none of R^{21}, R^{22}, R^{23}, or R^{24} is H.

51. The compound of any one of claims 44-50, wherein each of R^{20}, R^{21}, R^{22}, R^{23}, and R^{24} is methyl; or each of R^{21}, R^{22}, R^{23}, and R^{24} is methyl.

52. The compound of any one of claims 44-51, wherein X^1 is chloro or fluoro.

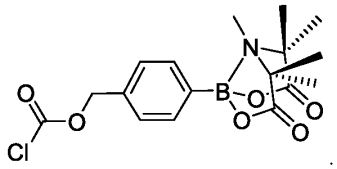
53. The compound of claim 52, wherein X^1 is chloro.

54. The compound of any one of claims 44-51, wherein X^1 is OR^j.

55. The compound of claim 54, wherein R^j is selected from the group consisting of methyl, ethyl, nitrophenyl, pentafluorophenyl, and $-N(C(O)CH_2)_2$.

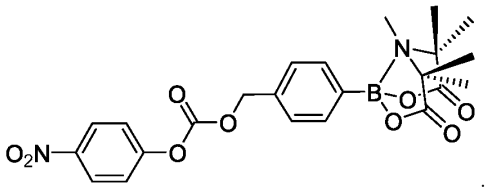
56. The compound of claim 55, wherein R^j is nitrophenyl.

57. The compound of claim 44, wherein the compound is:

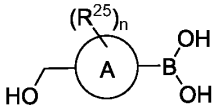


.

58. The compound of claim 44, wherein the compound is:

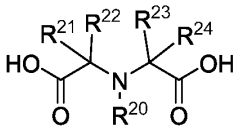


59. A method of making a compound of Formula (I), wherein the method comprises combining a compound of Formula (XVI):



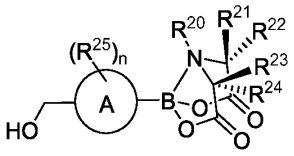
(**XVI**);

and a compound of Formula (XVII):



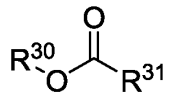
(**XVII**);

thereby forming a compound of Formula (XVIII):



(**XVIII**);

and further combining the compound of Formula (XVIII) and a compound of Formula (XIX):



(**XIX**);

thereby forming the compound of Formula (I);

wherein:

A is aryl or heteroaryl;

B is a boron having sp^3 hybridization;

n is an integer selected from 1, 2, 3, or 4;

X^1 is halogen or OR^j;

R^j is nitrophenyl;

R^{20} is selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, and aryl;

R^{21} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, and heteroaralkyl;

R^{22} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, and heteroaralkyl;

R^{23} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, and heteroaralkyl;

R^{24} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, and heteroaralkyl;

R^{25} is, independently for each occurrence, selected from the group consisting of H, alkyl, cycloalkyl, alkoxy, hydroxyl, halogen, acyl, aryl, heteroaryl, heterocyclyl, cyano, nitro, and sulfonyl;

R^{30} is haloalkyl or nitrophenyl; and

R^{31} is -(O)-haloalkyl or halogen.

60. The method of claim 59, wherein A is phenyl.

61. The method of claim 59 or 60, wherein R^{25} is H.

62. The method of any one of claims 59-61, wherein X^1 is chloro or fluoro.

63. The method of any one of claims 59-61, wherein X^1 is OR^j.

64. The method of claim 63, wherein R^j is 4-nitrophenyl.

65. The method of any one of claims 59-64, wherein each of R^{20}, R^{21}, R^{22}, R^{23}, and R^{24} is methyl; or each of R^{21}, R^{22}, R^{23}, and R^{24} is methyl.

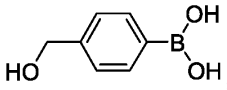
66. The method of any one of claims 59-65, wherein R^{30} is $-C(Cl)_3$.

67. The method of claim 66, wherein R^{31} is $-O(C(Cl)_3)$.

68. The method of any one of claims 59-67, wherein R^{30} is 4-nitrophenyl.

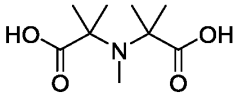
69. The method of claim 68, wherein R^{31} is chloro.

70. The method of claim 59, wherein the compound of Formula (XVI) is:



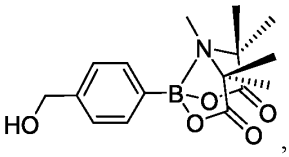
, or a salt thereof.

71. The method of claim 59, wherein the compound of Formula (XVII) is:



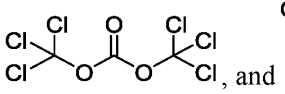
, or a salt thereof.

72. The method of claim 59, wherein the compound of Formula (XVIII) is:

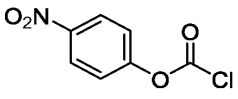


, or a salt thereof.

73. The method of claim 59, wherein the compound of Formula (XIX) is selected from the group consisting of:



, and



, or a salt thereof.