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Doctoral Dissertation

**Synthesis of Hypervalent Iodine Reagents Containing
Various Amino Groups and Their Applications to
Oxidative Amination Reactions**

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January 2026

Department of Applied Chemistry

Graduate School of Engineering

The University of Osaka

Synthesis of Hypervalent Iodine Reagents Containing Various Amino Groups and Their Applications to Oxidative Amination Reactions

(多様なアミノ基を有する超原子価ヨウ素反応剤の合成と
酸化のアミノ化反応への活用)

2026

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Preface

The studies presented in this thesis were conducted under the supervision of Professor Dr. Satoshi Minakata, Department of Applied Chemistry, Graduate School of Engineering, The University of Osaka during the period of 2020–2026.

The objectives of this thesis are the development of synthetic methods for hypervalent iodine reagents containing various amino groups and their application to oxidative amination reactions. The author hopes that the fundamental work described in this thesis will contribute to the further development of hypervalent iodine chemistry, synthetic methods for amines, and other related areas of chemistry.

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January, 2026

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General Introduction

1. Utility of Amines in Medicinal and Organic Synthetic Chemistry

Amino groups ($-NR_2$) are an indispensable functional group for biologically active molecules including pharmaceuticals (Figure 1)¹: Approximately one-third of approved small-molecule drugs contain aromatic amines, while aliphatic amines are present in about 40% of these compounds, with a substantial overlap between the two.^{1,j,k} Moreover, primary and secondary amines are also valuable as synthetic intermediates for a wide range of nitrogen-containing organic molecules, including tertiary amines, amides, sulfonamides, and azaheterocycles. Therefore, the development of the method for the synthesis of amines has been an important research topic in organic chemistry (Scheme 1).

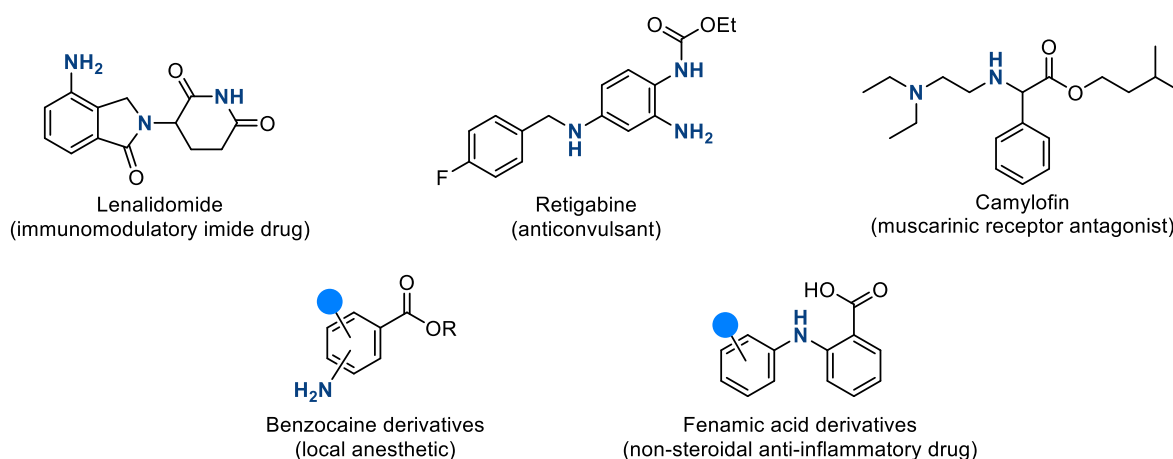
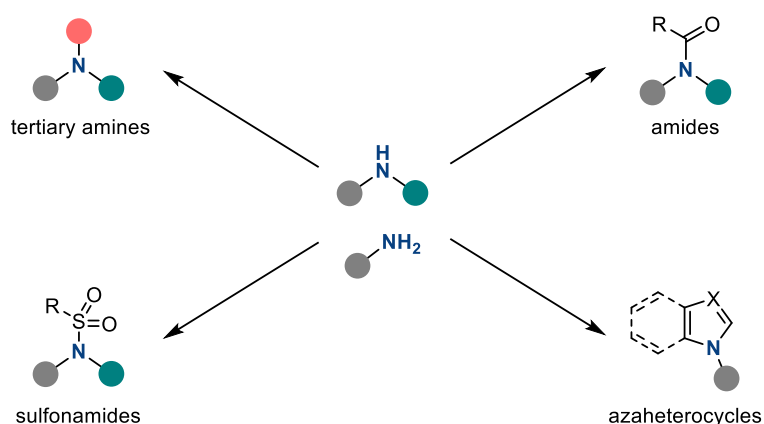


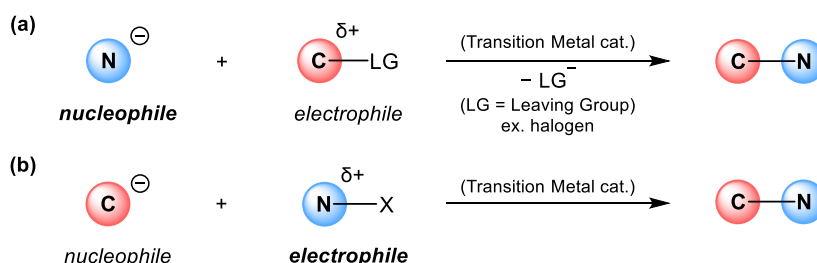
Figure 1. Nitrogen-containing molecules of pharmaceuticals and natural products



Scheme 1. Utility of primary and secondary amines as synthetic intermediates

2. C–N Bond Formation for the Synthesis of Nitrogen-Containing Organic Molecules

For the synthesis of a variety of nitrogen-containing organic molecules, carbon (C)–nitrogen (N) bond formation reactions (amination reactions) represent one of the most fundamental and straightforward approaches.² Representative reaction patterns for C–N bond formation are depicted in Scheme 2. General methods involve the reaction of nitrogen nucleophiles with carbon electrophiles and transition-metal-catalyzed cross coupling reactions (Scheme 2a). On the other hand, the reaction of carbon nucleophiles with umpolung-type aminating reagents bearing an electron-withdrawing group at the nitrogen atom is an alternative approach, which is categorized as oxidative (electrophilic) amination (Scheme 2b).³ For such reactions, azo- and nitroso-compounds are widely used as an electrophilic aminating reagent (Figure 2). In these cases, the resulting aminated product is hydrazine or hydroxylamine derivatives, and thus a further conversion, including reductive deprotection is required to access the target amines. Meanwhile, hydroxylamine and chloramine derivatives can introduce amino groups through substitution reaction, but existing reagents have limited variation of *N*-substituents, thereby limiting their application in amine synthesis.



Scheme 2. Overview of Amination Reaction

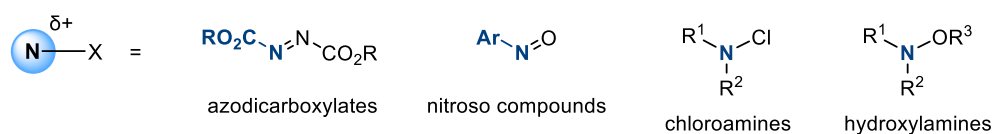


Figure 2. Typical electrophilic aminating reagents

3. Hypervalent Iodine(III) Compounds

Iodine, the heaviest halogen element practically available for organic synthesis, can have a wide range of oxidation states beyond the octet rule, up to a maximum of seven valence states, due to its large atomic radius and low electronegativity. Especially, hypervalent iodine(III) compounds are readily

prepared and represent a powerful tool for oxidative transformations in organic synthesis, in which the oxidation process is promoted by the reduction of I(III) to I(I).^{3,4} The most widely used iodine(III) compounds are iodobenzene derivatives (PhIX_2), whose structure consists of an aryl group, two electronegative ligands (X) occupying the apical positions, and two lone pairs at the equatorial positions (Figure 3). The unique reactivity of hypervalent iodine(III) reagents arises from the presence of a weak and highly polarized hypervalent (three-center-four-electron) bond (I–X) at the apical positions, allowing the ligands (X) to act as readily transferable functional groups in oxidative functionalization reactions.

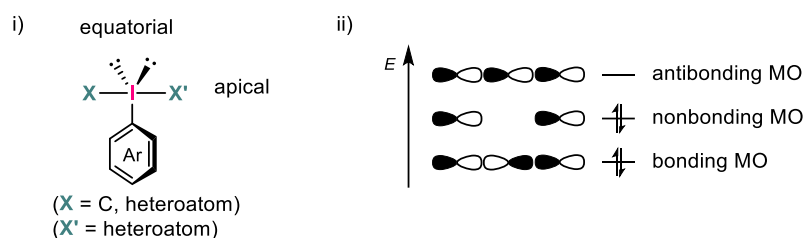
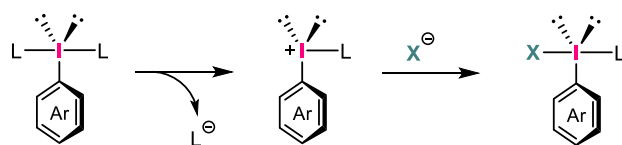


Figure 3. Features of iodine(III) compounds: i) typical structure, ii) three-center-four-electron bond

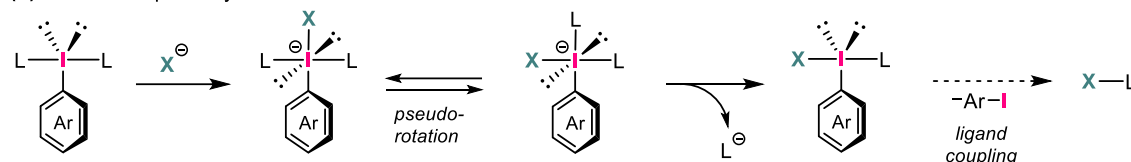
Iodine(III) compounds exhibit behavior not only as simple oxidants but also as an oxidative functionalization reagent by transferring ligands. A ligand exchange on the hypervalent iodine center has been used as the most straightforward approach for preparing reagents for various functional group transfer reactions (Scheme 3). The ligand exchange process is classified into two distinct mechanistic pathways, dissociative and associative; however, the dissociative pathway is generally considered unlikely because it involves the formation of unstable dicoordinated iodonium cation intermediate (Scheme 3a). As for the associative pathway, the reaction is initiated by the addition of a nucleophile to the positively charged iodine(III) to form tetracoordinated iodate anion, followed by pseudo-rotation and elimination of the ligand, providing target reagents (Scheme 3b).

(a) dissociative pathway

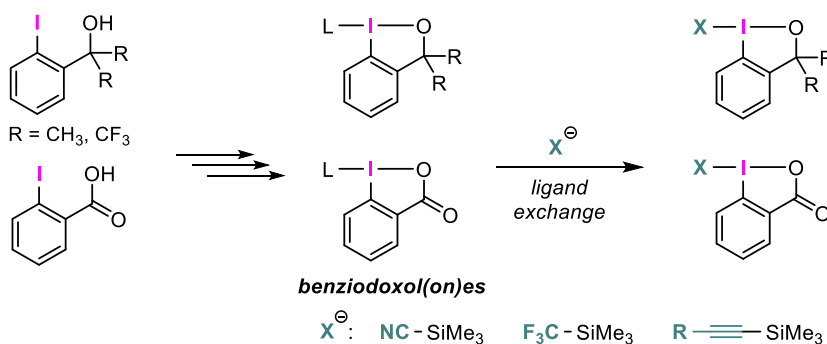


L = OR or halogen

(b) associative pathway

**Scheme 3.** Ligand exchange pathway.

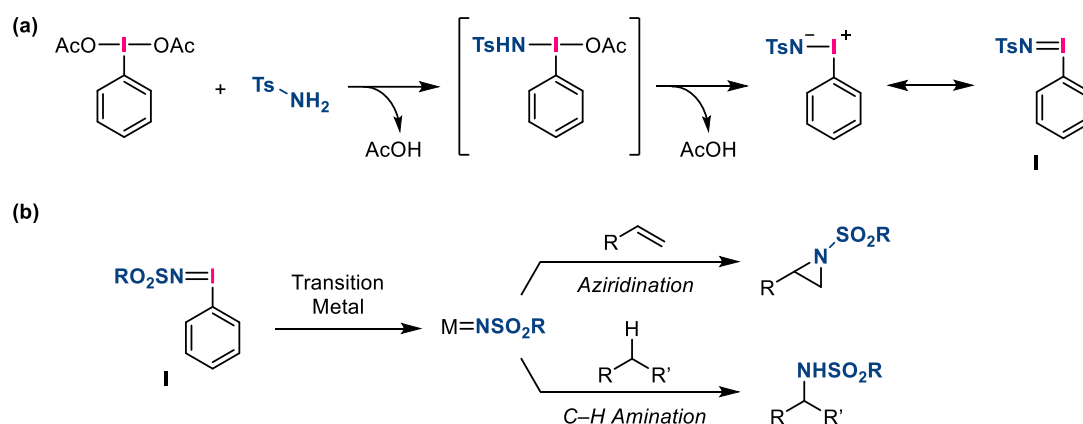
In the ligand exchange process, undesirable pseudo-rotation of ligands and a ligand coupling via reductive elimination often pose problems in forming the target iodine(III) compound. To suppress these processes, employing heterocyclic iodine(III) compounds, especially, five-membered I–O bond containing heterocycles (benziodoxol(on)e) that have higher thermal stability, are useful (Scheme 4).^{4g} Indeed, the use of benziodoxol(on)e scaffolds made it possible to synthesize otherwise unstable hypervalent iodine(III) compounds containing cyano, trifluoromethyl, and alkynyl groups through the ligand exchange using the corresponding silylated nucleophiles.

**Scheme 4.** Benziodoxol(on)es

4. Hypervalent Iodine(III)-Based Aminating Reagents

Given the reactivities that are described above, iodine(III) reagents containing I–N bonds are promising reagents for oxidative amination.⁵ Indeed, several such iodine(III) reagents have been synthesized and applied to oxidative amination reactions. The first example is *N*-tosyliminoiodane (**I**), which is synthesized from (diacetoxy)iodobenzene and *p*-toluenesulfonamide (Scheme 5a).^{6d} These

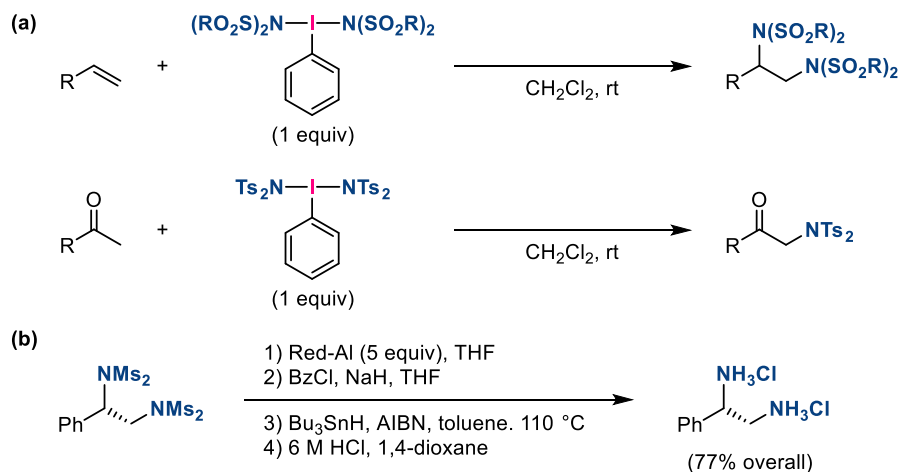
reagents have been widely used in the oxidative amination, especially in aziridination of alkenes and C–H amination through a nitrene or nitrenoid formation (Scheme 5b).⁶



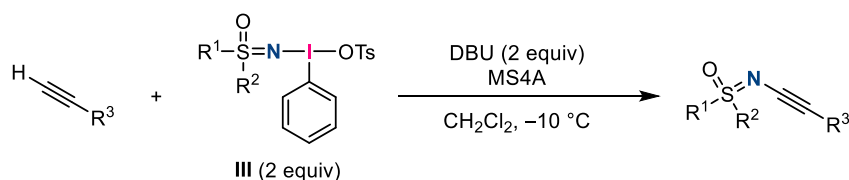
Scheme 5. a) Synthesis of iminoiodinanes, b) Their use in oxidative amination

In past decades, several hypervalent iodine(III) reagents containing transferable nitrogen functional groups have been developed, most of which possess protected nitrogen functionalities incorporating electron-withdrawing groups, such as bissulfonimido (**II**),^{7,8} sulfoximido (**III**),⁹ and azido (**IV**) (Figure 4).¹⁰ However, the use of these reagents often necessitates laborious deprotection and further transformation steps to access the desired amine products, thereby limiting their synthetic practicality. In addition, the use of azido reagents (**IV**) requires careful handling due to their inherent hazards.^{10d}

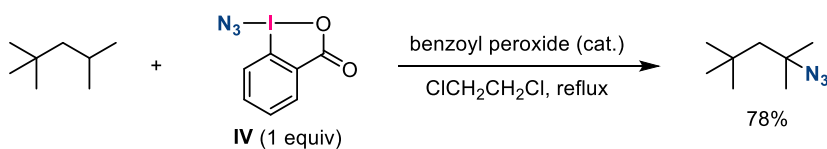
For instance, bissulfonimidoiodanes (**II**) enabled oxidative diamination of alkenes and α -amination of ketones (Scheme 6a).⁷ However, the aminated product of this method requires multistep deprotection steps (Scheme 6b), thus hampering further elaboration of the aminated products.^{7a} In addition, sulfoximidoiodanes (**III**), and azidoiodanes (**IV**) also allowed various oxidative C–H amination reactions (Scheme 7 and 8).^{9,10}



Scheme 6. Oxidative aminations of bisulfonimidoiodanes

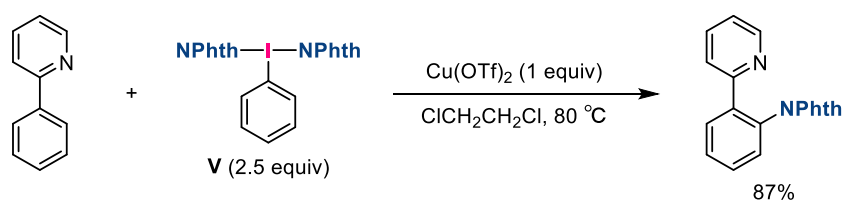


Scheme 7. Sulfoximidoiodane

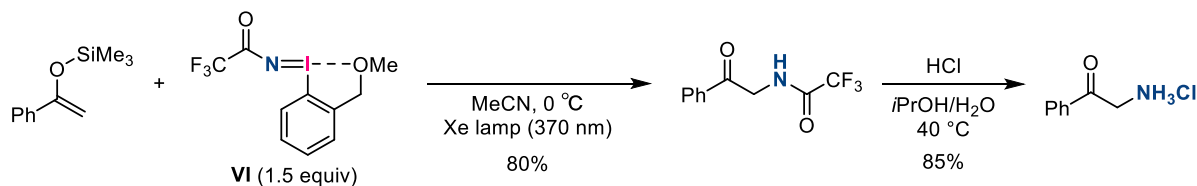
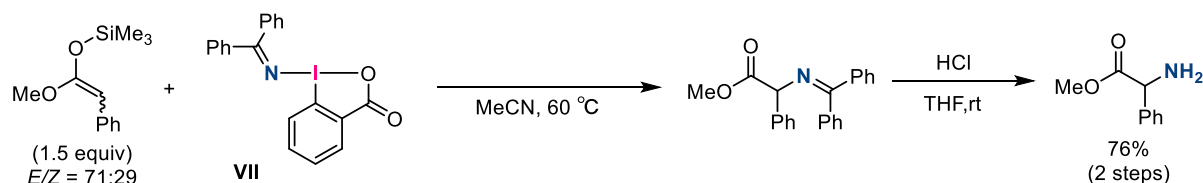


Scheme 8. Azidoiodane

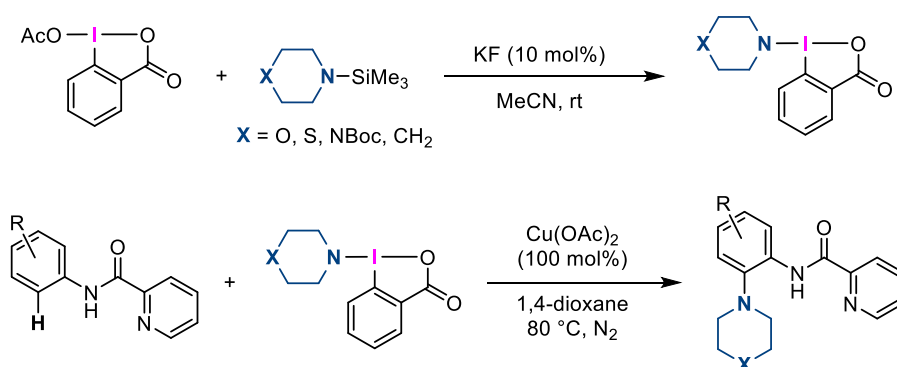
To deal with these limitations, hypervalent iodine(III) reagents containing amino functionalities that can be readily converted to NH_2 group, such as phthalimide (V),^{11,12} trifluoroacetamide (VI),¹³ and (diarylmethylene)amino groups (VII)¹⁴ have been developed (Scheme 9–11). However, these approaches still require a deprotection step, which hinders the direct synthesis of structurally complex amines.

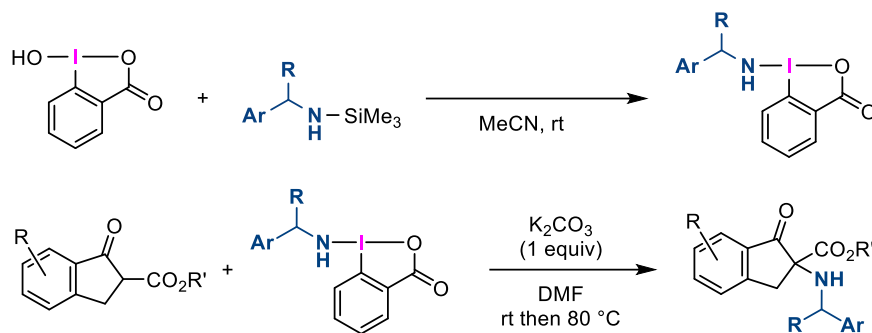


Scheme 9. Phthalimidoiodanes

**Scheme 10.** *N*-trifluoroacetyliminoiododanane**Scheme 11.** (Diarylmethylene)amino benziodoxolones

Nevertheless, hypervalent iodine(III) reagents containing simple unprotected amino groups (–NR₂) have remained largely unexplored, despite their high potential for direct and practical amination. Recently, iodine(III) compounds derived from secondary amines have been synthesized using a thermally stable iodoxolone framework and *N*-silyl amines (Scheme 12). These reagents were applied to copper-catalyzed C(sp²)–H amination of 2-picolinamides.¹⁵ In addition, benzylic primary amines derived iodine(III) compounds were synthesized and applied to amination of stabilized enolates (Scheme 13).¹⁶ However, the variation of amino groups in hypervalent iodine-based aminating reagents is still limited. Therefore, development of synthesis and application of hypervalent iodine(III) reagents containing amino groups remains a challenging task.

**Scheme 12.** Synthesis and application of aminobenziodoxolones derived from secondary amines



Scheme 13. Synthesis and application of aminobenziodoxolones derived from benzylic primary amines

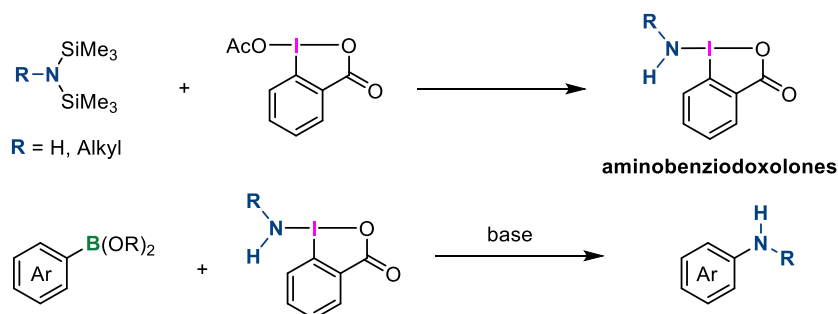
5. Aim of This Thesis

On the basis of these backgrounds, this study aimed to develop iodine(III) compounds capable of directly introducing unprotected and diverse amino groups as powerful tools for oxidative amination reactions, enabling straightforward and practical access to valuable amine derivatives, including biologically active molecules and pharmaceuticals.

6. Synopsis of This Thesis

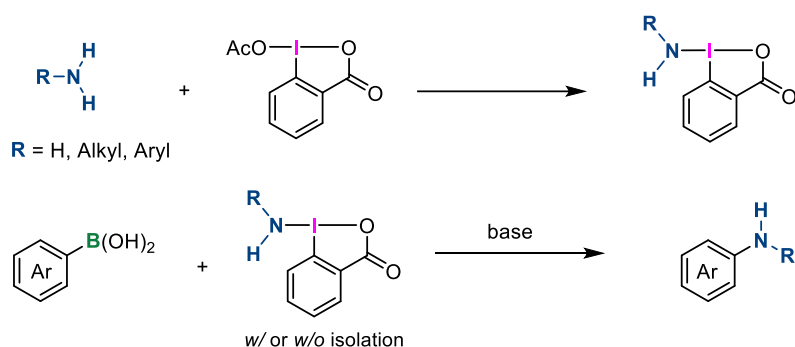
The author has developed the method for the synthesis of novel hypervalent iodine reagents containing various amino groups and oxidative amination reactions utilizing these reagents. This thesis consists of General Introduction, three Chapters, and Conclusion.

Chapter 1 describes the synthesis of hypervalent iodine(III) reagents containing amino ($-\text{NH}_2$, NHR) groups (aminobenziodoxolones) using disilazanes and their application to oxidative amination of arylboronic acid derivatives (Scheme 14).



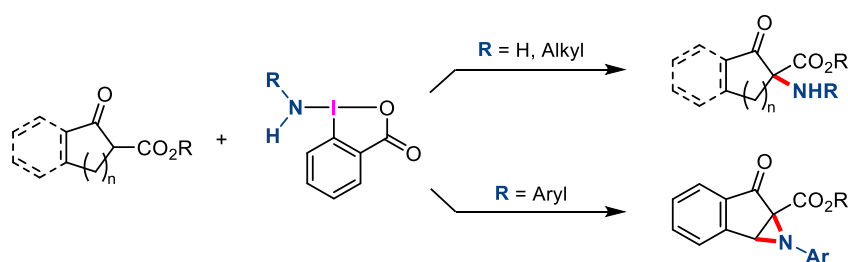
Scheme 14. Synthesis of aminobenziodoxolones using disilazanes and amination of arylboronic acid derivatives

Chapter 2 deals with the versatile synthetic method of aminobenziodoxolones using amines and its application to the practical method for arylamine synthesis (Scheme 15).



Scheme 15. Synthesis of aminobenziodoxolones from amines and application to versatile arylamine synthesis

Chapter 3 discloses the oxidative α -amination and aziridination of cyclic β -ketoesters using aminobenziodoxolones (Scheme 16).



Scheme 16. α -Amination and aziridination of β -ketoesters using aminobenziodoxolones

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Chapter 1

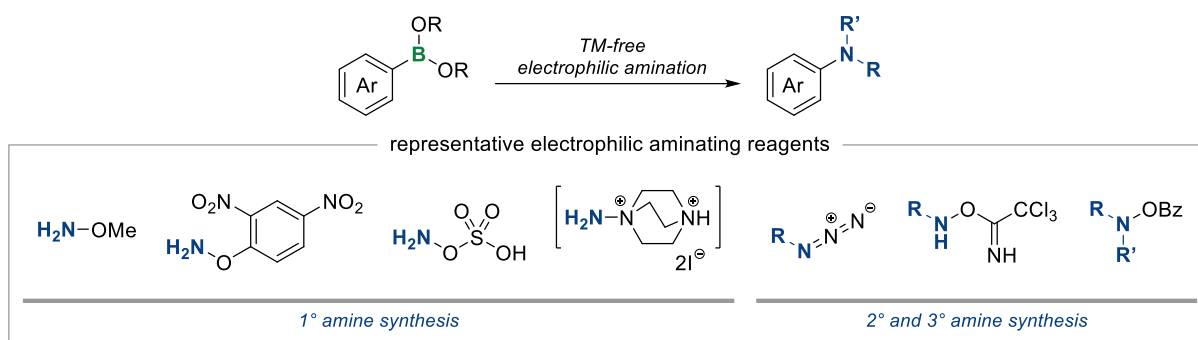
Synthesis of Aminobenziodoxolones Using Disilazanes and Their Use in the Electrophilic Amination of Arylboronic Acid Derivatives

1-1. Introduction

The development of methodologies for the synthesis of arylamines is a research topic of great interest in organic synthesis as they are important building blocks that are ubiquitous in natural products, pharmaceuticals, agrochemicals, and organic materials.¹ The most fundamental approach to accessing arylamines is C(aryl)–N bond-forming reactions. Classical methods include nucleophilic aromatic substitution (S_NAr) with amines² and electrophilic nitration of aromatic compounds.³ Despite their reliability, these reactions often suffer from low levels of functional group compatibility due to the harsh reaction conditions. Over the past few decades, transition-metal (TM)-catalyzed C(aryl)–N bond-forming reactions such as Buchwald-Hartwig⁴ and Ullmann-Goldberg-type⁵ coupling have been the most widely used examples. In addition, electrophilic amination of organometallic reagents⁶ and C(aryl)–H amination⁷ have also found wide application in arylamine synthesis. The use of TMs, however, has a serious drawback, particularly in the production of pharmaceuticals where trace metal contaminants must be completely removed entirely, resulting in additional cost and operational complexity.⁸ In this context, practical TM-free methods are in high demand.

Electrophilic amination of arylboron reagents has attracted considerable attention — particularly the use of readily available and easily handled boronic acid derivatives.⁹ In recent decades, TM-free approaches have been developed using various electrophilic aminating reagents such as hydroxyamine derivatives,¹⁰ an aminoazanium,¹¹ azides,¹² and others^{13,14} (Scheme 1) as alternatives to TM-catalyzed reactions (e.g. Chan-Lam-Evans coupling).¹⁵ Existing methods, however, continue to offer only limited applicability in reactions involving electron-deficient (hetero)arylboronic acids and

pinacol boronates. In addition, the examples of synthesized secondary amines remain scarce.^{10c,e,14} The electrophilic amination of arylboron reagents generally proceeds via the formation of a tetravalent borate complex with a B–N dative bond that is followed by 1,2-aryl migration, and, therefore, an aminating reagent that possesses both nucleo- and electrophilic characteristics is required.



Scheme 1. Transition-metal-free electrophilic amination of arylboronic acid derivatives

The author envisioned that hypervalent iodine(III) compounds containing a nucleophilic amino functionality attached to the iodine(III) center with high leaving ability¹⁶ would qualify as an aminating reagent for such amination.¹⁷ As described in the general introduction, the development of iodine(III) reagents containing nucleophilic aliphatic amino groups was reported only recently,^{18,19} but the scope of amines is still limited, notably an NH_2 -substituted one has never been reported. Herein, the author reports the syntheses of hypervalent iodine(III) compounds containing amino groups, which includes one with an NH_2 group, and describes their use in the electrophilic amination of arylboronic acids and boronates (Scheme 2). The amination developed in this study provides a powerful tool for the synthesis of primary and secondary (hetero)arylamines, which are difficult to access using existing methods.



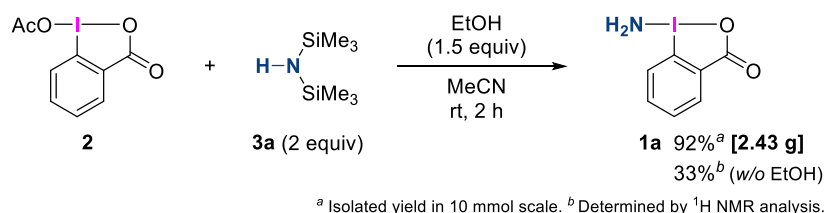
Scheme 2. This work: Utilizing hypervalent iodine-based aminating reagents

1-2. Results and Discussion

1-2-1. Synthesis of NH_2 -substituted Benziodoxolone using Hexamethyldisilazane

The initial investigation was the synthesis of an NH_2 -substituted hypervalent iodine reagent, which

is a promising reagent for the direct synthesis of primary amines but has never been synthesized. An iodine reagent having a benziodoxolone skeleton was selected in consideration of the stability of the target compound.^{18b,20} A ligand exchange of the acetoxy group of 1-acetoxy-1,2-benzodioxol-3-(1*H*)-one (**2**) with commercially available hexamethyldisilazane (**3a**) as an ammonia surrogate was then examined, which resulted in a low yield of **1a** with the formation of unidentified inseparable byproducts. The addition of EtOH (1.5 equiv) as a proton source was found to be effective in suppressing the byproduct formation and improving the yield of **1a** up to 92% in a 10 mmol scale synthesis (Scheme 3). Single crystals of **1a** suitable for X-ray crystallographic analysis were grown via slow diffusion from an acetonitrile solution. The structural data clearly confirmed that the sp³-hybridized NH₂ group is bound to the iodine center with an I–N bond length of 2.025(6) Å (Figure 1), which approximates the sum of the covalent radii of N and I (2.10 Å).²¹ The single-bond characteristics of the I–N bond were also supported by Wiberg bond index (WBI) analysis (WBI(N–I) = 0.789) (vide infra). In the crystal packing, the **1a** forms intermolecular secondary bonding interactions that include hydrogen bonding between the NH₂ group and the oxygen atoms and also halogen bonding between the iodine atom and the oxygen atom (Figure 2).



Scheme 3. Synthesis of hypervalent iodine compound containing NH₂ group

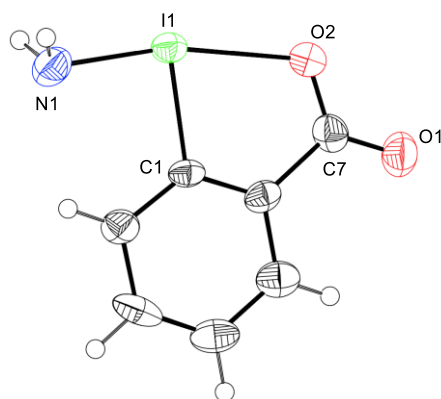


Figure 1. Crystal structure of **1a**. Thermal ellipsoids are shown at the 50% probability level. Selected bond lengths [Å] and angles [deg]: I1–N1 2.025(6), I1–O2 2.385(5), I1–C1 2.113(5), N1–I1–O2 166.59(18), N1–I1–C1 92.38(2), C1–I1–O2 74.29(18), C7–O2–I1 114.3(4).

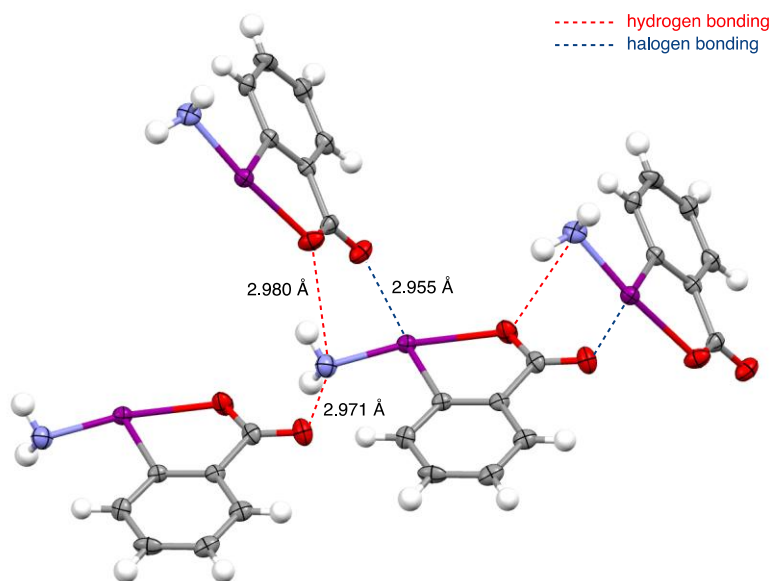


Figure 2. Intermolecular secondary bonding interactions of **1a** in the solid state.

The synthesized reagents **1a** are reasonably stable under ambient conditions in the solid state.²² Differential scanning calorimetry (DSC) analysis was performed to check the stability of **1a** (Figure 3). The DSC result showed that the decomposition started at 130 °C with a heat release of 572 kJ/kg.

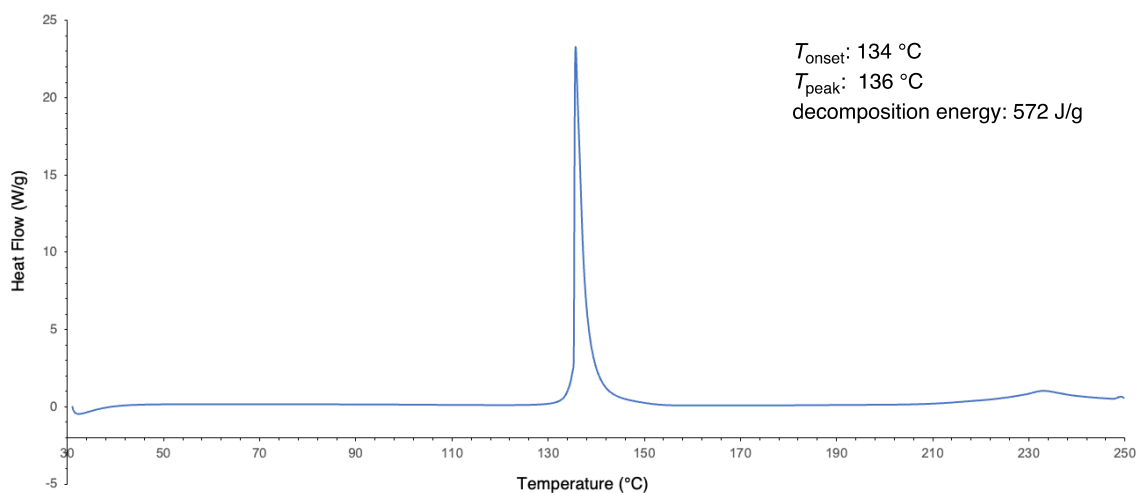


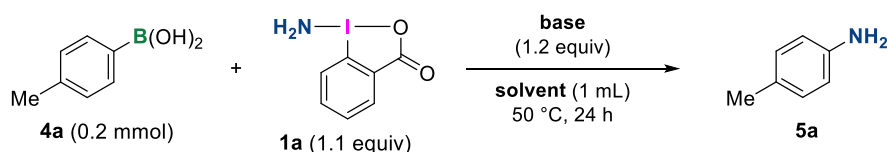
Figure 3. DSC analysis of **1a**

1-2-2. Electrophilic Amination of Arylboronic Acid Derivatives for Primary Amine Synthesis

The author then turned his attention to the electrophilic amination of arylboronic acids using synthesized hypervalent iodine(III) reagent **1a** to provide a primary amine (Table 1). The reaction of 4-

methylphenylboronic acid (**4a**) with **1a** in THF at 50 °C resulted in the formation of **5a** in a low yield (entry 1). Screening of the reaction conditions revealed that the addition of a base is effective in promoting amination (entries 2–5), and the use of Cs₂CO₃ drastically improved the yield of **5a** up to 94% (entry 4). The amination also proceeded at room temperature with slightly lower efficiency (entry 6). Reducing the amount of Cs₂CO₃ resulted in a lower yield of **5a** (entry 7). Examining the reaction in other solvents showed that THF is suitable for this amination (entries 8–11).

Table 1. Optimization of reaction conditions for the amination of boronic acid **4a**



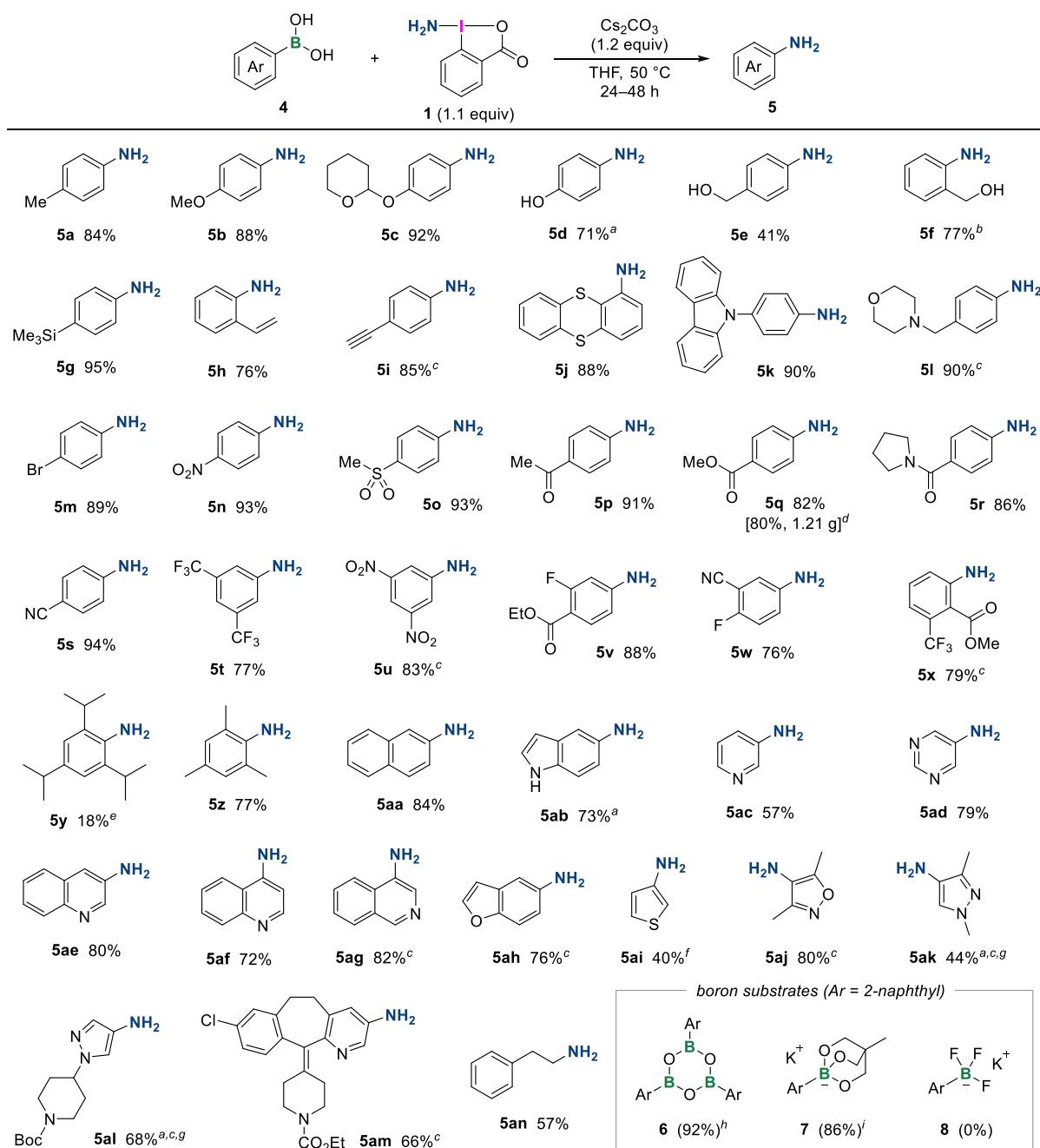
entry	base	solvent	yield (%) ^a
1	none	THF	9
2	Na ₂ CO ₃	THF	18
3	K ₂ CO ₃	THF	79
4 ^b	Cs ₂ CO ₃	THF	94 (84)
5	NEt ₃	THF	48
6 ^c	Cs ₂ CO ₃	THF	70
7 ^d	Cs ₂ CO ₃	THF	65
8	Cs ₂ CO ₃	1,4-dioxane	87
9	Cs ₂ CO ₃	MeCN	65
10	Cs ₂ CO ₃	toluene	70
11	Cs ₂ CO ₃	DMSO	26

^a Determined by ¹H NMR analysis of the crude product. A value in parenthesis is an isolated yield.

^b The reaction was conducted on a 0.4 mmol scale. ^c The reaction was conducted at room temperature.

^d Cs₂CO₃ (0.6 equiv) was used.

With the optimized reaction conditions in hand, we explored the scope of the amination of arylboronic acids and their derivatives using **1a** (Scheme 3). A number of arylboronic acids bearing both electron-donating and -withdrawing groups on the aryl rings were efficiently aminated. Remarkably, highly electron-deficient substrates, which have generally shown low reactivity in previously reported methods^{3,10,11} were transformed into the corresponding anilines in high yields (**5n**–**5x**). Various functional groups including heterocycle (**5c**, **5j–5l**), hydroxy (**5d**, **5e**), trimethylsilyl (**5g**), alkene (**5h**), alkyne (**5i**), nitro (**5n**, **5u**), sulfonyl (**5o**), several types of carbonyl (**5p–5r**, **5v**, **5x**), and nitrile (**5s**, **5w**) moieties are well tolerated. The sterically demanding anilines **5y** and **5z** could also be synthesized. It is noteworthy that although the amination of heteroarylboronic acids is difficult to



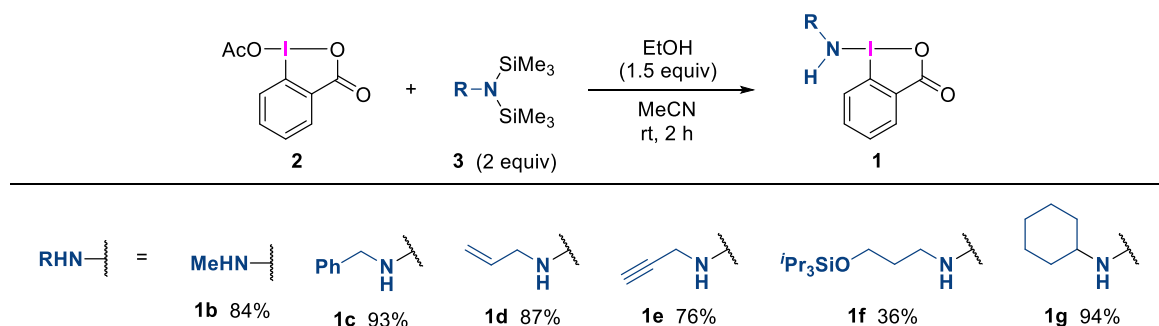
Scheme 4. Substrate scope. Reactions were conducted on a 0.2–0.4 mmol scale. Yields are isolated yields. Yields in parentheses were determined by ^1H NMR analysis of the crude product. ^a The reaction was conducted at room temperature. ^b Benzo[*c*][1,2]oxaborol-1(3*H*)-ol was used as a substrate. ^c Pinacol boronic acid esters were used as a substrate. ^d The reaction was conducted on a 10 mmol scale. ^e The reaction was conducted at 70 °C. ^f Yield of the isolated product after Boc protection. ^g **1a** (1.5 equiv) and Cs_2CO_3 (1.5 equiv) were used. ^h **6** (0.33 equiv) was used. ⁱ The reaction was conducted in the absence of Cs_2CO_3 .

achieve using the existing methods,^{10,11} the present method was successfully applied to the amination of substrates containing indole (**5ab**), pyridine (**5ac**), pyrimidine (**5ad**), (iso)quinoline (**5ae–5ag**), benzofuran (**5ah**), thiophene (**5ai**), isoxazole (**5aj**), and pyrazole (**5ak**, **5al**) skeletons. The synthetic utility of this amination was further highlighted by the synthesis of the loratadine derivative **5am**.

Although the reported methods of the amination of less-reactive pinacol boronic acid esters usually require the use of strong bases,^{10a,11} they readily underwent amination under the mild reaction conditions (**5i**, **5l**, **5u**, **5x**, **5ag**, **5ah**, **5aj**, **5ak**, **5al**, **5am**), ensuring the synthetic usefulness of the present method. A gram-scale reaction afforded **5q** without loss of efficiency, which demonstrates the scalability of the reaction. It is also found that the present method can be applied to the amination of an alkylboronic acid (**5an**). In addition, boroxine **6** and (triol)borate salt **7** were also suitable substrates, and, interestingly, the latter case required no addition of Cs₂CO₃. Meanwhile, trifluoroborate salt **8** did not undergo the amination.

1-2-3. Synthesis of Amino Group substituted Benziodoxolones

Based on the method for the synthesis of NH₂-substituted aminobenziodoxolone **1a** using hexamethyldisilazane, various disilazanes **3**, prepared from primary amines,²³ could also be used in the ligand exchange process to synthesize derivatives containing methyl (**1b**), benzyl (**1c**), allyl (**1d**), propargyl (**1e**), siloxy (**1f**), and sterically hindered cyclohexyl (**1g**) groups (Scheme 5).

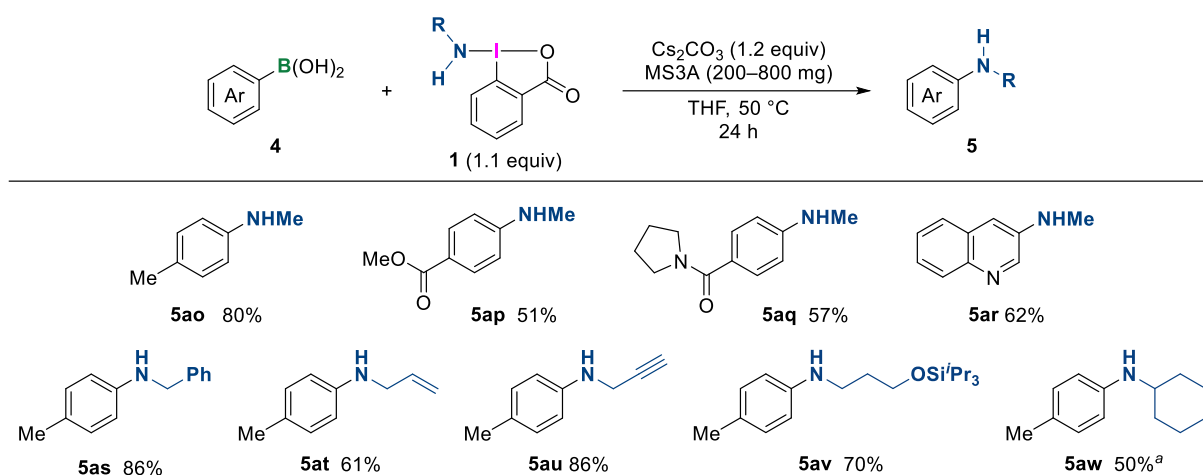


Scheme 5. Synthesis of hypervalent iodine reagents containing amino groups

1-2-4. Electrophilic Amination of Arylboronic Acids for Secondary Amine Synthesis

The use of primary amine-derived reagents **1** were also applicable to the amination of arylboronic acid derivatives, allowing for the synthesis of secondary amines (Scheme 6). The reaction of boronic acid **4a** with **1b** under the standard reaction conditions resulted in a low yield of **5an** along with some amounts of *p*-cresol as a byproduct, but the addition of molecular sieves was effective in suppressing the side reaction and improving the yield of **5ao** up to 80%. By employing the modified reaction

conditions, secondary amines **5ao–5aw** were successfully synthesized in moderate to good yields.



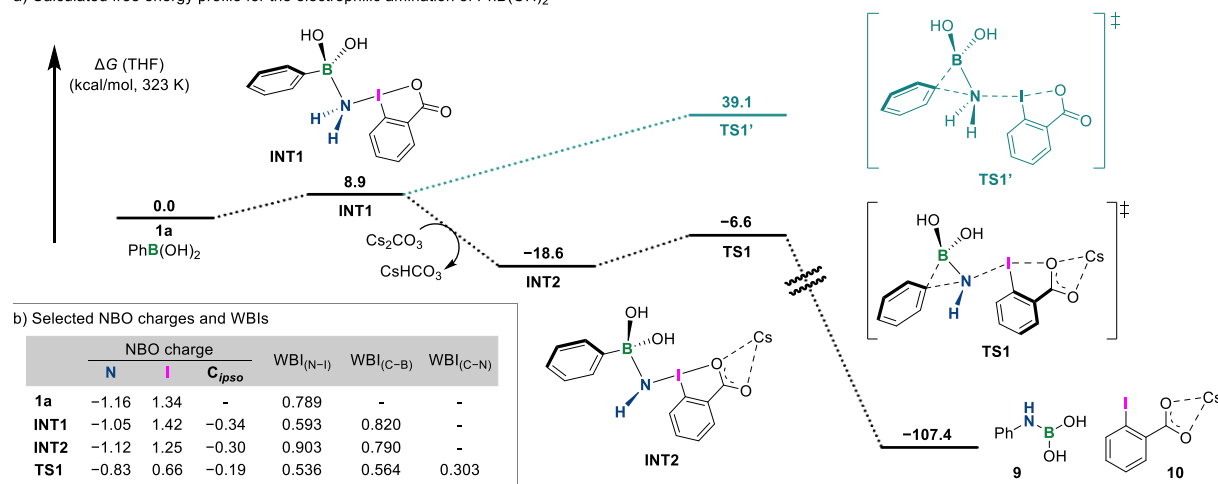
Scheme 6. Amination of (Hetero)arylboronic Acids for Secondary Amine Synthesis ^a The reaction was conducted at 70 °C.

1-2-5. Mechanistic Investigations

Based on the previous studies on the electrophilic amination of boronic acids,^{10–14} the author proposed that the reaction would be initiated by the formation of a tetravalent borate complex through a B–N dative bond, which would then be followed by 1,2-aryl migration. To elucidate the mechanistic details of the present electrophilic amination, density functional theory (DFT) calculations were performed at the M06-2X/6-311++g(d,p)-SDD(I,Cs),SMD(THF)//M06-2X/6-31+g(d,p)-LANL2DZ(I,Cs),SMD(THF) level of theory using phenylboronic acid as a model substrate, and the resultant energy profile is shown in Figure 4a. The Natural bond orbital (NBO) analysis was first performed to understand the electronic characteristics of **1a** (Figure 4b). The NBO charge of the sp^3 -hybridized nitrogen atom of **1a** was calculated to be -1.16 , which supports the presumption of its nucleophilic nature. The coordination of the amino group of **1a** to the boron center of $\text{PhB}(\text{OH})_2$ to form **INT1**, was determined to be an endothermic process (8.9 kcal/mol).^{10b,d} The 1,2-aryl migration from **INT1** via **TS1'** has a large free-energy barrier of 39.1 kcal/mol relative to the separated $\text{PhB}(\text{OH})_2$ and **1a**, which is consistent with experimental results showing low efficiency for amination in the absence of a base. Meanwhile, in the presence of Cs_2CO_3 , both the abstraction of the proton at the nitrogen atom and the coordination of the carboxyl group to the cesium cation occur to form the thermodynamically

more stable **INT2** (Figure 5). The 1,2-aryl migration from this complex via **TS1** has a much lower free energy barrier (12.0 kcal/mol) than that of **TS1'**, which led to the formations of **9** and **10**. It is suggested that Cs_2CO_3 acts as a base, and the resulting cesium cation then acts as a Lewis acid to promote the elimination of ortho-iodobenzoate, which then allows an efficient 1,2-aryl migration. The WBI and calculated bond distances in **TS1** clearly show that cleavages of the C–B bond ($\text{WBI}(\text{C–B}) = 0.564$, $d = 1.72 \text{ \AA}$) and the N–I bond ($\text{WBI}(\text{N–I}) = 0.536$, $d = 2.42 \text{ \AA}$) occur simultaneously with the formation of the Ph–N bond ($\text{WBI}(\text{C–N}) = 0.303$, $d = 2.07 \text{ \AA}$), which suggests a concerted 1,2-aryl migration mechanism (Figure 4b and 4c). Furthermore, NBO analysis of **TS1** revealed that there is a strong σ -donation interaction (81.6 kcal/mol) between the bonding orbital of $\sigma(\text{C–B})$ and the antibonding orbital of $\sigma^*(\text{N–I})$, which supports the electrophilic amination mechanism (Figure 6). The decrease in the NBO charge on the iodine atom from 1.25 in **INT2** to 0.66 in **TS1** indicates the reduction of I(III) to I(I). The amination of a pinacol boronate with **1a** also proceeds efficiently. Indeed, DFT calculations of the reaction pathway were performed, and the resultant reaction energy profile was similar to that of the reaction of a boronic acid (Figure 7).

a) Calculated free energy profile for the electrophilic amination of $\text{PhB}(\text{OH})_2$



c) Optimized geometries and selected distances

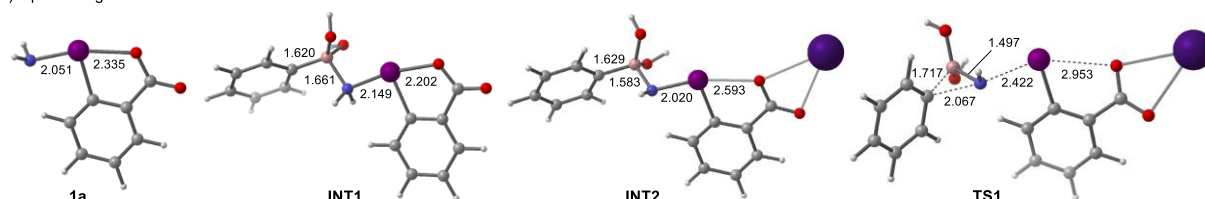


Figure 4. DFT calculation studies. Free energies (kcal/mol) are computed at the M06-2X/6-311++g(d,p)-SDD(I,Cs),SMD(THF)//M06-2X/6-31+g(d,p)-LANL2DZ(I,Cs),SMD(THF) level of theory.

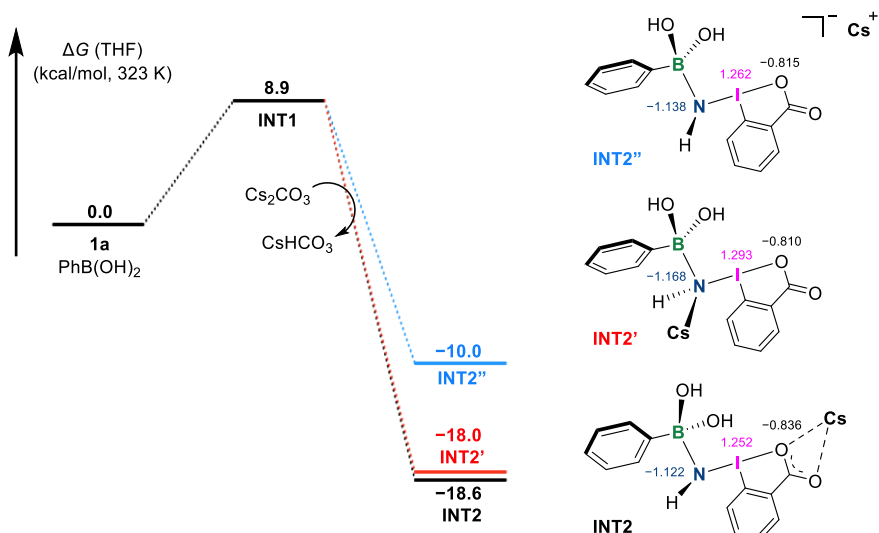
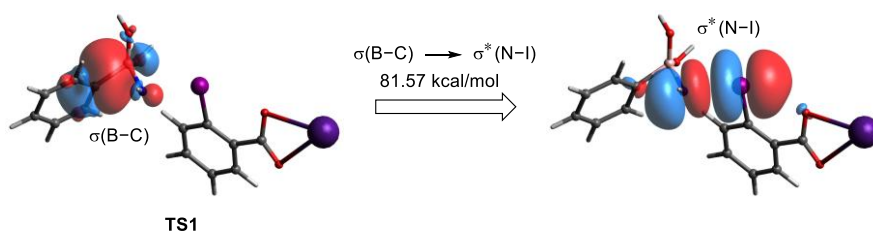


Figure 5. Formation of INT2 To confirm the structure of INT2, DFT calculations were performed to optimize the structures by changing the coordination mode of the cesium cation.



A donation interaction between the filled $\sigma(\text{B}-\text{C})$ orbital and the vacant $\sigma^*(\text{N}-\text{I})$.

Figure 6. NBO analysis of TS1

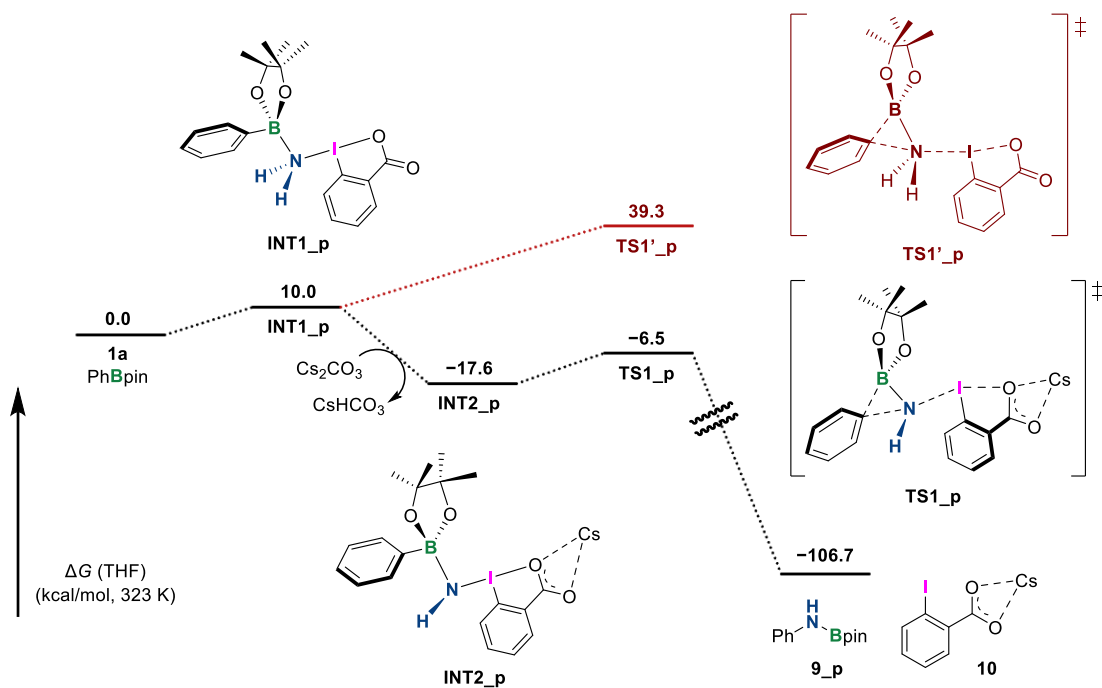
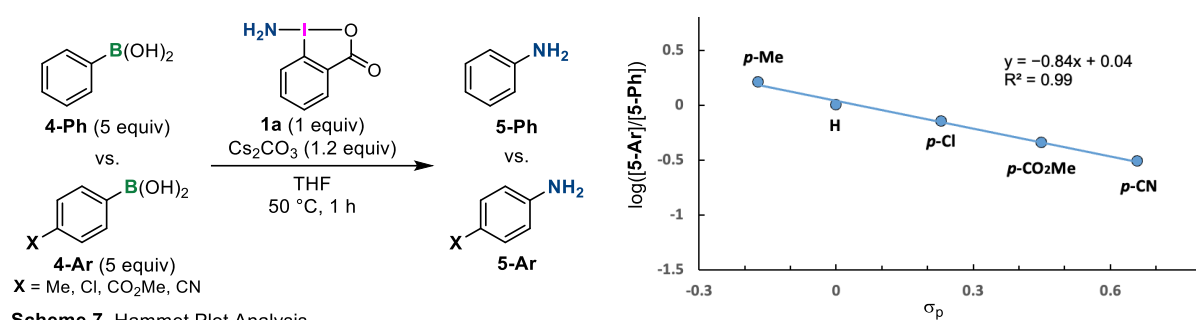


Figure 7. DFT calculation studies for pinacol boronate

To gain insight into the nature of the **TS1**, a Hammett study was performed using a series of para-substituted arylboronic acids (Scheme 7). More electron-rich substrates showed higher reactivity, and a linear correlation between the $\log([5\text{-Ar}]/[5\text{-Ph}])$ and Hammett constants (σ_{para}) was observed with a negative slope ($\rho = -0.84$, $R^2 = 0.99$),²⁴ indicating that a buildup in the positive charge at the aryl group occurs in **TS1**. This result is consistent with calculation showing that the positive charge of the aryl group, particularly at the *ipso* carbon, increases from -0.30 in **INT2** to -0.19 in **TS1**. The amination of a pinacol boronate with **1a** also proceeds efficiently.



1-3. Conclusion

In conclusion, the author has developed an electrophilic amination of arylboronic acids and boronates utilizing newly synthesized aminobenziodoxolones that exhibit both nucleophilic and electrophilic reactivity. The addition of Cs_2CO_3 is key to the promotion of the reaction, and the Cs-mediated electrophilic amination mechanism was supported by DFT calculations. This reaction has a broad substrate scope with good functional group tolerance.

1-4. Experimental Section

General Remarks

New compounds were characterized by ^1H NMR, $^{13}\text{C}\{^1\text{H}\}$ NMR, $^{19}\text{F}\{^1\text{H}\}$ NMR, IR, MS, and HRMS. ^1H , $^{13}\text{C}\{^1\text{H}\}$, and $^{19}\text{F}\{^1\text{H}\}$ NMR spectra were recorded on a JEOL JMT-400/54/SS spectrometer (^1H NMR, 400 MHz; $^{13}\text{C}\{^1\text{H}\}$ NMR, 100 MHz; $^{19}\text{F}\{^1\text{H}\}$ NMR, 377 MHz). ^1H NMR chemical shifts were determined relative to Me_4Si (0.0 ppm) as an internal standard in CDCl_3 or the signals of residual undeuterated dimethyl sulfoxide (2.49 ppm) in dimethyl sulfoxide- d_6 . $^{13}\text{C}\{^1\text{H}\}$ NMR chemical shifts were determined relative to CDCl_3 (77.00 ppm) or dimethyl sulfoxide- d_6 (39.50 ppm). $^{19}\text{F}\{^1\text{H}\}$ NMR

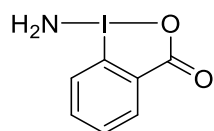
chemical shifts were determined relative to C_6F_6 (-164.9 ppm in CDCl_3) as an external standard. The multiplicities are abbreviated as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad) and combinations thereof. Infrared spectra were recorded on a SHIMADZU IRAffinity-1 FT-IR Spectrometer. High-resolution mass spectra (HRMS) were obtained on JEOL JMS-700 (magnetic sector type mass spectrometer) and JMS-T100LP. Elemental analyses were performed by J-SCIENCE LAB JM10 and Mitsubishi Chemical Analytech XS-2100H. Melting points were determined on a Stanford Research Systems MPA100 OptiMelt Automated Melting Point System. The X-ray diffraction data of the single crystal were collected on a two-dimensional X-ray detector (PILATUS 200K/R) equipped in Rigaku XtaLAB PRO diffractometer using thin multi-layer mirror monochromated Cu-K α radiation ($\lambda = 1.54187$ Å). All reactions were carried out under nitrogen. Products were purified by chromatography on silica gel BW-300 (Fuji Silysia Chemical Ltd.) or Chromatorex NH (Fuji Silysia Chemical Ltd.). Analytical thin-layer chromatography (TLC) was performed on pre-coated silica gel glass plates (Merck silica gel 60 F254 and Fuji Silysia Chromatorex NH, 0.25 mm thickness). Compounds were visualized with UV lamp or treatment with an ethanolic solution of phosphomolybdic acid followed by heating.

Materials

Hypervalent iodine reagent **2** was prepared according to the reported procedure.²⁵ Disilazanes **3c**,^{23b} **3e**,^{23a} and **3g**^{23b} were prepared according to the reported procedure. Pinacol boronic acid ester **4x** was prepared according to the reported procedure.²⁶ Boroxine **6** was prepared according to the reported procedure.²⁷ Dehydrated acetonitrile and THF were used from a solvent purification system. All other solvents and reagents were purchased and used as obtained.

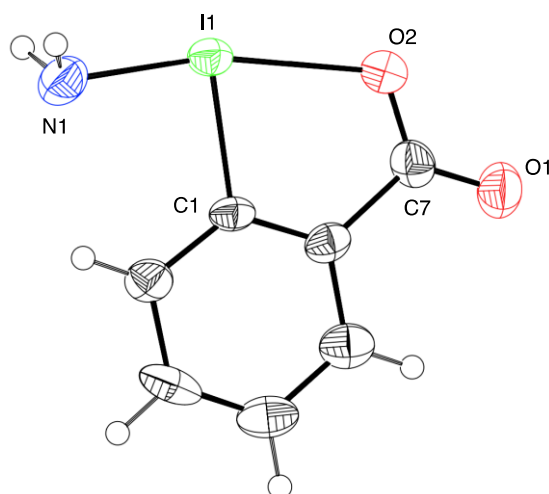
Synthesis of hypervalent iodine reagents

1-amino-1,2-benziodoxol-3(1*H*)-one (**1a**)



To a solution of 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (3.06 g, 10 mmol, 1.0 equiv) in MeCN (50 mL), hexamethyldisilazane (3.22 g, 20 mmol, 2.0 equiv) and ethanol (880 μL , 15 mmol, 1.5 equiv) were added. The mixture was stirred at room temperature for 2 h. Then, the precipitation was washed with MeCN and dried under vacuum to give the product as a white solid (2.43 g, 92% yield). Recrystallization from MeCN gave single crystals suitable for X-ray analysis.

mp. 124.2–125.8 °C (decomposed); ^1H NMR: (400 MHz, $\text{DMSO-}d_6$) δ 8.05–7.95 (m, 2H), 7.90–7.78 (m, 1H), 7.68–7.57 (m, 1H), 4.66 (brs, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, $\text{DMSO-}d_6$) δ 166.8, 133.4, 133.0, 130.8, 129.9, 125.5, 117.3; IR: (ATR) 3287, 3179, 3069, 3049, 1584, 1553, 1452, 1435, 1339, 1298, 1250, 1150, 1115, 1013, 893, 883, 829, 812 cm^{-1} ; HRMS (FAB+) m/z : $[\text{M}+\text{H}]^+$ Calculated for $\text{C}_7\text{H}_7\text{NO}_2\text{I}$ 263.9521; Found 263.9517; Analysis Calculated for $\text{C}_7\text{H}_6\text{NO}_2\text{I}$: C, 31.96; H, 2.30; N, 5.33; I, 48.25; Found: C, 31.95; H, 2.39; N, 5.33; I, 48.14



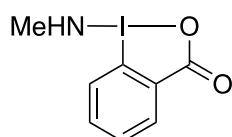
The structure of **1a** was determined by X-ray structural analysis. Thermal ellipsoids are drawn at the 50% probability level. CCDC 2306493 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

CCDC number	2306493
Empirical formula	$\text{C}_7\text{H}_6\text{NO}_2\text{I}$
Formula weight	263.03
Temperature/K	223.15
Crystal system	monoclinic
Space group	C2/c
$a/\text{\AA}$	11.1468(3)
$b/\text{\AA}$	9.8634(2)
$c/\text{\AA}$	15.3812(4)
$\alpha/^\circ$	90

$\beta/^\circ$	109.525(3)
$\gamma/^\circ$	90
Volume/ $\text{\AA}^3$	1593.85(7)
Z	8
$\rho_{\text{calc}}/\text{g/cm}^3$	2.192
μ/mm^{-1}	31.177
F(000)	992.0
Crystal size/ mm^3	$0.165 \times 0.122 \times 0.083$
Radiation	Cu K α ($\lambda = 1.54184$)
2Θ range for data collection/ $^\circ$	12.21 to 154.842
Index ranges	$-13 \leq h \leq 14, -9 \leq k \leq 12, -15 \leq l \leq 19$
Reflections collected	4934
Independent reflections	1617 [$R_{\text{int}} = 0.0388, R_{\text{sigma}} = 0.0346$]
Data/restraints/parameters	1617/5/106
Goodness-of-fit on F^2	1.157
Final R indexes [$I > 2\sigma(I)$]	$R_1 = 0.0528, wR_2 = 0.1472$
Final R indexes [all data]	$R_1 = 0.0573, wR_2 = 0.1615$
Largest diff. peak/hole / $e \text{\AA}^{-3}$	1.93/-1.86

The stability of **1a** was determined by DSC7000X (Hitachi High-Tech Science). **1a** (1.743 mg) was loaded into a gold-plated high-pressure crucible. The sealed crucible was loaded onto the machine and was scanned from 30 to 250 $^\circ\text{C}$ at a heating rate of 5 $^\circ\text{C}/\text{min}$. Data such as T_{onset} (temperature at which an exothermic signal is detected), the decomposition energy, and the peak temperature were recorded.

1-(methylamino)-1,2-benziodoxol-3(1H)-one (**1b**)

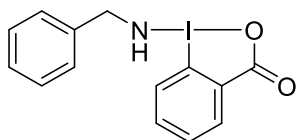


To a solution of 1-acetoxy-1,2-benziodoxol-3-(1H)-one (918 mg, 3.0 mmol, 1.0 equiv) in MeCN (30 mL), heptamethyldisilazane (1.08 g, 6.0 mmol, 2.0 equiv) and ethanol (265 μL , 4.5 mmol, 1.5 equiv) were added. The mixture was stirred at room temperature for 2 h. Then, the precipitation was washed

with MeCN and dried under vacuum to give the product as a white solid (701 mg, 84% yield).

mp. 122.5–124.0 °C (decomposed); ^1H NMR: (400 MHz, DMSO- d_6) δ 8.02 (dd, J = 7.6, 1.6 Hz, 1H), 7.97 (d, J = 7.6 Hz, 1H), 7.84 (ddd, J = 7.6, 7.6, 1.6 Hz, 1H), 7.64 (ddd, J = 7.6, 7.6, 1.2 Hz, 1H), 5.33 (q, J = 6.0 Hz, 1H), 3.27 (d, J = 6.0 Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, DMSO- d_6) δ 166.9, 133.5, 133.3, 131.4, 130.1, 125.5, 116.6, 38.9; IR: (ATR) 3242, 3071, 3059, 2957, 2932, 2893, 2864, 2789, 1597, 1584, 1562, 1463, 1433, 1410, 1339, 1300, 1246, 1157, 1144, 1015, 970, 833 cm^{-1} ; HRMS (FAB+) m/z : $[\text{M}+\text{H}]^+$ Calculated for $\text{C}_8\text{H}_9\text{NO}_2\text{I}$ 277.9678; Found 277.9685; Analysis Calculated for $\text{C}_8\text{H}_8\text{NO}_2\text{I}$: C, 34.68; H, 2.91; N, 5.06; I, 45.80; Found: C, 34.57; H, 3.05; N, 5.04; I, 45.82

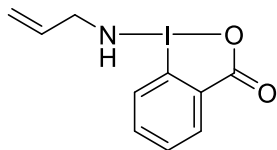
1-(benzylamino)-1,2-benziodoxol-3(1H)-one (1c)



To a solution of 1-acetoxy-1,2-benziodoxol-3-(1H)-one (614 mg, 2.0 mmol, 1.0 equiv) in MeCN (20 mL), *N*-benzyl-*N,N*-bis(trimethylsilyl)amine (1.02 g, 4.0 mmol, 2.0 equiv) and ethanol (180 μL , 3.0 mmol, 1.5 equiv) were added. The mixture was stirred at room temperature for 2 h. Then, the precipitation was washed with MeCN and dried under vacuum to give the product as a white solid (658 mg, 93% yield).

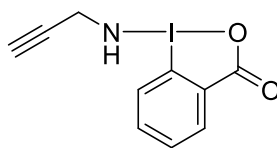
^1H NMR: (400 MHz, DMSO- d_6) δ 8.04 (d, J = 7.2 Hz, 1H), 7.99 (dd, J = 7.2, 1.6 Hz, 1H), 7.82 (ddd, J = 7.2, 7.2, 1.6 Hz, 1H), 7.62 (dd, J = 7.2, 7.2 Hz, 1H), 7.45–7.37 (m, 2H), 7.37–7.22 (m, 3H), 5.83 (t, J = 6.4 Hz, 1H), 4.47 (d, J = 6.4 Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, DMSO- d_6) δ 166.8, 140.7, 133.4, 133.2, 131.2, 130.0, 128.5, 128.4, 127.5, 125.7, 116.9, 54.5

The analytical data for this compound were in excellent agreement with the reported data.^{19b}

1-(allylamino)-1,2-benziodoxol-3(1*H*)-one (1d)

To a solution of 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (620 mg, 2.0 mmol, 1.0 equiv) in MeCN (20 mL), *N*-allyl-*N,N*-bis(trimethylsilyl)amine (840 mg, 4.0 mmol, 2.0 equiv) and ethanol (180 μ L, 3.0 mmol, 1.5 equiv) were added. The mixture was stirred at room temperature for 2 h. Then, the precipitation was washed with MeCN and dried under vacuum to give the product as a white solid (535 mg, 87% yield).

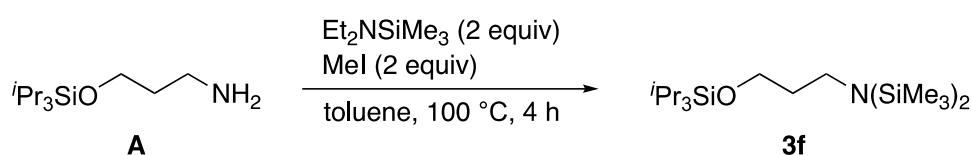
mp. 95.0–96.5 °C (decomposed); ^1H NMR: (400 MHz, DMSO- d_6) δ 8.04 (d, J = 8.0 Hz, 1H), 8.01 (dd, J = 8.0, 1.2 Hz, 1H), 7.85 (ddd, J = 8.0, 8.0, 1.2 Hz, 1H), 7.64 (ddd, J = 8.0, 8.0, 1.2 Hz, 1H), 5.97–5.80 (m, 1H), 5.58 (t, J = 6.0 Hz, 1H), 5.26 (dd, J = 16.4, 1.2 Hz, 1H), 5.16 (dd, J = 9.6, 1.2 Hz, 1H), 3.95 (dd, J = 6.0, 6.0 Hz, 2H); ^{13}C { ^1H } NMR: (100 MHz, DMSO- d_6) δ 166.9, 137.3, 133.4, 133.3, 131.3, 130.1, 125.6, 117.5, 117.0, 53.3; IR: (ATR) 3277, 2972, 2900, 1602, 1584, 1564, 1435, 1423, 1335, 1300, 1227, 1113, 1024, 1013, 923, 831, 772 cm^{-1} ; HRMS (FAB+) m/z : $[\text{M}+\text{H}]^+$ Calculated for $\text{C}_{10}\text{H}_{11}\text{NO}_2\text{I}$ 303.9834; Found 303.9833; Analysis Calculated for $\text{C}_{10}\text{H}_{10}\text{NO}_2\text{I}$: C, 39.63; H, 3.33; N, 4.62; I, 41.87; Found: C, 39.28; H, 3.21; N, 4.68; I, 41.66

1-(prop-2-yn-1-ylamino)-1,2-benziodoxol-3(1*H*)-one (1e)

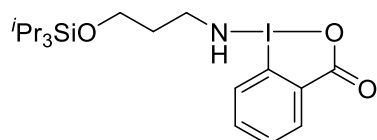
To a solution of 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (308 mg, 1.0 mmol, 1.0 equiv) in MeCN (10 mL), *N*-(prop-2-yn-1-yl)-*N,N*-bis(trimethylsilyl)amine (404 mg, 2.0 mmol, 2.0 equiv) and ethanol (90 μ L, 1.5 mmol, 1.5 equiv) were added. The mixture was stirred at room temperature for 2 h. Then, the precipitation was washed with MeCN and dried under vacuum to give the product as a pale yellow solid (230 mg, 76% yield).

mp. 94.0–95.0 °C (decomposed); ^1H NMR: (400 MHz, $\text{DMSO}-d_6$) δ 8.09 (d, $J = 7.2$ Hz, 1H), 8.01 (dd, $J = 7.2, 1.6$ Hz, 1H), 7.85 (ddd, $J = 7.2, 7.2, 1.6$ Hz, 1H), 7.64 (ddd, $J = 7.2, 7.2, 0.8$ Hz, 1H), 5.65 (t, $J = 4.8$ Hz, 1H), 4.17 (dd, $J = 4.8, 2.4$ Hz, 2H), 3.30 (t, $J = 2.4$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, $\text{DMSO}-d_6$) δ 167.0, 133.22, 133.17, 131.1, 130.1, 126.1, 117.3, 82.8, 75.8, 39.4; IR: (ATR) 3298, 3285, 3161, 2926, 1609, 1585, 1562, 1325, 1300, 1246, 1144, 1032, 966, 907, 829, 812 cm^{-1} ; HRMS (FAB+) m/z : $[\text{M}+\text{H}]^+$ Calculated for $\text{C}_{10}\text{H}_9\text{NO}_2\text{I}$ 301.9678; Found 301.9673; Analysis Calculated for $\text{C}_{10}\text{H}_8\text{NO}_2\text{I}$: C, 39.89; H, 2.68; N, 4.65; I, 42.15; Found: C, 39.61; H, 2.75; N, 4.59; I, 42.07

1-((3-((triisopropylsilyl)oxy)propyl)amino)-1-benzo-1,2-iodaoxol-3-(1*H*)-one (1f)



To a solution of 3-((triisopropylsilyl)oxy)propan-1-amine (613 mg, 2.5 mmol, 2.0 equiv) and *N,N*-diethyl-1,1,1-trimethylsilanamine (780 mg, 5.0 mmol, 1.0 equiv) in toluene (2 mL), MeI (791 mg, 5.0 mmol, 2.0 equiv) was added. The vial was sealed and placed in an aluminum block, which was preheated at 100 °C, and then the mixture was stirred at 100 °C for 4 h. The precipitation was removed by filtration, and the filtrate was concentrated under reduced pressure to give the mixture of **3f** and the starting amine **A** (717 mg, **A**:**3f** = 1:1), which contains 1.25 mmol of **3f**.

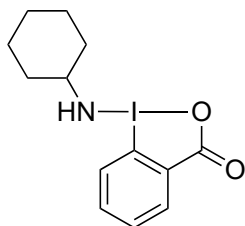


To a solution of 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (153 mg, 0.5 mmol, 1.0 equiv) in MeCN (10 mL), the mixture of **A** and **3f** (717 mg, 1.25 mmol of **3f**) and ethanol (45 μL , 0.75 mmol, 1.5 equiv) were added. The mixture was stirred at room temperature for 2 h. Then, the precipitation was washed with MeCN and dried under vacuum to give the product as a white solid (85.1 mg, 36% yield).

mp. 114.0–116.5 °C (decomposed); ^1H NMR: (400 MHz, CDCl_3) δ 8.31 (d, $J = 7.2$ Hz, 1H), 8.10–8.00 (m, 1H), 7.75 (dd, $J = 7.2, 7.2$ Hz, 1H), 7.62 (dd, $J = 7.2, 7.2$ Hz, 1H), 4.65 (brs, 1H), 3.89 (t, $J = 5.6$ Hz, 2H), 3.68–3.52 (m, 2H), 1.85 (tt, $J = 5.6, 5.6$ Hz, 2H), 1.20–0.90 (m, 21H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz,

CDCl₃) δ 168.9, 133.3, 132.8, 132.3, 130.2, 125.2, 116.4, 61.3, 50.8, 36.0, 18.0, 11.8; IR: (ATR) 3246, 2940, 2864, 1601, 1584, 1564, 1460, 1437, 1339, 1300, 1094, 1069, 1012, 966, 881, 833 cm⁻¹; HRMS (FAB+) m/z : [M+H]⁺ Calculated for C₁₉H₃₃NO₃ISi 478.1274; Found 478.1289

1-(cyclohexylamino)-1,2-benziodoxol-3(1*H*)-one (1g)



To a solution of 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (313 mg, 1.0 mmol, 1.0 equiv) in MeCN (10 mL), *N*-cyclohexyl-*N,N*-bis(trimethylsilyl)amine (494 mg, 2.0 mmol, 2.0 equiv) and ethanol (90 μ L, 1.5 mmol, 1.5 equiv) were added. The mixture was stirred at room temperature for 2 h. Then, the precipitation was washed with MeCN and dried under vacuum to give the product as a white solid (331 mg, 94% yield).

mp. 120.2–122.0 °C (decomposed); ¹H NMR: (400 MHz, DMSO-*d*₆) δ 8.07 (d, J = 7.6 Hz, 1H), 8.00 (d, J = 6.8 Hz, 1H), 7.84 (dd, J = 7.2, 7.2 Hz, 1H), 7.62 (dd, J = 7.2, 7.2 Hz, 1H), 5.54 (d, J = 4.4 Hz, 1H), 3.17–3.00 (m, 1H), 2.00–1.80 (m, 2H), 1.80–1.60 (m, 2H), 1.60–1.40 (m, 1H), 1.35–1.00 (m, 5H); ¹³C{¹H} NMR: (100 MHz, DMSO-*d*₆) δ 166.8, 133.7, 133.1, 131.2, 130.0, 125.4, 117.2, 58.2, 34.8, 25.3, 24.5; IR: (ATR) 3150, 3057, 2924, 2911, 2845, 1599, 1584, 1562, 1462, 1435, 1366, 1337, 1298, 1256, 1244, 1061, 1026, 1013, 959, 829 cm⁻¹; HRMS (FAB+) m/z : [M+H]⁺ Calculated for C₁₃H₁₇NO₂I 346.0304; Found 346.0299; Analysis Calculated for C₁₃H₁₆NO₂I: C, 45.24; H, 4.67; N, 4.06; I, 36.76; Found: C, 45.07; H, 4.64; N, 4.03; I, 36.55

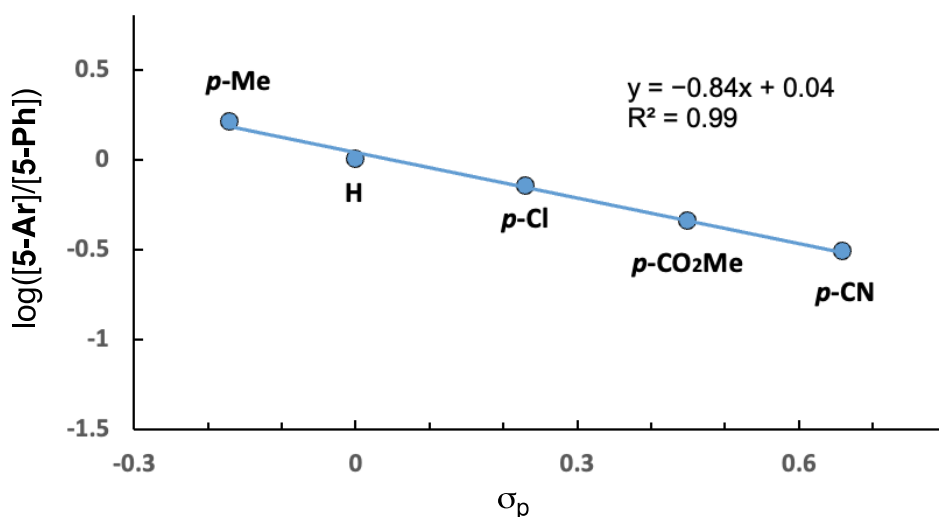
Hammett analysis

An oven-dried reaction vial containing a magnetic stir bar was charged with phenylboronic acid (1.0 mmol, 5.0 equiv), *para*-substituted arylboronic acid (1.0 mmol, 5.0 equiv), amino- λ^3 -iodane **1a** (0.2 mmol, 1.0 equiv), Cs₂CO₃ (0.24 mmol, 1.2 equiv), and THF (10 mL). The vial was sealed and placed in

an aluminum block, which was preheated at 50 °C. After the mixture was stirred at 50 °C for 1 h, the reaction was quenched by passing the solution through a short column (silica gel) using EtOAc as the eluent. The solution was then concentrated under reduced pressure to give the crude product, which was analyzed by ^1H NMR spectroscopy using 1,1,2,2-tetrachloroethane as an internal standard. The resulting ^1H resonances of the protons of **5-Ar** were integrated relative to those of **5-Ph** to calculate the ratio of products (Table S1). The values of $\log([\mathbf{5-Ar}]/[\mathbf{5-Ph}])$ were plotted versus the σ_p value, and a linear fit was created to obtain the Hammett-slope ($\rho = -0.84$).

Table S1. Data for Hammett-plot

X	σ_p	$[\mathbf{5-Ar}]/[\mathbf{5-Ph}]$	$[\mathbf{5-Ar}]/[\mathbf{5-Ph}]$	$[\mathbf{5-Ar}]/[\mathbf{5-Ph}]$	$\log([\mathbf{5-Ar}]/[\mathbf{5-Ph}])$
Me	-0.17	1.74	1.51	1.63	0.21
H	0.00	1	1	1	0
Cl	0.23	0.70	0.69	0.70	-0.15
CO ₂ Me	0.45	0.46	0.45	0.46	-0.34
CN	0.66	0.30	0.32	0.31	-0.51



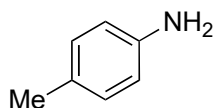
Typical procedure and product data

General procedure I: An oven-dried reaction vial containing a magnetic stir bar was charged with aryl boron compound (1.0 equiv), amino- λ^3 -iodane (1.1 equiv), Cs_2CO_3 (1.2 equiv), and THF. Then, the vial was sealed and placed in an aluminum block, which was preheated at the indicated temperature. After the mixture was stirred at the temperature for the indicated time, sat. NaHCO_3 aq. was added, and the mixture was extracted with CHCl_3 (3×15 mL). The combined organic layers were dried over Na_2SO_4 , filtrated, and concentrated under reduced pressure to give the crude product, which was analyzed by ^1H NMR spectroscopy using 1,1,2,2-tetrachloroethane as an internal standard. Purification by flash column chromatography on NH silica gel (hexane/EtOAc) gave the product.

General procedure II: A reaction flask equipped with a magnetic stirring bar was charged with MS3A and flamed-dried under vacuum. After cooling down to room temperature, aryl boron compound (1.0 equiv), amino- λ^3 -iodane (1.1 equiv), Cs_2CO_3 (1.2 equiv), and THF were added. Then, the flask was sealed and placed in an aluminum block, which was preheated at the indicated temperature. After the mixture was stirred at the temperature for the indicated time, the reaction was quenched by passing the solution through a short column (silica gel) using EtOAc as the eluent. The solution was then concentrated under reduced pressure to give the crude product, which was analyzed by ^1H NMR spectroscopy using 1,1,2,2-tetrachloroethane as an internal standard. Purification by flash column chromatography on NH silica gel (hexane/EtOAc) gave the product.

Product data

p-toluidine (5a)

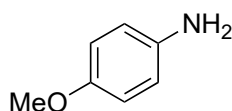


According to the general procedure I, the reaction using (4-methyl phenyl)boronic acid (54.0 mg, 0.40 mmol, 1.0 equiv), **1a** (117.4 mg, 0.44 mmol, 1.1 equiv), Cs_2CO_3 (159.8 mg, 0.48 mmol, 1.2 equiv), and THF (2 mL) was conducted at 50 °C for 24 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 98:2) gave the product as a pale red solid (35.9 mg, 84% yield).

^1H NMR: (400 MHz, CDCl_3) δ 6.96 (d, $J = 8.0$ Hz, 2H), 6.61 (d, $J = 8.0$ Hz, 2H), 3.52 (brs, 2H), 2.24 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 143.8, 129.7, 127.8, 115.2, 20.4

The analytical data for this compound were in excellent agreement with the reported data.^{10b}

4-methoxyaniline (5b)

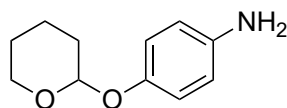


According to the general procedure **I**, the reaction using (4-methoxy phenyl)boronic acid (60.8 mg, 0.40 mmol, 1.0 equiv), **1a** (116.7 mg, 0.44 mmol, 1.1 equiv), Cs_2CO_3 (160.2 mg, 0.48 mmol, 1.2 equiv), and THF (2 mL) was conducted at 50 °C for 24 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 9:1) gave the product as a pale yellow solid (43.5 mg, 88% yield).

^1H NMR: (400 MHz, CDCl_3) δ 6.80–6.70 (m, 2H), 6.70–6.60 (m, 2H), 3.75 (s, 3H), 3.39 (brs, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 152.8, 139.9, 116.4, 114.8, 55.7

The analytical data for this compound were in excellent agreement with the reported data.^{10b}

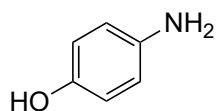
4-((tetrahydro-2H-pyran-2-yl)oxy)aniline (5c)



According to the general procedure **I**, the reaction using (4-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)boronic acid (89.1 mg, 0.40 mmol, 1.0 equiv), **1a** (116.3 mg, 0.44 mmol, 1.1 equiv), Cs_2CO_3 (159.2 mg, 0.48 mmol, 1.2 equiv), and THF (2 mL) was conducted at 50 °C for 24 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 85:15) gave the product as a yellow oil (71.7 mg, 92% yield).

^1H NMR: (400 MHz, CDCl_3) δ 6.89 (d, $J = 8.4$ Hz, 2H), 6.62 (d, $J = 8.4$ Hz, 2H), 5.25 (dd, $J = 3.6, 3.6$ Hz, 1H), 4.05–3.81 (m, 1H), 3.70–3.10 (m, 3H), 2.10–1.92 (m, 1H), 1.92–1.75 (m, 2H), 1.75–1.45 (m, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 150.0, 140.9, 118.0, 116.1, 97.5, 62.1, 30.5, 25.2, 19.0

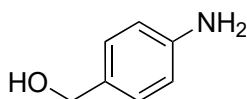
The analytical data for this compound were in excellent agreement with the reported data.²⁸

4-aminophenol (5d)

An oven-dried reaction vial containing a magnetic stir bar was charged with 4-hydroxyphenylboronic acid (55.5 mg, 0.40 mmol, 1.0 equiv), **1a** (116.8 mg, 0.44 mmol, 1.1 equiv), Cs₂CO₃ (158.7 mg, 0.48 mmol, 1.2 equiv), and THF (2 mL). Then, the vial was sealed, and the mixture was stirred at room temperature for 48 h, sat. NH₄Cl aq. was added, and the mixture was extracted with EtOAc (3 × 15 mL). The combined organic layers were dried over Na₂SO₄, filtrated, and concentrated under reduced pressure to give the crude product, which was analyzed by ¹H NMR spectroscopy using 1,1,2,2-tetrachloroethane as an internal standard. Purification by flash column chromatography on silica gel (hexane/EtOAc = 7:3) gave the product as a white solid (31.2 mg, 71% yield).

¹H NMR: (400 MHz, DMSO-*d*₆) δ 8.31 (brs, 1H), 6.58–6.22 (m, 4H), 4.36 (brs, 2H); ¹³C{¹H} NMR: (100 MHz, DMSO-*d*₆) δ 148.2, 140.7, 115.5, 115.2

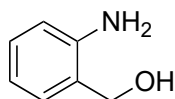
The analytical data for this compound were in excellent agreement with the reported data.²⁹

(4-aminophenyl)methanol (5e)

According to the general procedure **I**, the reaction using (4-(hydroxymethyl)phenyl)boronic acid (61.0 mg, 0.40 mmol, 1.0 equiv), **1a** (116.6 mg, 0.44 mmol, 1.1 equiv), Cs₂CO₃ (157.2 mg, 0.48 mmol, 1.2 equiv), and THF (2 mL) was conducted at 50 °C for 24 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 4:6) gave the product as a pale yellow solid (20.4 mg, 41% yield).

¹H NMR: (400 MHz, CDCl₃) δ 7.16 (d, *J* = 8.8 Hz, 2H), 6.67 (d, *J* = 8.8 Hz, 2H), 4.55 (s, 2H), 3.60 (brs, 2H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 146.0, 131.0, 128.8, 115.1, 65.3

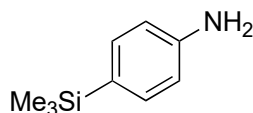
The analytical data for this compound were in excellent agreement with the reported data.^{10d}

(2-aminophenyl)methanol (5f)

According to the general procedure **I**, the reaction using 2-(hydroxymethyl)phenylboronic acid cyclic monoester (54.2 mg, 0.40 mmol, 1.0 equiv), **1a** (115.9 mg, 0.44 mmol, 1.1 equiv), Cs₂CO₃ (162.1 mg, 0.48 mmol, 1.2 equiv), and THF (2 mL) was conducted at 50 °C for 24 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 7:3) gave the product as a pale yellow solid (37.7 mg, 77% yield).

¹H NMR: (400 MHz, CDCl₃) δ 7.14 (ddd, *J* = 7.6, 7.6, 1.6 Hz, 1H), 7.07 (dd, *J* = 7.6, 1.6 Hz, 1H), 6.80–6.60 (m, 2H), 4.67 (s, 2H), 4.17 (brs, 2H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 146.0, 129.3, 129.2, 124.8, 118.1, 116.0, 64.3

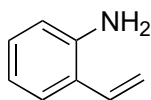
The analytical data for this compound were in excellent agreement with the reported data.^{10d}

4-(trimethylsilyl)aniline (5g)

According to the general procedure **I**, the reaction using (4-trimethylsilyl)boronic acid (79.0 mg, 0.40 mmol, 1.0 equiv), **1a** (117.0 mg, 0.44 mmol, 1.1 equiv), Cs₂CO₃ (157.0 mg, 0.48 mmol, 1.2 equiv), and THF (2 mL) was conducted at 50 °C for 24 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 99:1) gave the product as a yellow oil (63.0 mg, 95% yield).

¹H NMR: (400 MHz, CDCl₃) δ 7.38–7.27 (m, 2H), 6.74–6.62 (m, 2H), 3.69 (brs, 2H), 0.22 (s, 9H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 147.0, 134.5, 128.4, 114.5, –0.9

The analytical data for this compound were in excellent agreement with the reported data.³⁰

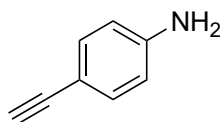
2-vinylaniline (5h)

According to the general procedure **I**, the reaction using (2-vinylphenyl)boronic acid (59.2 mg, 0.40 mmol, 1.0 equiv), **1a** (115.9 mg, 0.44 mmol, 1.1 equiv), Cs₂CO₃ (160.3 mg, 0.48 mmol, 1.2 equiv), and THF (2 mL) was conducted at 50 °C for 24 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 99:1) gave the product as a yellow oil (36.3 mg, 76% yield).

¹H NMR: (400 MHz, CDCl₃) δ 7.33–7.22 (m, 1H), 7.08 (ddd, *J* = 8.0, 8.0, 1.6 Hz, 1H), 6.83–6.70 (m, 2H), 6.68 (d, *J* = 8.0 Hz, 1H), 5.62 (dd, *J* = 17.6, 1.6 Hz, 1H), 5.31 (dd, *J* = 11.2, 1.6 Hz, 1H), 3.74 (brs, 2H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 143.6, 132.7, 128.7, 127.3, 124.1, 118.9, 116.0, 115.7

The analytical data for this compound were in excellent agreement with the reported data.³⁰

4-ethynylaniline (**5i**)

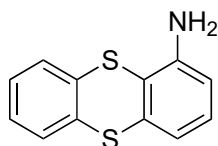


According to the general procedure **I**, the reaction using 2-(4-ethynylphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (46.1 mg, 0.20 mmol, 1.0 equiv), **1a** (59.1 mg, 0.22 mmol, 1.1 equiv), Cs₂CO₃ (82.6 mg, 0.24 mmol, 1.2 equiv), and THF (1 mL) was conducted at 50 °C for 24 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 8:2) gave the product as a pale yellow solid (20.1 mg, 85% yield).

¹H NMR: (400 MHz, CDCl₃) δ 7.30 (d, *J* = 8.0 Hz, 2H), 6.60 (d, *J* = 8.0 Hz, 2H), 3.81 (brs, 2H), 2.96 (s, 1H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 147.0, 133.5, 114.6, 111.3, 84.3, 74.9

The analytical data for this compound were in excellent agreement with the reported data.³¹

thianthren-1-amine (**5j**)



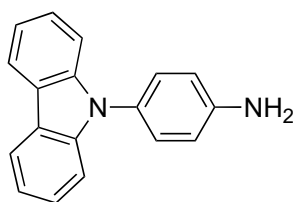
According to the general procedure **I**, the reaction using 1-thianthrenylboronic acid (103.7 mg, 0.40 mmol, 1.0 equiv), **1a** (116.8 mg, 0.44 mmol, 1.1 equiv), Cs₂CO₃ (159.9 mg, 0.48 mmol, 1.2 equiv), and

THF (2 mL) was conducted at 50 °C for 24 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 9:1) gave the product as a pale yellow solid (81.0 mg, 88% yield).

^1H NMR: (400 MHz, CDCl_3) δ 7.60–7.45 (m, 2H), 7.35–7.18 (m, 2H), 7.05 (dd, J = 8.0 Hz, 1H), 6.96 (dd, J = 7.6, 1.2 Hz, 1H), 6.67 (dd, J = 7.6, 1.2 Hz, 1H), 4.22 (brs, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 145.2, 136.9, 136.7, 134.9, 129.0, 128.8, 128.3, 127.8, 127.5, 119.1, 119.0, 113.8

The analytical data for this compound were in excellent agreement with the reported data.^{14e}

4-(9*H*-carbazol-9-yl)aniline (5k)

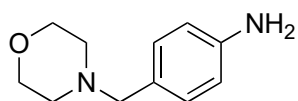


According to the general procedure **I**, the reaction using (4-(9*H*-carbazol-9-yl)phenyl)boronic acid (57.7 mg, 0.20 mmol, 1.0 equiv), **1a** (58.8 mg, 0.22 mmol, 1.1 equiv), Cs_2CO_3 (81.9 mg, 0.24 mmol, 1.2 equiv), and THF (1 mL) was conducted at 50 °C for 24 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 7:3) gave the product as a yellow oil (46.7 mg, 90% yield).

^1H NMR: (400 MHz, CDCl_3) δ 8.12 (d, J = 8.0 Hz, 2H), 7.47–7.35 (m, 2H), 7.35–7.17 (m, 6H), 6.83 (d, J = 8.0 Hz, 2H), 3.49 (brs, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 145.9, 141.5, 128.5, 128.1, 125.7, 123.0, 120.1, 119.4, 115.9, 109.8

The analytical data for this compound were in excellent agreement with the reported data.³²

4-(morpholinomethyl)aniline (5l)



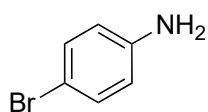
According to the general procedure **I**, the reaction using 4-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl)morpholine (60.5 mg, 0.20 mmol, 1.0 equiv), hypervalent iodine reagent **x** (58.1 mg, 0.22 mmol, 1.1 equiv), Cs_2CO_3 (81.4 mg, 0.24 mmol, 1.2 equiv), and THF (1 mL) was conducted at 50 °C

for 24 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 7:3) gave the product as a white solid (34.5 mg, 90% yield).

^1H NMR: (400 MHz, CDCl_3) δ 7.09 (d, J = 8.0 Hz, 2H), 6.64 (d, J = 8.0 Hz, 2H), 3.85–3.50 (m, 4H), 3.62 (brs, 2H), 3.38 (s, 2H), 2.55–2.20 (m, 4H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 145.5, 130.4, 127.5, 114.9, 67.0, 63.0, 53.5

The analytical data for this compound were in excellent agreement with the reported data.³³

4-bromoaniline (5m)

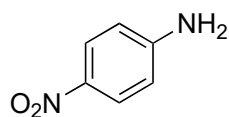


According to the general procedure **I**, the reaction using (4-bromophenyl)boronic acid (79.9 mg, 0.40 mmol, 1.0 equiv), **1a** (117.5 mg, 0.44 mmol, 1.1 equiv), Cs_2CO_3 (156.6 mg, 0.48 mmol, 1.2 equiv), and THF (2 mL) was conducted at 50 °C for 48 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 8:2) gave the product as a pale red solid (61.0 mg, 89% yield).

^1H NMR: (400 MHz, CDCl_3) δ 7.30–7.15 (m, 2H), 6.62–6.48 (m, 2H), 3.65 (brs, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 145.4, 132.0, 116.7, 110.2

The analytical data for this compound were in excellent agreement with the reported data.^{10b}

4-nitroaniline (5n)



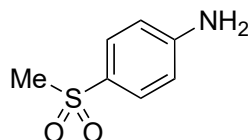
According to the general procedure **I**, the reaction using (4-nitrophenyl)boronic acid (66.2 mg, 0.40 mmol, 1.0 equiv), **1a** (116.1 mg, 0.44 mmol, 1.1 equiv), Cs_2CO_3 (158.9 mg, 0.48 mmol, 1.2 equiv), and THF (2 mL) was conducted at 50 °C for 48 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 7:3) gave the product as a yellow solid (51.0 mg, 93% yield).

^1H NMR: (400 MHz, CDCl_3) δ 8.07 (d, J = 8.8 Hz, 2H), 6.63 (d, J = 8.8 Hz, 2H), 4.40 (brs, 2H);

$^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 152.4, 139.1, 126.3, 113.3

The analytical data for this compound were in excellent agreement with the reported data.^{13b}

4-(methylsulfonyl)aniline (**5o**)

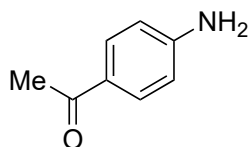


According to the general procedure **I**, the reaction using (4-(methylsulfonyl)phenyl)boronic acid (80.0 mg, 0.40 mmol, 1.0 equiv), **1a** (119.3 mg, 0.45 mmol, 1.1 equiv), Cs_2CO_3 (160.0 mg, 0.48 mmol, 1.2 equiv), and THF (2 mL) was conducted at 50 °C for 48 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 1:1) gave the product as a white solid (63.4 mg, 93% yield).

^1H NMR: (400 MHz, CDCl_3) δ 7.70 (d, J = 8.8 Hz, 2H), 6.72 (d, J = 8.8 Hz, 2H), 4.21 (brs, 2H), 3.01 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 151.3, 129.5, 128.8, 114.1, 45.0

The analytical data for this compound were in excellent agreement with the reported data.³⁴

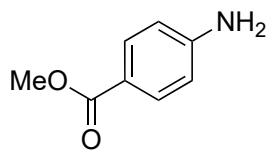
1-(4-aminophenyl)ethan-1-one (**5p**)



According to the general procedure **I**, the reaction using (4-acetylphenyl)boronic acid (65.6 mg, 0.40 mmol, 1.0 equiv), **1a** (116.5 mg, 0.44 mmol, 1.1 equiv), Cs_2CO_3 (158.5 mg, 0.48 mmol, 1.2 equiv), and THF (2 mL) was conducted at 50 °C for 48 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 7:3) gave the product as a white solid (49.3 mg, 91% yield).

^1H NMR: (400 MHz, CDCl_3) δ 7.81 (d, J = 8.4 Hz, 2H), 6.65 (d, J = 8.4 Hz, 2H), 4.11 (brs, 2H), 2.51 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 196.5, 151.0, 130.8, 127.9, 113.7, 26.1

The analytical data for this compound were in excellent agreement with the reported data.³⁴

methyl 4-aminobenzoate (5q)

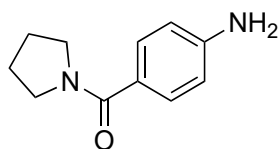
According to the general procedure **I**, the reaction using (4-(methoxycarbonyl)phenyl)boronic acid (71.5 mg, 0.40 mmol, 1.0 equiv), **1a** (116.6 mg, 0.44 mmol, 1.1 equiv), Cs₂CO₃ (160.7 mg, 0.48 mmol, 1.2 equiv), and THF (2 mL) was conducted at 50 °C for 48 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 85:15) gave the product as a pale yellow solid (49.0 mg, 82% yield).

Gram scale synthesis: A heat-gun-dried reaction flask containing a magnetic stir bar was charged with (4-(methoxycarbonyl)phenyl)boronic acid (1.80 g, 10 mmol, 1.0 equiv), **1a** (2.90 g, 11 mmol, 1.1 equiv), Cs₂CO₃ (3.92 g, 12 mmol, 1.2 equiv), and THF (20 mL). Then, the flask was sealed and placed in an aluminum block, which was preheated at 50 °C. After the mixture was stirred at 50 °C for 24 h, sat. NaHCO₃ aq. was added, and the mixture was extracted with CHCl₃ (3 × 50 mL). The combined organic layers were dried over Na₂SO₄, filtrated, and concentrated under reduced pressure to give the crude product. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 7:3) gave the product as a pale yellow solid (1.21 g, 80% yield).

¹H NMR: (400 MHz, CDCl₃) δ 7.90–7.78 (m, 2H), 6.72–6.57 (m, 2H), 4.05 (brs, 2H), 3.85 (s, 3H);

¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 167.1, 150.8, 131.6, 119.6, 113.8, 51.6

The analytical data for this compound were in excellent agreement with the reported data.^{10b}

(4-aminophenyl)(pyrrolidin-1-yl)methanone (5r)

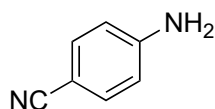
According to the general procedure **I**, the reaction using (4-(pyrrolidine-1-carbonyl)phenyl)boronic acid (78.1 mg, 0.40 mmol, 1.0 equiv), **1a** (116.7 mg, 0.44 mmol, 1.1 equiv), Cs₂CO₃ (155.4 mg, 0.48 mmol,

1.2 equiv), and THF (2 mL) was conducted at 50 °C for 24 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 3:7) gave the product as a yellow solid (65.6 mg, 86% yield).

^1H NMR: (400 MHz, CDCl_3) δ 7.41 (d, J = 8.4 Hz, 2H), 6.65 (d, J = 8.4 Hz, 2H), 3.86 (brs, 2H), 3.72–3.33 (m, 4H), 2.10–1.85 (m, 4H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 169.7, 148.1, 129.3, 126.8, 113.9, 49.8, 46.3, 26.5, 24.4

The analytical data for this compound were in excellent agreement with the reported data³⁵

4-aminobenzonitrile (5s)

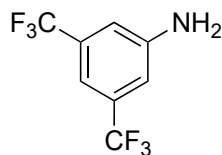


According to the general procedure **I**, the reaction using (4-cyanophenyl)boronic acid (58.6 mg, 0.40 mmol, 1.0 equiv), **1a** (116.1 mg, 0.44 mmol, 1.1 equiv), Cs_2CO_3 (158.7 mg, 0.48 mmol, 1.2 equiv), and THF (2 mL) was conducted at 50 °C for 48 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 7:3) gave the product as a white solid (44.6 mg, 94% yield).

^1H NMR: (400 MHz, CDCl_3) δ 7.42 (d, J = 8.8 Hz, 2H), 6.65 (d, J = 8.8 Hz, 2H), 4.16 (brs, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 150.3, 133.8, 120.1, 114.4, 100.2

The analytical data for this compound were in excellent agreement with the reported data.^{10b}

3,5-bis(trifluoromethyl)aniline (5t)



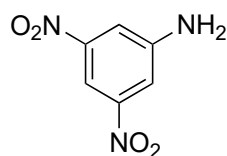
According to the general procedure **I**, the reaction using (3,5-bis(trifluoromethyl)phenyl)boronic acid (103.6 mg, 0.40 mmol, 1.0 equiv), **1a** (116.8 mg, 0.44 mmol, 1.1 equiv), Cs_2CO_3 (155.3 mg, 0.48 mmol, 1.2 equiv), and THF (2 mL) was conducted at 50 °C for 48 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 9:1) gave the product as a colorless oil (71.0 mg,

77% yield).

^1H NMR: (400 MHz, CDCl_3) δ 7.21 (s, 1H), 7.03 (s, 2H), 4.07 (brs, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 147.3, 132.5 (q, $J_{\text{CF}} = 32.9$ Hz), 123.4 (q, $J_{\text{CF}} = 271.1$ Hz), 114.1 (m), 111.5 (m)

The analytical data for this compound were in excellent agreement with the reported data.³⁶

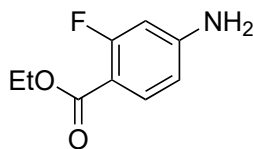
3,5-dinitroaniline (5u)



According to the general procedure **I**, the reaction using 2-(3,5-dinitrophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (58.5 mg, 0.20 mmol, 1.0 equiv), **1a** (58.5 mg, 0.22 mmol, 1.1 equiv), Cs_2CO_3 (81.9 mg, 0.24 mmol, 1.2 equiv), and THF (1 mL) was conducted at 50 °C for 48 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 7:3) gave the product as a yellow solid (30.9 mg, 83% yield).

m.p.: 146.0–147.8 °C; ^1H NMR: (400 MHz, CDCl_3) δ 8.36 (t, $J = 2.0$ Hz, 1H), 7.77 (d, $J = 2.0$ Hz, 2H), 4.42 (brs, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 149.4, 148.3, 113.7, 107.8; IR: (ATR) 3468, 3375, 3235, 3103, 1738, 1639, 1526, 1460, 1341, 1240, 1057, 1045, 1001, 881, 814 cm^{-1} ; HRMS (EI) m/z : M^+ Calculated for $\text{C}_6\text{H}_5\text{N}_3\text{O}_4$ 183.0280; Found 183.0274

ethyl 4-amino-2-fluorobenzoate (5v)

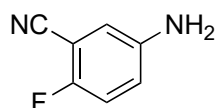


According to the general procedure **I**, the reaction using (4-(ethoxycarbonyl)-3-fluorophenyl)boronic acid (43.0 mg, 0.20 mmol, 1.0 equiv), **1a** (59.5 mg, 0.22 mmol, 1.1 equiv), Cs_2CO_3 (81.8 mg, 0.24 mmol, 1.2 equiv), and THF (1 mL) was conducted at 50 °C for 24 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 7:3) gave the product as a white solid (32.7 mg,

88% yield).

TLC: R_f = 0.30 (NH, hexane/EtOAc = 7:3); m.p.: 115.8–116.5 °C; ^1H NMR: (400 MHz, CDCl_3) δ 7.76 (dd, J = 8.0, 8.0 Hz, 1H), 6.41 (dd, J = 8.0, 2.0 Hz, 1H), 6.33 (dd, J = 16.8, 2.0 Hz, 1H), 4.33 (q, J = 7.2 Hz, 2H), 4.15 (brs, 2H), 1.36 (t, J = 7.2 Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 164.4 (d, J_{CF} = 4.1 Hz), 163.9 (d, J_{CF} = 256.9 Hz), 152.3 (d, J_{CF} = 12.3 Hz), 133.7 (d, J_{CF} = 2.5 Hz), 109.9 (d, J_{CF} = 2.5 Hz), 108.1 (d, J_{CF} = 9.9 Hz), 101.7 (d, J_{CF} = 25.6 Hz), 60.5, 14.3; $^{19}\text{F}\{^1\text{H}\}$ NMR: (377 MHz, CDCl_3) δ -110.6; IR: (ATR) 3421, 3340, 3219, 2986, 1690, 1632, 1609, 1568, 1510, 1456, 1441, 1368, 1346, 1294, 1267, 1076, 1024, 966, 881, 870, 849, 837 cm^{-1} ; HRMS (EI) m/z : M^+ Calculated for $\text{C}_9\text{H}_{10}\text{FNO}_2$ 183.0696; Found 183.0693

5-amino-2-fluorobenzonitrile (5w)

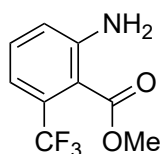


According to the general procedure **I**, the reaction using (3-cyano-4-fluorophenyl)boronic acid (66.4 mg, 0.40 mmol, 1.0 equiv), **1a** (117.5 mg, 0.44 mmol, 1.1 equiv), Cs_2CO_3 (155.8 mg, 0.48 mmol, 1.2 equiv), and THF (2 mL) was conducted at 50 °C for 24 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 7:3) gave the product as a pale yellow solid (41.4 mg, 76% yield).

^1H NMR: (400 MHz, CDCl_3) δ 7.07–6.92 (m, 1H), 6.92–6.75 (m, 2H), 3.74 (brs, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 156.5 (d, J_{CF} = 247.8 Hz), 143.1 (d, J_{CF} = 2.5 Hz), 121.6 (d, J_{CF} = 6.6 Hz), 117.6, 117.0 (d, J_{CF} = 20.6 Hz), 114.3, 101.2 (d, J_{CF} = 17.2 Hz)

The analytical data for this compound were in excellent agreement with the reported data.³⁷

methyl 2-amino-6-(trifluoromethyl)benzoate (5x)

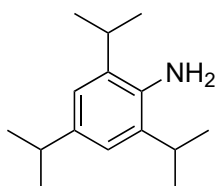


According to the general procedure **I**, the reaction using 2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-

yl)-6-(trifluoromethyl)benzoate (66.0 mg, 0.20 mmol, 1.0 equiv), **1a** (58.5 mg, 0.22 mmol, 1.1 equiv), Cs₂CO₃ (80.5 mg, 0.24 mmol, 1.2 equiv), and THF (2 mL) was conducted at 50 °C for 24 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 85:15) gave the product as a colorless oil (34.5 mg, 79% yield).

TLC: R_f = 0.13 (NH, hexane/EtOAc = 9:1); ¹H NMR: (400 MHz, CDCl₃) δ 7.28 (dd, J = 8.0, 8.0 Hz, 1H), 7.05 (d, J = 8.0 Hz, 1H), 6.87 (d, J = 8.0 Hz, 1H), 4.81 (brs, 2H), 3.91 (s, 3H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 168.0, 147.3, 131.3, 130.0 (q, J_{CF} = 31.1 Hz), 123.7 (q, J_{CF} = 271.7 Hz), 120.0, 116.1 (q, J_{CF} = 5.5 Hz), 113.3, 54.4; ¹⁹F{¹H} NMR: (377 MHz, CDCl₃) δ -62.0; IR: (ATR) 3487, 3389, 1711, 1616, 1472, 1435, 1342, 1279, 1155, 1126, 1090, 1049, 959, 914, 831, 806, 779 cm⁻¹; HRMS (ESI+) m/z : [M+Na]⁺ Calculated for C₉H₈NO₂F₃Na 242.0399; Found 242.0406

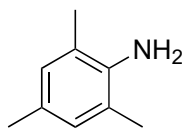
2,4,6-triisopropylaniline (**5y**)



According to the general procedure **I**, the reaction using (2,4,6-triisopropylphenyl)boronic acid (99.6 mg, 0.40 mmol, 1.0 equiv), **1a** (117.0 mg, 0.44 mmol, 1.1 equiv), Cs₂CO₃ (162.2 mg, 0.48 mmol, 1.2 equiv), and THF (2 mL) was conducted at 70 °C for 48 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 99:1) gave the product as a yellow oil (15.9 mg, 18% yield).

¹H NMR: (400 MHz, CDCl₃) δ 6.90 (s, 2H), 3.62 (brs, 2H), 2.93 (sep, J = 6.8 Hz, 2H), 2.83 (sep, J = 6.8 Hz, 1H), 1.28 (d, J = 6.8 Hz, 12H), 1.23 (d, J = 6.8 Hz, 6H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 138.7, 128.0, 132.4, 120.7, 33.8, 28.1, 24.4, 22.5

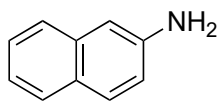
The analytical data for this compound were in excellent agreement with the reported data.³⁸

2,4,6-trimethylaniline (5z)

According to the general procedure **I**, the reaction using (2,4,6-trimethylphenyl)boronic acid (32.7 mg, 0.20 mmol, 1.0 equiv), **1a** (58.7 mg, 0.22 mmol, 1.1 equiv), Cs₂CO₃ (81.1 mg, 0.24 mmol, 1.2 equiv), and THF (1 mL) was conducted at 50 °C for 24 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 99:1) gave the product as a red oil (20.8 mg, 77% yield).

¹H NMR: (400 MHz, CDCl₃) δ 6.77 (s, 2H), 3.44 (brs, 2H), 2.21 (s, 3H), 2.16 (s, 6H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 140.1, 128.8, 127.1, 121.8, 20.3, 17.6

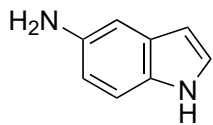
The analytical data for this compound were in excellent agreement with the reported data.^{10b}

naphthalen-2-amine (5aa)

According to the general procedure **I**, the reaction using naphthalen-2-ylboronic acid (69.2 mg, 0.40 mmol, 1.0 equiv), **1a** (116.5 mg, 0.44 mmol, 1.1 equiv), Cs₂CO₃ (160.1 mg, 0.48 mmol, 1.2 equiv), and THF (2 mL) was conducted at 50 °C for 24 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 9:1) gave the product as a pale red solid (48.2 mg, 84% yield).

¹H NMR: (400 MHz, CDCl₃) δ 7.69 (d, *J* = 8.0 Hz, 1H), 7.66 (d, *J* = 8.0 Hz, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.45–7.30 (m, 1H), 7.30–7.12 (m, 1H), 6.98 (d, *J* = 2.4 Hz, 1H), 6.94 (dd, *J* = 8.4, 2.4 Hz, 1H), 3.83 (brs, 2H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 144.1, 134.9, 129.2, 127.9, 127.7, 126.3, 125.8, 122.4, 118.2, 108.5

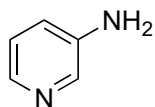
The analytical data for this compound were in excellent agreement with the reported data.^{10b}

1*H*-indol-5-amine (5ab)

According to the general procedure **I**, the reaction using indole-5-boronic acid (65.0 mg, 0.40 mmol, 1.0 equiv), **1a** (117.4 mg, 0.44 mmol, 1.1 equiv), Cs₂CO₃ (166.2 mg, 0.51 mmol, 1.3 equiv), and THF (2 mL) was conducted at room temperature for 24 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 7:3) gave the product as a pale yellow solid (38.5 mg, 73% yield).

¹H NMR: (400 MHz, CDCl₃) δ 7.95 (brs, 1H), 7.18 (d, *J* = 8.8 Hz, 1H), 7.11 (dd, *J* = 2.4, 2.4 Hz, 1H), 6.94 (d, *J* = 1.2 Hz, 1H), 6.66 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.42–6.28 (m, 1H), 3.46 (brs, 2H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 139.5, 130.7, 128.8, 124.7, 113.0, 111.5, 105.6, 101.6

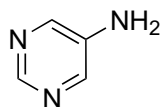
The analytical data for this compound were in excellent agreement with the reported data.³⁹

pyridin-3-amine (5ac)

According to the general procedure **I**, the reaction using pyridin-3-ylboronic acid (48.5 mg, 0.40 mmol, 1.0 equiv), **1a** (116.9 mg, 0.44 mmol, 1.1 equiv), Cs₂CO₃ (159.7 mg, 0.48 mmol, 1.2 equiv), and THF (2 mL) was conducted at 50 °C for 48 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 7:3) gave the product as a pale yellow solid (21.2 mg, 57% yield).

¹H NMR: (400 MHz, CDCl₃) δ 8.10 (d, *J* = 2.8 Hz, 1H), 8.02 (dd, *J* = 4.8, 1.2 Hz, 1H), 7.10–7.05 (m, 1H), 6.97 (ddd, *J* = 8.0, 2.8, 1.2 Hz, 1H), 3.70 (brs, 2H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 142.4, 140.0, 137.5, 123.7, 121.4

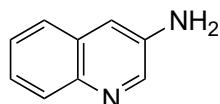
The analytical data for this compound were in excellent agreement with the reported data.³⁴

pyrimidin-5-amine (5ad)

An oven-dried reaction vial containing a magnetic stir bar was charged with pyrimidin-5-ylboronic acid (49.3 mg, 0.40 mmol, 1.0 equiv), hypervalent iodine reagent **1a** (119.8 mg, 0.44 mmol, 1.1 equiv), Cs₂CO₃ (160.1 mg, 0.48 mmol, 1.2 equiv), and THF (2 mL). Then, the vial was sealed and placed in an aluminum block, which was preheated at 50 °C, then the mixture was stirred at 50 °C for 48 h. The precipitation was removed by filtration, and the filtrate was then concentrated under reduced pressure to give the product as a pale yellow solid (30.0 mg, 79% yield).

¹H NMR: (400 MHz, CDCl₃) δ 8.66 (s, 1H), 8.22 (s, 2H), 3.75 (brs, 2H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 149.7, 142.9, 140.4

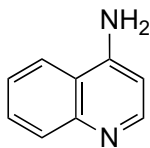
The analytical data for this compound were in excellent agreement with the reported data.³⁴

quinolin-3-amine (5ae)

An oven-dried reaction vial containing a magnetic stir bar was charged with quinoline-3-boronic acid (34.3 mg, 0.20 mmol, 1.0 equiv), **1a** (57.7 mg, 0.22 mmol, 1.1 equiv), Cs₂CO₃ (80.7 mg, 0.24 mmol, 1.2 equiv), and THF (1 mL). The vial was sealed and placed in an aluminum block, which was preheated at 50 °C, then the mixture was stirred at 50 °C for 24 h. The precipitation was removed by filtration, and the filtrate was concentrated under reduced pressure to give the crude product. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 7:3) gave the product as a yellow solid (23.1 mg, 80% yield).

¹H NMR: (400 MHz, CDCl₃) δ 8.51 (d, *J* = 2.8 Hz, 1H), 8.00–7.85 (m, 1H), 7.62–7.55 (m, 1H), 7.48–7.39 (m, 2H), 7.24 (d, *J* = 2.8 Hz, 1H), 3.91 (brs, 2H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 143.1, 142.8, 139.7, 129.12, 129.10, 126.9, 125.8, 125.6, 115.0

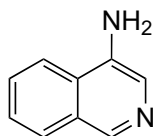
The analytical data for this compound were in excellent agreement with the reported data.⁴⁰

quinolin-4-amine (5af)

An oven-dried reaction vial containing a magnetic stir bar was charged with quinoline-4-boronic acid (69.4 mg, 0.40 mmol, 1.0 equiv), **1a** (117.4 mg, 0.44 mmol, 1.1 equiv), Cs₂CO₃ (156.4 mg, 0.48 mmol, 1.2 equiv), and THF (2 mL). The vial was sealed and placed in an aluminum block, which was preheated at 50 °C, then the mixture was stirred at 50 °C for 24 h. The precipitation was removed by filtration, and the filtrate was concentrated under reduced pressure to give the crude product. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 6:4) gave the product as a pale yellow solid (41.4 mg, 72% yield).

¹H NMR: (400 MHz, CDCl₃) δ 8.54 (d, *J* = 5.2 Hz, 1H), 8.01 (d, *J* = 8.8 Hz, 1H), 7.77 (d, *J* = 8.8 Hz, 1H), 7.70–7.60 (m, 1H), 7.50–7.40 (m, 1H), 6.60 (d, *J* = 5.2 Hz, 1H), 4.77 (brs, 2H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 150.7, 149.5, 148.9, 129.9, 129.3, 124.8, 120.1, 118.8, 103.7

The analytical data for this compound were in excellent agreement with the reported data.⁴⁰

isoquinolin-4-amine (5ag)

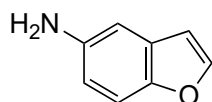
An oven-dried reaction vial containing a magnetic stir bar was charged with 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)isoquinoline (51.0 mg, 0.20 mmol, 1.0 equiv), **1a** (58.5 mg, 0.22 mmol, 1.1 equiv), Cs₂CO₃ (81.9 mg, 0.24 mmol, 1.2 equiv), and THF (1 mL). The vial was sealed and placed in an aluminum block, which was preheated at 50 °C, then the mixture was stirred at 50 °C for 24 h. The precipitation was removed by filtration, and the filtrate was concentrated under reduced pressure to give the crude product. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 7:3) gave the product as a pale yellow solid (23.7 mg, 82% yield).

¹H NMR: (400 MHz, CDCl₃) δ 8.74, (s, 1H), 8.04 (s, 1H), 7.91 (d, *J* = 8.8 Hz, 1H), 7.80 (d, *J* = 8.8 Hz,

1H), 7.70–7.60 (m, 1H), 7.60–7.50 (m, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 143.4, 136.7, 129.0, 128.6, 128.2, 127.8, 127.0, 126.1, 120.0

The analytical data for this compound were in excellent agreement with the reported data.³⁴

benzofuran-5-amine (5ah)

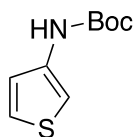


An oven-dried reaction vial containing a magnetic stir bar was charged with 2-(benzofuran-5-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (49.2 mg, 0.20 mmol, 1.0 equiv), **1a** (59.0 mg, 0.22 mmol, 1.1 equiv), Cs_2CO_3 (80.2 mg, 0.24 mmol, 1.2 equiv), and THF (1 mL). The vial was sealed and placed in an aluminum block, which was preheated at 50 °C, then the mixture was stirred at 50 °C for 24 h. The precipitation was removed by filtration, and the filtrate was concentrated under reduced pressure to give the crude product. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 9:1) gave the product as a pale yellow oil (20.2 mg, 76% yield).

^1H NMR: (400 MHz, CDCl_3) δ 7.52 (d, J = 1.6 Hz, 1H), 7.32–7.20 (m, 1H), 6.90–6.80 (m, 1H), 6.66 (dd, J = 8.8, 2.4 Hz, 1H), 6.59 (d, J = 1.6 Hz, 1H), 3.55 (brs, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 149.5, 145.4, 142.0, 128.2, 113.6, 111.6, 106.1, 106.0

The analytical data for this compound were in excellent agreement with the reported data.^{14e}

tert-butyl thiophen-3-ylcarbamate (5ai)



An oven-dried reaction vial containing a magnetic stir bar was charged with thiophen-3-ylboronic acid (51.0 mg, 0.40 mmol, 1.0 equiv), **1a** (117.3 mg, 0.44 mmol, 1.1 equiv), Cs_2CO_3 (154.7 mg, 0.48 mmol, 1.2 equiv), and THF (2 mL). The vial was sealed and placed in an aluminum block, which was preheated at 50 °C, then the mixture was stirred at 50 °C for 24 h. The precipitation was removed by

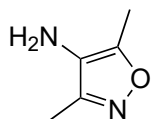
filtration, and the filtrate was concentrated under reduced pressure to give the crude product. To a solution of the crude product in THF (4 mL), triethylamine (140 μ L, 1.0 mmol, 2.5 equiv) and di-*tert*-butyl dicarbonate (149.0 mg, 0.68 mmol, 1.7 equiv) were added. After the mixture was stirred at room temperature for 24 h, the excess of di-*tert*-butyl dicarbonate was quenched by the addition of MeOH (2 mL). The solvent was removed under reduced pressure to give the crude product. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 9:1) gave the product as a pale yellow solid (32.0 mg, 40% yield).

^1H NMR: (400 MHz, CDCl_3) δ 7.30–7.23 (m, 2H), 6.98–6.85 (m, 1H), 6.72 (brs, 1H), 1.51 (s, 9H);

$^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 152.7, 136.0, 124.6, 120.6, 107.2, 28.3

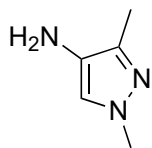
The analytical data for this compound were in excellent agreement with the reported data.⁴⁰

3,5-dimethylisoxazol-4-amine (5aj)



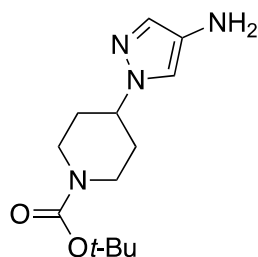
An oven-dried reaction vial containing a magnetic stir bar was charged with 3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)isoxazole (88.4 mg, 0.40 mmol, 1.0 equiv), **1a** (117.4 mg, 0.44 mmol, 1.1 equiv), Cs_2CO_3 (157.6 mg, 0.48 mmol, 1.2 equiv), and THF (2 mL). Then, the vial was sealed and placed in an aluminum block, which was preheated at 50 $^\circ\text{C}$., then the mixture was stirred at 50 $^\circ\text{C}$ for 24 h. The precipitation was removed by filtration, and the filtrate was concentrated under reduced pressure to give the crude product. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 7:3) gave the product as a yellow oil (36.0 mg, 80% yield).

TLC: R_f = 0.20 (NH, hexane/EtOAc = 7:3); ^1H NMR: (400 MHz, CDCl_3) δ 2.50 (brs, 2H), 2.28 (s, 3H), 2.20 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 155.1, 154.2, 120.6, 10.2, 9.3; IR: (ATR) 3329, 1658, 1479, 1427, 1271, 1211, 1015, 901, 754 cm^{-1} ; HRMS (EI+) m/z : M^+ Calculated for $\text{C}_5\text{H}_8\text{N}_2\text{O}$ 112.0637; Found 112.0639

1,3-dimethyl-1*H*-pyrazol-4-amine (5ak)

An oven-dried reaction vial containing a magnetic stir bar was charged with 1,3-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-pyrazole (88.0 mg, 0.40 mmol, 1.0 equiv), **1a** (162.7 mg, 0.62 mmol, 1.5 equiv), Cs₂CO₃ (206 mg, 0.63 mmol, 1.5 equiv), and THF (2 mL). The vial was sealed, and the mixture was stirred at room temperature for 48 h. The precipitation was removed by filtration, and the filtrate was concentrated under reduced pressure to give the crude product. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 7:3) gave the product as a red oil (19.5 mg, 44% yield).

TLC: R_f = 0.10 (NH, hexane/EtOAc = 1:1); ¹H NMR: (400 MHz, CDCl₃) δ 6.93 (s, 1H), 3.73 (s, 3H), 2.64 (brs, 2H), 2.17 (s, 3H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 138.9, 126.1, 119.9, 38.7, 10.5; IR: (ATR) 3319, 3211, 2924, 1730, 1622, 1582, 1437, 1416, 1360, 1325, 1233, 1001, 812, 766 cm⁻¹; HRMS (CI) m/z : [M+H]⁺ Calculated for C₅H₁₀N₃ 112.0875; Found 112.0871

***tert*-butyl 4-(4-amino-1*H*-pyrazol-1-yl)piperidine-1-carboxylate (5al)**

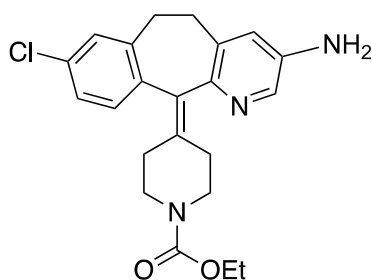
According to the general procedure **I**, the reaction using *tert*-butyl 4-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-pyrazol-1-yl)piperidine-1-carboxylate (75.6 mg, 0.20 mmol, 1.0 equiv), **1a** (79.0 mg, 0.30 mmol, 1.5 equiv), Cs₂CO₃ (110.1 mg, 0.33 mmol, 1.5 equiv), and THF (1 mL) was conducted at room temperature for 24 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 7:3) gave the product as a red oil (36.0 mg, 68% yield).

¹H NMR: (400 MHz, DMSO-*d*₆) δ 7.05 (s, 1H), 6.89 (s, 1H), 4.11 (tt, J = 12.0, 4.0 Hz, 1H), 4.04–3.90

(m, 2H), 3.79 (br, 2H), 2.83 (br, 2H), 1.91–1.84 (m, 2H), 1.66 (dddd, $J = 12.0, 12.0, 12.0, 4.0$ Hz, 2H), 1.39 (s, 9H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, DMSO- d_6) δ 153.9, 130.6, 128.9, 114.4, 78.8, 57.7, 42.5, 31.9, 28.1

The analytical data for this compound were in excellent agreement with the reported data.⁴¹

ethyl 4-(3-amino-8-chloro-5,6-dihydro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-ylidene)piperidine-1-carboxylate (5am)

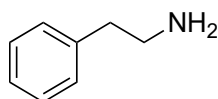


Ethyl 4-(8-chloro-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,6-dihydro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-ylidene)piperidine-1-carboxylate (**4am**) was prepared by the reported procedure.⁴² Purification by flash column chromatography on silica gel (hexane/EtOAc = 3:7) gave the product (90.0 mg).

According to the general procedure **I**, the reaction using **4am** (90.0 mg, 0.177 mmol, 1.0 equiv), **1a** (52.8 mg, 0.20 mmol, 1.1 equiv), Cs_2CO_3 (72.2 mg, 0.22 mmol, 1.2 equiv), and THF (2 mL) was conducted at 50 °C for 24 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 7:3) gave the product as a white solid (46.2 mg, 66% yield).

^1H NMR: (400 MHz, DMSO- d_6) δ 7.71 (d, $J = 2.4$ Hz, 1H), 7.28 (d, $J = 2.4$ Hz, 1H), 7.17 (dd, $J = 8.0, 2.4$ Hz, 1H), 7.01 (d, $J = 8.0$ Hz, 1H), 6.65 (d, $J = 2.4$ Hz, 1H), 5.26–5.10 (br, 2H), 4.02 (q, $J = 7.2$ Hz, 2H), 3.65–3.50 (m, 2H), 3.30–3.00 (m, 4H), 2.80–2.60 (m, 2H), 2.36–2.05 (m, 4H), 1.16 (t, $J = 7.2$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, DMSO- d_6) δ 154.5, 143.9, 143.6, 140.6, 139.4, 134.9, 133.7, 133.1, 132.8, 131.1, 130.1, 128.5, 125.5, 121.0, 60.6, 44.5, 31.1, 30.9, 30.4, 30.2, 14.6 (one sp^3 signal was not observed because of overlapping)

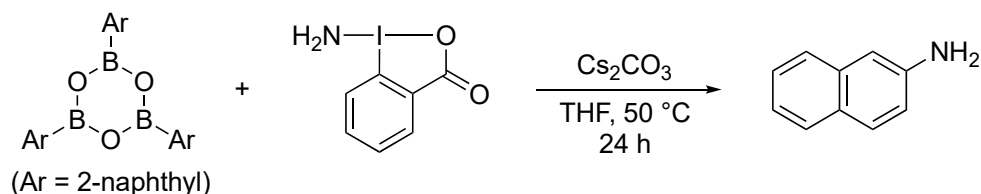
The analytical data for this compound were in excellent agreement with the reported data.⁴³

2-phenylethan-1-amine (5an)

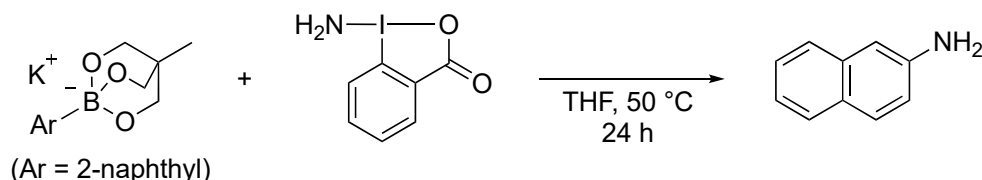
According to the general procedure **I**, the reaction using phenethylboronic acid (60.6 mg, 0.40 mmol, 1.0 equiv), **1a** (116.1 mg, 0.44 mmol, 1.1 equiv), Cs₂CO₃ (163.3 mg, 0.48 mmol, 1.2 equiv), and THF (2 mL) was conducted at 50 °C for 24 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 7:3) gave the product as a colorless oil (27.6 mg, 57% yield).

¹H NMR: (400 MHz, CDCl₃) δ 7.34–7.28 (m, 2H), 7.25–7.16 (m, 3H), 2.97 (t, *J* = 6.8 Hz, 2H), 2.75 (t, *J* = 6.8 Hz, 2H), 1.31 (brs, 2H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 139.8, 128.8, 128.4, 126.1, 43.6, 40.1

The analytical data for this compound were in excellent agreement with the reported data.^{13b}

amination of a boroxine as a substrate

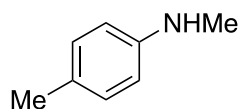
According to the general procedure **I**, the reaction using 2,4,6-tri-2-naphthalenylboroxine (31.4 mg, 0.067 mmol, 0.33 equiv), **1a** (58.4 mg, 0.22 mmol, 1.1 equiv), Cs₂CO₃ (76.6 mg, 0.24 mmol, 1.2 equiv), and THF (1 mL) was conducted at 50 °C for 24 h. The crude product was analyzed by ¹H NMR spectroscopy using 1,1,2,2-tetrachloroethane as an internal standard (92% yield).

amination of a (triol)borate as a substrate

According to the general procedure **I**, the reaction using potassium 2-naphthyltriolborate (59.1 mg, 0.20 mmol, 1.0 equiv), **1a** (57.7 mg, 0.22 mmol, 1.1 equiv), and THF (1 mL) was conducted at 50 °C for 24

h. The crude product was analyzed by ^1H NMR spectroscopy using 1,1,2,2-tetrachloroethane as an internal standard (86% yield).

***N*,4-dimethylaniline (5ao)**

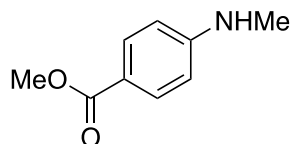


According to the general procedure **II**, the reaction using MS3A (404 mg), 4-methylphenylboronic acid (55.0 mg, 0.40 mmol), **1b** (122.0 mg, 0.44 mmol), Cs_2CO_3 (162.3 mg, 0.48 mmol), and THF (2 mL) was conducted at 50 °C for 24 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 99:1) gave the product as a colorless oil (38.6 mg, 80% yield).

^1H NMR: (400 MHz, CDCl_3) δ 7.00 (d, J = 8.8 Hz, 2H), 6.62–6.43 (m, 2H), 3.53 (brs, 1H), 2.80 (s, 3H), 2.24 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 147.1, 129.7, 126.5, 112.6, 31.1, 20.4

The analytical data for this compound were in excellent agreement with the reported data.⁴⁴

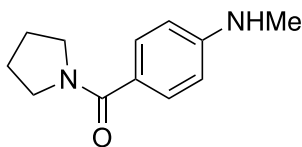
methyl 4-(methylanino)benzoate (5ap)



According to the general procedure **II**, the reaction using MS3A (808 mg), (4-(methoxycarbonyl)phenyl)boronic acid (72.6 mg, 0.40 mmol), **1b** (124.0 mg, 0.44 mmol), Cs_2CO_3 (156.5 mg, 0.48 mmol), and THF (2 mL) was conducted at 50 °C for 24 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 9:1) gave the product as a white solid (33.6 mg, 51% yield).

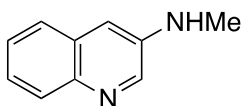
^1H NMR: (400 MHz, CDCl_3) δ 7.88 (d, J = 8.8 Hz, 2H), 6.55 (d, J = 8.8 Hz, 2H), 4.20 (brs, 1H), 3.85 (s, 3H), 2.89 (d, J = 4.0 Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 167.4, 152.8, 131.5, 118.1, 111.0, 51.5, 30.1

The analytical data for this compound were in excellent agreement with the reported data.⁴⁴

(4-(methylanino)phenyl)(pyrrolidin-1-yl)methanone (5aq)

According to the general procedure **II**, the reaction using MS3A (205 mg), (4-(pyrrolidine-1-carbonyl)phenyl)boronic acid (44.0 mg, 0.20 mmol), **1b** (61.0 mg, 0.22 mmol), Cs₂CO₃ (77.3 mg, 0.24 mmol), and THF (2 mL) was conducted at 50 °C for 24 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 1:1) gave the product as a pale yellow solid (23.4 mg, 57% yield).

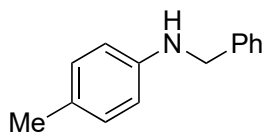
m.p.: 146.5–147.7 °C; TLC: *R_f* = 0.15 (NH, hexane/EtOAc = 1:1); ¹H NMR: (400 MHz, CDCl₃) δ 7.45 (d, *J* = 8.8 Hz, 2H), 6.56 (d, *J* = 8.8 Hz, 2H), 4.03 (brs, 1H), 3.80–3.40 (m, 4H), 2.85 (s, 3H), 2.10–1.80 (m, 4H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 169.9, 150.6, 129.3, 125.1, 111.1, 49.9, 46.3, 30.3, 26.5, 24.4; IR: (ATR) 3288, 2976, 2957, 2924, 2866, 2808, 1593, 1557, 1531, 1491, 1398, 1346, 1333, 1283, 1227, 1186, 1109, 1072, 1032, 922, 851, 831, 764 cm⁻¹; HRMS (EI) *m/z*: M⁺ Calculated for C₁₂H₁₆N₂O 204.1263; Found 204.1262

N-methylquinolin-3-amine (5arr)

According to the general procedure **II**, the reaction using MS3A (405 mg), quinolin-3-ylboronic acid (69.5 mg, 0.40 mmol), **1b** (122.4 mg, 0.44 mmol), Cs₂CO₃ (155.0 mg, 0.48 mmol), and THF (2 mL) was conducted at 50 °C for 24 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 8:2) gave the product as a pale yellow solid (39.2 mg, 62% yield).

¹H NMR: (400 MHz, CDCl₃) δ 8.43 (d, *J* = 2.4 Hz, 1H), 7.95 (d, *J* = 8.4 Hz, 1H), 7.72–7.55 (m, 1H), 7.55–7.32 (m, 2H), 7.00 (d, *J* = 2.4 Hz, 1H), 4.10 (brs, 1H), 2.94 (d, *J* = 4.8 Hz, 3H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 143.3, 142.5, 142.0, 129.5, 128.9, 126.9, 125.9, 124.8, 109.4, 30.3

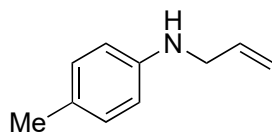
The analytical data for this compound were in excellent agreement with the reported data.⁴⁵

***N*-benzyl-4-methylaniline (5as)**

According to the general procedure **II**, the reaction using MS3A (201 mg), 4-methylphenylboronic acid (27.2 mg, 0.20 mmol), **1c** (78.0 mg, 0.22 mmol), Cs₂CO₃ (78.7 mg, 0.24 mmol), and THF (2 mL) was conducted at 50 °C for 24 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 99:1) gave the product as a colorless oil (34.0 mg, 86% yield).

¹H NMR: (400 MHz, CDCl₃) δ 7.45–7.20 (m, 5H), 6.98 (d, *J* = 8.0 Hz, 2H), 6.55 (d, *J* = 8.0 Hz, 2H), 4.29 (s, 2H), 3.89 (brs, 1H), 2.23 (s, 3H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 145.9, 139.6, 129.7, 128.6, 127.5, 127.1, 126.7, 113.0, 48.6, 20.4

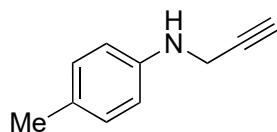
The analytical data for this compound were in excellent agreement with the reported data.⁴⁶

***N*-allyl-4-methylaniline (5att)**

According to the general procedure **II**, the reaction using MS3A (417 mg), 4-methylphenylboronic acid (55.0 mg, 0.40 mmol), **1d** (134.9 mg, 0.44 mmol), Cs₂CO₃ (159.0 mg, 0.48 mmol), and THF (4 mL) was conducted at 50 °C for 24 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 99:1) gave the product as a colorless oil (36.2 mg, 61% yield).

¹H NMR: (400 MHz, CDCl₃) δ 6.99 (d, *J* = 8.4 Hz, 2H), 6.56 (d, *J* = 8.4 Hz, 2H), 6.05–5.85 (m, 1H), 5.27 (d, *J* = 17.6 Hz, 1H), 5.15 (d, *J* = 10.4 Hz, 1H), 3.76 (d, *J* = 5.2 Hz, 2H), 3.64 (brs, 1H), 2.24 (s, 3H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 145.8, 135.6, 129.7, 126.7, 116.1, 113.2, 46.9, 20.4

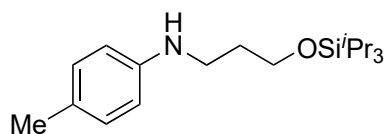
The analytical data for this compound were in excellent agreement with the reported data.⁴⁷

4-methyl-*N*-(prop-2-yn-1-yl)aniline (5au)

According to the general procedure **II**, the reaction using MS3A (405 mg), 4-methylphenylboronic acid (54.1 mg, 0.40 mmol), **1e** (132.7 mg, 0.44 mmol), Cs₂CO₃ (164.0 mg, 0.50 mmol), and THF (4 mL) was conducted at 50 °C for 24 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 99:1) gave the product as a pale yellow solid (29.8 mg, 52% yield).

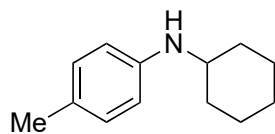
¹H NMR: (400 MHz, CDCl₃) δ 7.03 (d, *J* = 8.0 Hz, 2H), 6.68–6.55 (m, 2H), 3.98–3.83 (m, 2H), 3.72 (brs, 1H), 2.25 (s, 3H), 2.20 (t, *J* = 2.4 Hz, 1H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 144.5, 129.7, 128.0, 113.7, 81.2, 71.2, 33.9, 20.4

The analytical data for this compound were in excellent agreement with the reported data.⁴⁸

4-methyl-*N*-(3-((triisopropylsilyl)oxy)propyl)aniline (5av)

According to the general procedure **II**, the reaction using MS3A (215 mg), 4-methylphenylboronic acid (27.6 mg, 0.20 mmol), **1f** (106.4 mg, 0.22 mmol), Cs₂CO₃ (90.9 mg, 0.28 mmol), and THF (2 mL) was conducted at 50 °C for 24 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 99:1) gave the product as a colorless oil (44.9 mg, 70% yield).

TLC: *R_f* = 0.73 (NH, hexane/EtOAc = 9:1); ¹H NMR: (400 MHz, CDCl₃) δ 6.97 (d, *J* = 8.4 Hz, 2H), 6.53 (d, *J* = 8.4 Hz, 2H), 3.99 (brs, 1H), 3.84 (t, *J* = 5.6 Hz, 2H), 3.24 (t, *J* = 6.4 Hz, 2H), 2.23 (s, 3H), 1.90–1.80 (m, 2H), 1.20–0.95 (m, 21H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 146.4, 129.7, 126.1, 112.8, 62.4, 42.4, 32.1, 20.4, 18.0, 11.9; IR: (ATR) 3399, 2041, 2292, 2891, 2864, 1620, 1520, 1462, 1383, 1317, 1258, 1096, 1070, 1013, 995, 881, 804 cm⁻¹; HRMS (EI) *m/z*: M⁺ Calculated for C₁₉H₃₅NOSi 321.2488; Found 321.2495

***N*-cyclohexyl-4-methylaniline (5aw)**

According to the general procedure **II**, the reaction using MS3A (406 mg), 4-methylphenylboronic acid (27.5 mg, 0.20 mmol), **1g** (77.8 mg, 0.22 mmol), Cs₂CO₃ (82.8 mg, 0.24 mmol), and THF (2 mL) was conducted at 70 °C for 24 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 99:1) gave the product as a colorless oil (18.8 mg, 50% yield).

¹H NMR: (400 MHz, CDCl₃) δ 6.96 (d, *J* = 8.4 Hz, 2H), 6.51 (d, *J* = 8.4 Hz, 2H), 3.34 (brs, 1H), 3.25–3.15 (m, 1H), 2.22 (s, 3H), 2.08–1.96 (m, 2H), 1.82–1.70 (m, 2H), 1.70–1.58 (m, 1H), 1.43–1.28 (m, 2H), 1.28–1.00 (m, 3H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 145.1, 129.7, 126.1, 113.5, 52.0, 33.5, 26.0, 25.0, 20.3

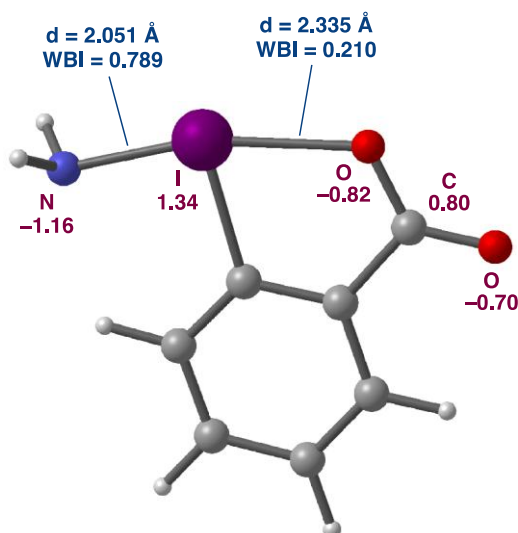
The analytical data for this compound were in excellent agreement with the reported data.⁴⁹

Computational studies

Density functional theory (DFT) computations were performed in Gaussian 16, Revision C.01.⁵⁰ Molecular geometries were optimized using M06-2X density functional in the 6-31+g(d,p)-LANL2DZ(I,Cs) basis set with the SMD solvation model (THF). Harmonic frequency calculations were performed at the same level of theory as that used for geometry optimization to characterize the stationary points as either minima (no imaginary frequencies) or first-order saddle points (one imaginary frequency). Intrinsic Reaction Coordinate (IRC) calculations were performed to confirm that the first-order saddle points found were real transition states connecting the reactants and the products. The thermal energy corrections for the optimized geometries were calculated at M06-2X level of theory in the 6-311++g(d,p)-SDD(I,Cs) basis set with the SMD solvation model (THF). The zero-point energies (ZPE) and thermal energy corrections were calculated using vibrational frequencies with GoodVibes v3.1.1⁵¹ employing a quasi-harmonic approximation for entropy calculation at pressure of 1.0 atm and temperature of 323.15 K with frequency cut-off value of 100 cm⁻¹, as proposed by Grimme.

Natural bond orbital (NBO) analyses were performed by NBO version 3.0 or 7.0 programs as including in Gaussian. Molecular structure visualizations were obtained using CYLview.⁵²

Selected distances, WBIs, and NBO charges of 1a



Calculated energies and thermochemical parameters

structure	E [hartree]	H [hartree]	TS [hartree]	G [hartree]
1a	-486.805527	-486.673093	0.053538	-486.726631
PhB(OH)₂	-408.235782	-408.100488	0.046078	-408.146566
INT1	-895.052952	-894.782394	0.076545	-894.858939
Cs₂CO₃	-304.139043	-304.114231	0.051383	-304.165614
CsHCO₃	-284.597504	-284.562640	0.043325	-284.605965
INT2	-914.635855	-914.376279	0.086142	-914.462421
TS1	-914.613886	-914.356256	0.087047	-914.443304
TS1'	-895.001774	-894.733272	0.077584	-894.810856
9	-463.623113	-463.469460	0.049513	-463.518972
10	-451.131680	-451.025562	0.059511	-451.085073
Cs₊ cation	-20.034938	-20.032380	0.021096	-20.053476
INT2'	-914.635998	-914.376225	0.085230	-914.461455
INT2''	-894.575199	-894.318853	0.076513	-894.395367
PhBpin	-642.852064	-642.561208	0.061689	-642.622897
INT1_p	-1129.669212	-1129.243280	0.090378	-1129.333658

INT2_p	-1149.250988	-1148.836334	0.100916	-1148.937250
TS1_p	-1149.231100	-1148.818055	0.101522	-1148.919576
TS1'_p	-1129.619096	-1129.194974	0.091910	-1129.286884
9_p	-698.239140	-697.929750	0.064367	-697.994117

Cartesian coordinates of computed structures

1a				H	2.48644	2.14935	-0.03313
I	-1.45779	0.19383	-0.00000	H	0.00850	2.14678	-0.02933
O	-0.07585	2.07644	-0.00014	H	0.00866	-2.14688	0.02932
O	2.08799	2.67757	0.00009	H	2.48659	-2.14927	0.03314
C	0.52137	-0.58789	-0.00004	H	3.72894	0.00007	0.00002
C	0.75621	-1.95179	-0.00010	B	-1.73821	-0.00001	-0.00001
H	-0.07050	-2.65359	-0.00023	O	-2.38136	-1.20893	-0.03621
C	2.08675	-2.37662	-0.00003	H	-3.34639	-1.17497	-0.02851
H	2.30260	-3.44058	-0.00002	O	-2.38130	1.20895	0.03622
C	3.12946	-1.44849	0.00004	H	-3.34633	1.17496	0.02853
H	4.15918	-1.79139	0.00010				
C	2.85142	-0.08444	0.00003	INT1			
H	3.64485	0.65646	0.00003	I	0.86995	-0.92658	-0.06249
C	1.52880	0.36327	-0.00000	O	2.92122	-1.72470	-0.12409
C	1.18825	1.84046	0.00003	O	5.08230	-1.14177	-0.07841
N	-2.23110	-1.70568	0.00013	C	2.05978	0.83682	-0.06061
H	-2.81307	-1.83147	0.82648	C	1.55264	2.12731	-0.08261
H	-2.81307	-1.83164	-0.82620	H	0.49062	2.34074	-0.10756
				C	2.46456	3.18527	-0.08652
PhB(OH)₂				H	2.08829	4.20312	-0.10417
C	1.94409	1.20836	-0.01803	C	3.83879	2.94495	-0.07232
C	0.54984	1.20424	-0.01646	H	4.53404	3.77801	-0.07428
C	-0.16959	-0.00006	-0.00001	C	4.31699	1.63848	-0.06452
C	0.54992	-1.20429	0.01645	H	5.38058	1.42166	-0.06408
C	1.94419	-1.20831	0.01803	C	3.42068	0.56954	-0.06362
C	2.64254	0.00004	0.00000	C	3.89432	-0.86034	-0.08657

H	-0.85571	0.92877	0.81797	O	3.53948	0.06890	0.00047
H	-1.10561	0.71962	-0.80506	H	3.82358	-0.85520	0.00051
N	-0.93607	0.22932	0.07644				
B	-2.16231	-0.82342	0.45800	INT2			
O	-1.83637	-1.94523	-0.40968	I	-0.35379	-0.43611	-0.22682
H	-2.14753	-2.76866	-0.01747	O	3.67524	1.60523	0.00449
O	-1.97090	-1.15209	1.85068	C	0.03316	1.66121	-0.14159
H	-2.68383	-0.82810	2.40974	C	-1.05326	2.52135	-0.15238
C	-3.54596	-0.05291	0.11834	H	-2.06062	2.11811	-0.20492
C	-4.31036	-0.40064	-1.00476	C	-0.80886	3.89414	-0.08831
C	-4.02551	0.99563	0.92201	H	-1.64776	4.58339	-0.09221
C	-5.50297	0.25816	-1.31251	C	0.49890	4.37464	-0.01685
H	-3.96118	-1.20791	-1.64475	H	0.68393	5.44317	0.03277
C	-5.21493	1.66347	0.62585	C	1.56749	3.48255	-0.00443
H	-3.46215	1.30393	1.80350	H	2.59400	3.83040	0.05430
C	-5.95873	1.29392	-0.49626	C	1.34921	2.10286	-0.06396
H	-6.07790	-0.03615	-2.18660	C	2.52247	1.13898	-0.03174
H	-5.56247	2.46896	1.26728	N	-2.34902	-0.18152	-0.41326
H	-6.88609	1.80876	-0.73082	H	-2.58073	-0.51098	-1.35246
				B	-3.17296	-0.93115	0.71106
Cs₂CO₃				O	-2.68241	-2.32544	0.72683
O	-1.12623	1.96731	0.04333	H	-3.11657	-2.82323	1.42863
O	0.00040	0.02679	0.14125	O	-2.98744	-0.27268	2.00222
Cs	-3.01428	-0.36106	-0.01251	H	-2.15511	-0.55134	2.39968
C	-0.00222	1.33397	0.03297	C	-4.72278	-0.77555	0.23492
O	1.11903	1.96124	-0.08506	C	-5.32388	-1.70779	-0.62429
Cs	3.01551	-0.35979	-0.00556	C	-5.50620	0.31846	0.63641
				C	-6.64243	-1.56283	-1.06512
CsHCO₃				H	-4.74457	-2.57121	-0.94785
O	1.59983	1.15449	-0.00036	C	-6.82447	0.47779	0.20520
O	1.62919	-1.10347	-0.00040	H	-5.06851	1.05413	1.30811
Cs	-1.28898	-0.00607	0.00005	C	-7.39846	-0.46570	-0.65032
C	2.15373	0.03828	-0.00015	H	-7.08137	-2.30444	-1.72818

H	-7.40721	1.33415	0.53585	C	6.81438	0.03837	2.02806
H	-8.42458	-0.34739	-0.98779	H	6.83447	-2.07840	2.43621
O	2.20983	-0.09346	-0.04252	H	6.55176	2.09565	1.43478
Cs	5.16729	-1.16881	-0.00073	H	7.64019	0.25576	2.69947
TS1				O	-2.52622	-0.11131	-0.47437
				Cs	-5.43075	-0.75806	0.49580
I	0.32882	-0.85942	-0.57350	TS1'			
O	-3.41365	1.61789	0.64869				
C	0.06320	1.24987	-0.41629				
C	1.20809	2.01939	-0.61094	I	0.98593	-1.09233	-0.02354
H	2.15514	1.54311	-0.84571	O	3.63964	-1.60326	-0.00956
C	1.11870	3.40612	-0.49902	O	5.52286	-0.37179	-0.00319
H	2.00698	4.01024	-0.65832	C	2.04528	0.76766	-0.01586
C	-0.10027	4.00425	-0.18350	C	1.30796	1.94907	-0.01789
H	-0.17276	5.08351	-0.08907	H	0.22313	1.94401	-0.01931
C	-1.22706	3.21145	0.00729	C	1.98272	3.16885	-0.02155
H	-2.18653	3.65214	0.25788	H	1.41174	4.09214	-0.02523
C	-1.17689	1.81663	-0.11903	C	3.37644	3.19405	-0.02169
C	-2.48533	1.03617	0.03972	H	3.90559	4.14179	-0.02584
N	2.63425	-0.63334	0.13258	C	4.08624	1.99851	-0.01702
H	2.59623	-1.43846	0.77022	H	5.17145	1.98576	-0.01628
B	3.59621	-0.90712	-0.98073	C	3.43705	0.75796	-0.01385
O	3.63904	-2.26732	-1.43358	C	4.28980	-0.52308	-0.00854
H	4.29054	-2.38043	-2.13492	H	-1.30720	0.38777	0.77387
O	3.66594	0.10691	-1.99549	H	-1.36429	0.21848	-0.91077
H	3.17132	-0.16878	-2.77634	N	-1.45817	-0.25172	-0.00766
C	4.69311	-0.52223	0.28288	B	-2.46115	-1.40320	0.12491
C	5.29837	-1.54875	1.01866	O	-2.49896	-2.16096	-1.04489
C	5.13711	0.79506	0.46196	H	-2.88964	-3.02930	-0.89084
C	6.36048	-1.27340	1.88143	O	-2.52603	-2.09839	1.33278
H	4.95072	-2.57154	0.89038	H	-2.63175	-1.56767	2.12988
C	6.20192	1.07398	1.31565	C	-3.48623	0.06513	0.03112
H	4.64931	1.59756	-0.08579	C	-4.08397	0.32217	-1.20701
				C	-3.90688	0.73604	1.18434

C	-5.18232	1.17691	-1.26755	C	3.50405	-0.35479	-0.01654
H	-3.72323	-0.18060	-2.09985	H	3.85324	-1.38216	-0.02507
C	-5.00680	1.58801	1.11560	C	4.41670	0.69919	-0.02222
H	-3.40501	0.58826	2.13865	H	5.48104	0.48516	-0.03420
C	-5.64281	1.80650	-0.10875	C	3.95836	2.01675	-0.01367
H	-5.67684	1.35339	-2.21789	H	4.66598	2.84040	-0.01926
H	-5.36075	2.08717	2.01227	C	2.59059	2.27656	0.00118
H	-6.49370	2.47878	-0.16121	H	2.22984	3.30199	0.00618
9				C	1.65603	1.23351	0.01024
				C	0.16557	1.55625	0.03054
				O	-0.38360	1.71588	-1.08620
				Cs	-2.94889	0.27105	-0.00964
N	-1.01690	-0.74829	-0.02884				
H	-1.13111	-1.75515	-0.05188				
B	-2.24066	-0.01194	0.00219				
O	-3.38639	-0.77771	-0.01439	Cs_cation			
H	-4.21622	-0.28796	0.00831	Cs	0.00000	0.00000	0.00000
O	-2.23110	1.36138	0.04722				
H	-3.10229	1.77478	0.07110	INT2'			
C	0.32214	-0.34445	-0.01462	I	1.18663	-1.50250	-0.14072
C	1.32121	-1.33205	0.01661	O	3.58191	-1.76920	-0.81048
C	0.71204	1.00416	-0.03337	O	5.52671	-0.64326	-0.67534
C	2.66787	-0.98396	0.02682	C	2.25838	0.12130	0.72359
H	1.02986	-2.37960	0.03479	C	1.59809	1.01188	1.55987
C	2.06511	1.33970	-0.02137	H	0.54132	0.88541	1.77240
H	-0.04019	1.78239	-0.05829	C	2.32830	2.06093	2.12153
C	3.05395	0.35713	0.00826	H	1.82970	2.76252	2.78367
H	3.41879	-1.76864	0.05059	C	3.68894	2.19894	1.84430
H	2.34439	2.38959	-0.03675	H	4.25342	3.01484	2.28479
H	4.10440	0.62978	0.01641	C	4.32484	1.28012	1.01401
10				H	5.38464	1.35651	0.79176
				C	3.61602	0.21795	0.44620
				C	4.32717	-0.81264	-0.42747
				H	-0.77289	-1.19785	1.41077
I	0.78182	-1.71596	0.00120	N	-0.61627	-0.78719	0.48738
O	-0.37414	1.61718	1.16141				
C	2.13942	-0.07272	0.00004				

B	-1.72965	-1.29327	-0.52499	N	-0.94978	-0.94978	-0.41199
O	-1.50787	-0.54916	-1.77035	H	-1.28333	-1.28333	-1.34885
H	-1.64442	-1.14867	-2.51104	B	-1.97211	-1.97211	0.71319
O	-1.56270	-2.72592	-0.83799	O	-1.96231	-1.96231	0.74810
H	-2.10087	-3.29104	-0.27462	H	-2.49835	-2.49835	1.48368
C	-3.15773	-0.94947	0.19244	O	-1.59170	-1.59170	2.00246
C	-4.09120	-0.09468	-0.41349	H	-0.84701	-0.84701	2.37596
C	-3.52357	-1.50616	1.43115	C	-3.39533	-3.39533	0.23745
C	-5.32350	0.19636	0.17850	C	-4.25157	-4.25157	-0.63254
H	-3.84593	0.34140	-1.38037	C	-3.80546	-3.80546	0.64889
C	-4.75133	-1.22877	2.03470	C	-5.45766	-5.45766	-1.07590
H	-2.83708	-2.18229	1.94235	H	-3.96593	-3.96593	-0.96183
C	-5.65746	-0.37035	1.40881	C	-5.00784	-5.00784	0.21637
H	-6.02572	0.85926	-0.32103	H	-3.16510	-3.16510	1.32903
H	-5.00307	-1.68041	2.99079	C	-5.84035	-5.84035	-0.65120
H	-6.61468	-0.15074	1.87319	H	-6.10036	-6.10036	-1.74807
Cs	-1.00399	2.26887	-0.81132	H	-5.29929	-5.29929	0.55523
				H	-6.77766	-6.77766	-0.99013

INT2"

I	0.84854	0.84854	-0.23018	PhBpin			
O	3.32016	3.32016	-0.03923	C	3.78885	1.19789	-0.16402
O	5.29543	5.29543	0.03291	C	2.39478	1.19441	-0.16299
C	1.90526	1.90526	-0.14888	C	1.67713	-0.00001	0.00004
C	1.17638	1.17638	-0.16978	C	2.39481	-1.19440	0.16304
H	0.09222	0.09222	-0.22555	C	3.78889	-1.19786	0.16402
C	1.87520	1.87520	-0.10934	C	4.48657	0.00003	-0.00002
H	1.32369	1.32369	-0.12131	H	4.33148	2.13011	-0.29146
C	3.26864	3.26864	-0.03143	H	1.85326	2.12867	-0.28957
H	3.80803	3.80803	0.01513	H	1.85333	-2.12869	0.28963
C	3.96749	3.96749	-0.00836	H	4.33155	-2.13007	0.29143
H	5.05089	5.05089	0.05624	H	5.57294	0.00003	-0.00003
C	3.29093	3.29093	-0.06451	C	-2.01336	0.77784	0.08515
C	4.05858	4.05858	-0.02009	C	-2.01332	-0.77784	-0.08520

B	0.11793	0.00000	0.00006	C	3.97202	0.17653	0.00134	
O	-0.63884	-1.12060	0.23209	C	4.02677	-0.63631	-1.26534	
O	-0.63881	1.12067	-0.23182	H	-0.16901	0.05152	1.80587	
C	-2.93978	1.52020	-0.86191	H	-0.13568	1.47668	0.97125	
H	-3.97604	1.20223	-0.70620	N	-0.29803	0.47117	0.88060	
H	-2.87919	2.59459	-0.66480	C	-2.48385	1.58802	-0.06935	
H	-2.67096	1.34550	-1.90576	C	-1.88920	2.36086	-1.08057	
C	-2.25897	1.21874	1.52567	C	-3.64156	2.09775	0.53393	
H	-2.05357	2.28994	1.60623	C	-2.42349	3.58769	-1.47587	
H	-3.29705	1.04192	1.82195	H	-0.99421	1.99191	-1.58261	
H	-1.60048	0.68899	2.22156	C	-4.18613	3.32589	0.14974	
C	-2.25859	-1.21883	-1.52575	H	-4.12440	1.51317	1.31409	
H	-2.05302	-2.29001	-1.60623	C	-3.57704	4.07493	-0.85737	
H	-3.29664	-1.04217	-1.82226	H	-1.94650	4.16179	-2.26577	
H	-1.60003	-0.68901	-2.22152	H	-5.08593	3.69754	0.63299	
C	-2.93991	-1.52021	0.86171	H	-3.99834	5.02901	-1.16134	
H	-3.97615	-1.20227	0.70580	C	-2.54223	-1.92592	-0.44751	
H	-2.87924	-2.59460	0.66469	C	-2.63473	-1.90734	1.11356	
H	-2.67128	-1.34542	1.90560	B	-1.87122	0.15962	0.35807	
INT1_p				O	-2.58952	-0.50943	1.40898	
				O	-1.68204	-0.81482	-0.71502	
				C	-3.92690	-2.48739	1.67158	
	I	1.10851	-0.36988	-0.50881	H	-4.05680	-3.52742	1.35225
	O	2.85299	-1.00599	-1.69211	H	-3.89693	-2.46890	2.76586
	O	5.08592	-0.90472	-1.80968	H	-4.79257	-1.90709	1.34427
	C	2.74219	0.45501	0.58017	C	-1.43941	-2.59792	1.77736
	C	2.62018	1.18969	1.75010	H	-0.48758	-2.27064	1.34548
	H	1.66453	1.40936	2.21045	H	-1.43887	-2.35069	2.84379
	C	3.79046	1.66062	2.35001	H	-1.49539	-3.68658	1.67719
H	3.71548	2.23794	3.26598	C	-1.92375	-3.18787	-1.03048	
C	5.03915	1.39709	1.78672	H	-2.50671	-4.07165	-0.74882	
H	5.93858	1.77083	2.26480	H	-1.91329	-3.12176	-2.12313	
C	5.13046	0.65489	0.61356	H	-0.89479	-3.32454	-0.68699	
H	6.08825	0.43301	0.15342					

C	-3.89362	-1.64876	-1.10928	C	5.00593	-1.82735	0.64363
H	-3.73029	-1.46500	-2.17550	B	-2.86059	-0.03047	-0.06661
H	-4.57812	-2.49656	-1.00453	O	-4.19520	0.07127	-0.67046
H	-4.36510	-0.75977	-0.67766	O	-2.64905	-1.47599	0.17198
INT2_p				C	-4.85631	-1.17354	-0.49350
				C	-3.67165	-2.19451	-0.50017
				C	-5.86536	-1.37338	-1.61752
				C	-5.58672	-1.15918	0.85429
I	0.01401	-0.04905	-0.82657	C	-3.95217	-3.48918	0.25387
O	4.34303	1.10256	-0.35630	C	-3.21049	-2.53067	-1.92472
C	0.84666	1.90665	-0.99159	H	-6.31023	-2.37433	-1.57318
C	-0.01103	2.96231	-1.25660	H	-6.67258	-0.63934	-1.52267
H	-1.07426	2.77661	-1.37658	H	-5.39860	-1.23915	-2.59661
C	0.53111	4.24490	-1.35513	H	-4.87503	-1.07885	1.68203
H	-0.12510	5.08497	-1.56133	H	-6.24464	-0.28465	0.88488
C	1.90172	4.44533	-1.18836	H	-6.19730	-2.05701	1.00022
H	2.31806	5.44483	-1.26568	H	-4.82687	-4.00546	-0.15863
C	2.73563	3.36309	-0.92069	H	-3.09087	-4.16084	0.16814
H	3.80462	3.49314	-0.78435	H	-4.12614	-3.29484	1.31515
C	2.21633	2.06951	-0.81761	H	-2.23656	-3.02943	-1.86842
C	3.12851	0.89396	-0.51951	H	-3.91049	-3.20295	-2.43303
N	-1.86917	0.56660	-1.15477	H	-3.10163	-1.62755	-2.53301
H	-2.12111	0.24168	-2.09027	TS1_p			
C	-2.62985	0.81344	1.30900				
C	-2.72267	2.21527	1.31601				
C	-2.34971	0.19251	2.53509				
C	-2.55160	2.96305	2.48232	I	0.31397	-0.54690	-0.43214
H	-2.93713	2.73271	0.38181	O	4.35204	1.51194	0.65818
C	-2.16868	0.92580	3.71166	C	0.73305	1.03595	0.93072
H	-2.27578	-0.89330	2.55909	C	-0.37580	1.61263	1.54607
C	-2.27066	2.31724	3.68892	H	-1.37461	1.23703	1.34510
H	-2.63517	4.04680	2.45380	C	-0.18249	2.67049	2.43363
H	-1.94982	0.41389	4.64579	H	-1.04347	3.11815	2.92118
H	-2.13306	2.89324	4.60004	C	1.10384	3.14330	2.68801
O	2.54616	-0.23606	-0.45734	H	1.25774	3.96996	3.37496

C	2.19294	2.54617	2.06177	H	-2.55213	-3.02937	2.72857
H	3.20451	2.89504	2.24211	H	-4.50230	-4.08838	1.30825
C	2.03619	1.46971	1.17854	H	-4.43634	-4.11893	-0.46335
C	3.30044	0.83366	0.59231	H	-2.93663	-3.98106	0.47023
N	-1.82825	0.39505	-0.95263	H	-5.85861	-2.15697	-0.88611
H	-1.76364	0.15709	-1.94904	H	-6.26059	-2.23501	0.84209
C	-3.83614	0.91854	-1.21001	H	-5.72364	-0.70246	0.11846
C	-4.39997	0.61807	-2.45519				
C	-4.15164	2.13713	-0.59725	TS1'_p			
C	-5.30110	1.49829	-3.05778	I	1.45131	-0.79503	0.16246
H	-4.15674	-0.32591	-2.93882	O	3.85190	-2.03351	0.06788
C	-5.05400	3.01727	-1.19165	O	5.99104	-1.39092	-0.20387
H	-3.69756	2.38329	0.35993	C	2.98699	0.68747	0.00347
C	-5.63021	2.69814	-2.42488	C	2.61216	2.02901	0.00376
H	-5.74787	1.24854	-4.01633	H	1.57361	2.33035	0.09289
H	-5.30573	3.95342	-0.70077	C	3.59837	3.00801	-0.10502
H	-6.33014	3.38523	-2.89177	H	3.31115	4.05486	-0.10411
O	3.18181	-0.32468	0.11517	C	4.93824	2.63796	-0.21073
C	6.17441	-0.59846	-0.75595	H	5.70915	3.39746	-0.29592
B	-2.98992	-0.30021	-0.32746	C	5.28338	1.29102	-0.20391
O	-3.15747	-0.15423	1.09268	H	6.31801	0.97272	-0.28165
O	-3.31180	-1.65417	-0.67680	C	4.31567	0.28503	-0.09411
C	-3.54674	-1.41906	1.63358	C	4.77258	-1.18430	-0.07773
C	-4.12400	-2.16471	0.38283	H	-0.38173	1.18631	0.99265
C	-4.55587	-1.19587	2.75228	H	-0.31406	1.24642	-0.70125
C	-2.30038	-2.10639	2.19506	N	-0.63306	0.72403	0.11738
C	-3.98600	-3.67925	0.43263	C	-2.46475	1.67918	0.07346
C	-5.58311	-1.78806	0.10721	C	-2.77144	2.30487	-1.13713
H	-4.95867	-2.14994	3.11075	C	-2.85367	2.22872	1.29775
H	-4.06543	-0.69696	3.59471	C	-3.56581	3.44985	-1.12279
H	-5.38443	-0.56631	2.41937	H	-2.43622	1.87480	-2.07752
H	-1.58998	-2.34299	1.39793	C	-3.64886	3.37290	1.30123
H	-1.81024	-1.42413	2.89763	H	-2.57910	1.74314	2.23090

C	-4.00187	3.98115	0.09360	C	2.34474	-0.87502	0.15170
H	-3.84235	3.92774	-2.05770	C	4.63094	0.70493	-0.09237
H	-3.98957	3.79150	2.24326	H	3.27406	2.36331	-0.30984
H	-4.61387	4.87794	0.10103	C	3.61300	-1.44920	0.21693
C	-3.20757	-1.67869	-0.86318	H	1.45930	-1.49218	0.24945
C	-2.87728	-2.02037	0.62900	C	4.76447	-0.67135	0.09666
B	-1.95702	-0.02147	0.02853	H	5.51333	1.33125	-0.18791
O	-2.39302	-0.75513	1.13784	H	3.69658	-2.52209	0.36633
O	-2.20064	-0.69047	-1.17587	H	5.74741	-1.12831	0.15003
C	-4.07623	-2.45593	1.45464	B	-0.35115	0.59170	-0.06932
H	-4.53460	-3.35039	1.01950	O	-0.67172	-0.73072	0.13984
H	-3.75344	-2.69915	2.47153	O	-1.45803	1.39820	-0.23674
H	-4.82852	-1.66624	1.51201	C	-2.09287	-0.85664	-0.12913
C	-1.74589	-3.03665	0.75903	C	-2.60780	0.59775	0.13026
H	-0.90003	-2.77367	0.11525	C	-2.67658	-1.91026	0.79520
H	-1.40082	-3.05247	1.79702	C	-2.23577	-1.28486	-1.58707
H	-2.08111	-4.04305	0.48997	C	-3.79239	1.01035	-0.72569
C	-3.06490	-2.84589	-1.82426	C	-2.89482	0.86905	1.60496
H	-3.73618	-3.66150	-1.53550	H	-3.76500	-1.95210	0.68246
H	-3.33426	-2.52423	-2.83483	H	-2.26860	-2.89177	0.53621
H	-2.04016	-3.22296	-1.84499	H	-2.43829	-1.70240	1.84038
C	-4.57731	-1.01978	-1.02452	H	-1.82903	-0.52781	-2.26536
H	-4.65390	-0.61201	-2.03702	H	-1.68076	-2.21521	-1.73717
H	-5.38507	-1.74368	-0.88135	H	-3.28357	-1.46132	-1.84714
H	-4.71479	-0.19926	-0.31211	H	-4.64587	0.35071	-0.53690
				H	-4.08832	2.03257	-0.47177
				H	-3.54889	0.97608	-1.78962
				H	-3.05497	1.94247	1.74056
				H	-3.79242	0.34041	1.93884
				H	-2.05403	0.56399	2.23651
9_p							
N	0.96183	1.13564	-0.11417				
H	1.01573	2.14096	-0.23273				
C	2.21053	0.50880	-0.04086				
C	3.37062	1.29039	-0.16081				

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Chapter 2

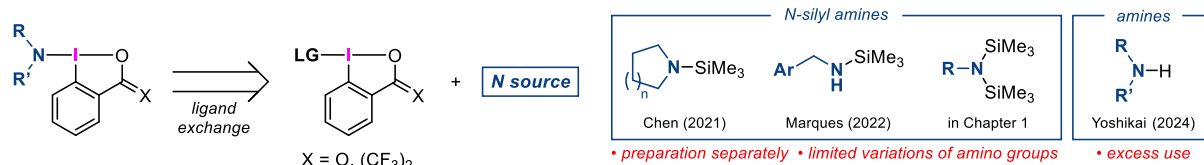
Versatile Method for the Synthesis of Aminobenziodoxolones Using Amines and Its Application to Electrophilic Amination of Arylboronic Acids

2-1. Introduction

In general, amines are sensitive to oxidants including hypervalent iodine oxidants and the and their reactions are often difficult to control or lead to overoxidation.^{1,2} Therefore, the direct conversion of amines into hypervalent iodine compounds containing an N–I bond (amino- λ^3 -iodanes) has remained a significant challenge. As described in the general introduction, amino- λ^3 -iodanes derived from secondary³ and benzylic primary amines⁴ have recently been synthesized by incorporating a thermally stable iodoxolone framework (Scheme 1A).^{5–8} In chapter 1, the author reported the method employing disilazanes as nitrogen sources, enabling the synthesis of unprecedented iodine(III) reagents bearing $-\text{NH}_2$ and $-\text{NHR}$ groups.⁹ However, the existing methods rely on the use of *N*-silyl amines, which demand careful preparation, thereby limiting their synthetic versatility and broader applicability.^{3,4,9–12} Building on this strategy, the author envisioned that leveraging the iodoxolone framework would allow access to aminobenziodoxolones directly from amines by overcoming their inherent reactivity toward oxidants. During this work, the direct use of simple alkylamines for the synthesis of amino-bis(trifluoromethyl)benziodoxoles has been reported; however, this protocol still necessitates an excess of amines.¹³ Therefore, the development of a synthetically practical and efficient method for the preparation of amino- λ^3 -iodanes employing a stoichiometric amount of amine remains an unmet and important challenge. In chapter 2, the author reports the development of a general and practical strategy for the synthesis of aminobenziodoxolones using readily available amines, including ammonia, primary aliphatic amines, and aromatic amines (Scheme 1Bi). This method enables the synthesis of a diverse range of aminobenziodoxolones, most of which have not been accessible via previously reported

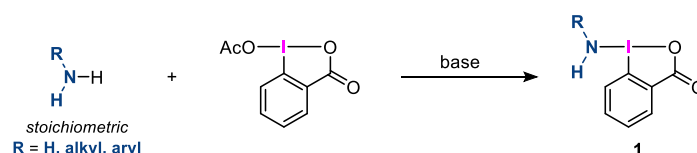
methods. Moreover, the broad and practical synthesis of aminobenziodoxolones achieved in this study significantly expands the scope of transition-metal (TM)-free electrophilic amination of arylboronic acid derivatives to access versatile arylamines (Scheme 1Bii), which serve as valuable building blocks widely found in natural products, pharmaceuticals, agrochemicals, and organic materials.¹⁴

A) Synthesis of aliphatic aminobenziodoxol(on)es

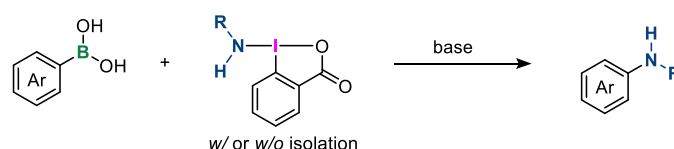


B) This work

i) Synthesis of aminobenziodoxolones using various amines



ii) TM-free oxidative amination of arylboronic acids from amines



Scheme 1 A) Overview of existing amino- λ^3 -iodanes. **B)** Synthesis of aminobenziodoxolones from amines and its application to amination of arylboronic acids.

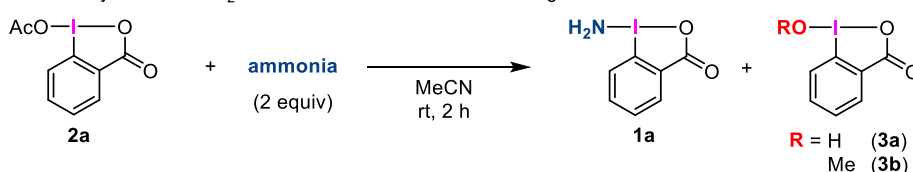
2-2. Results and Discussion

2-2-1. Synthesis of Aminobenziodoxolone Using Amines

The author initiated the investigation into synthesis of NH_2 -substituted benziodoxolone **1a** using ammonia (Table 1), offering a simpler and more practical alternative to the previously reported method using hexamethyldisilazane.⁹ Gratifyingly, treatment of 1-acetoxy-1,2-benzodioxol-3-(1*H*)-one (**2a**) with aqueous ammonia (2 equivalents of NH_3) underwent ligand exchange at the iodine center to furnish the desired product **1a** in 61% yield (entry 1). However, the presence of water also generated hydroxy-benziodoxolone **3a**, hindering the isolation of **1a** due to their low solubility in common organic solvents. Switching to a methanolic ammonia solution improved the yield of **1a** to 87%, albeit with minor formation of methoxy-benziodoxolone **3b** (entry 2). In this case, simple washing of the crude mixture with chloroform allowed for isolation of pure **1a** in 75% yield. To suppress undesired side

reactions derived from protic solvents, a 1,4-dioxane solution of ammonia was examined; however, this resulted in a low conversion of **2a** and a low yield of **1a** (entry 3). The author then turned his attention to the use of gaseous ammonia. Conducting the reaction in acetonitrile under an ammonia atmosphere proved highly effective, delivering **1a** in 92% isolated yield (entry 4). In addition, ammonium carbamate, a bench-stable and inexpensive ammonia equivalent, was also found to be applicable.¹⁵ Employing 1 equivalent of ammonium carbamate, corresponding to 2 equivalents of ammonia, furnished **1a** in high yield (entry 5). In contrast, other common ammonium salts, such as NH_4Cl and NH_4OAc , were ineffective.¹⁶ It should be noted that attempts to synthesize the corresponding NH_2 -substituted benziodoxoles were unsuccessful (Table 2), highlighting that the iodoxolone framework is essential for the successful preparation of NH_2 -substituted reagents. The reagent **1a** has been demonstrated to serve as an electrophilic aminating reagent, enabling the efficient synthesis of a broad range of primary amines.⁹ This practical and operationally simple method thus provides a new synthetic platform for the efficient utilization of ammonia in primary amine synthesis.

Table 1. Synthesis of NH_2 -substituted benziodoxolone **1a** using ammonia.



Entry	Ammonia source	Yield (%)	
		1a	3
1	NH_3 , 28% in water	61	27 (3a)
2	NH_3 , 2 M in MeOH	87 (75)	10 (3b)
3	NH_3 , 0.4 M in 1,4-dioxane	22	-
4	gaseous NH_3 (1 atm)	>95 (92)	-
5	$\text{H}_2\text{NCO}_2\text{NH}_4$ (1 equiv)	88 (88)	-

Yields were determined by ^1H NMR analysis of the crude product on a 0.1–0.2 mmol scale. Values in parentheses are isolated yields on 0.5 mmol (entry 2), 2 mmol (entry 4), and 1 mmol (entry 5) scales.

Table 2. Comparison of the reactivity of hypervalent iodine compounds

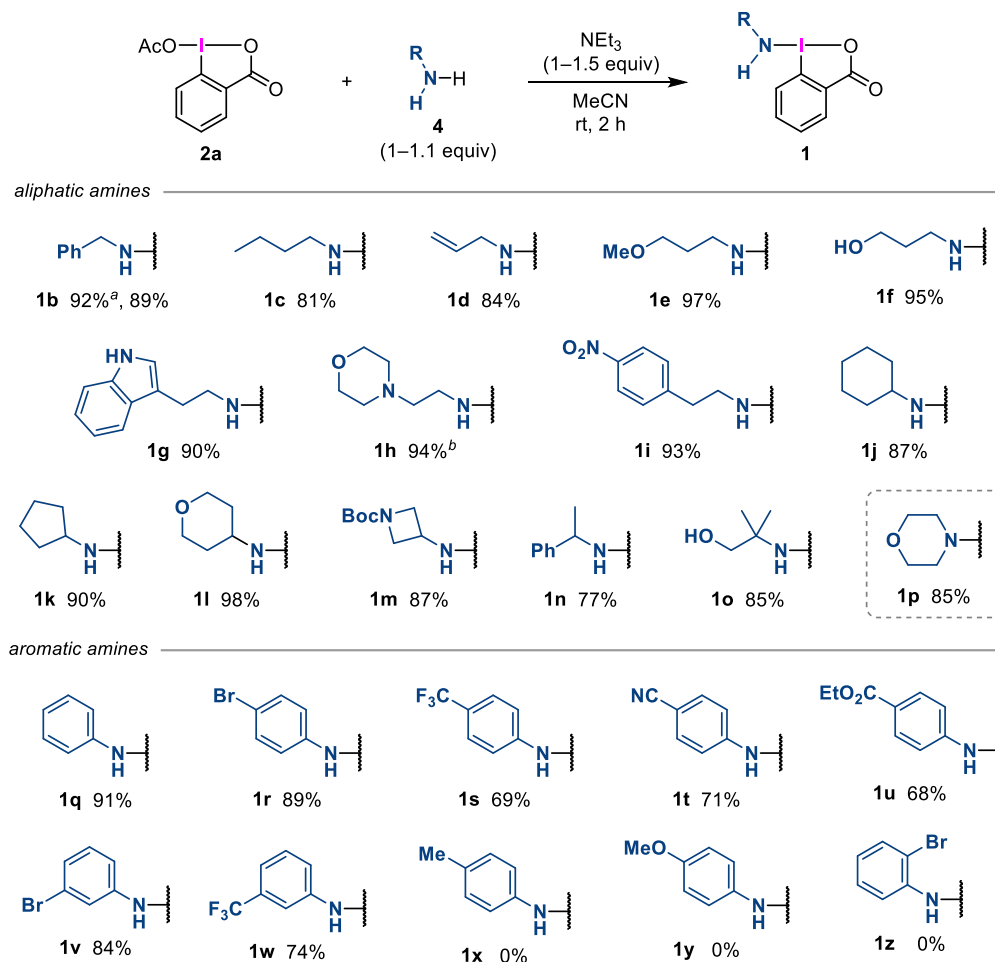
Entry	AcO—I ^{III}	Yield (%)	Recovery (%)
1	2a	1a 87	0
2	2b	0	quant.
3	2c	0	80

2b

2c

Yields were determined by ^1H NMR analysis of the crude product.

Encouraged by the successful synthesis of **1a** using ammonia, the author next sought to expand the scope of the method for the synthesis of aminobenziodoxolones from simple amines (Scheme 2). As expected, the reaction with 2 equivalents of benzylamine (**4b**) afforded the corresponding product **1b** in high yield. To reduce the amount of amine substrates required, the author screened bases capable of scavenging the *in-situ* generated acetic acid. Among those tested, triethylamine proved effective, enabling the formation of **1b** in high yield with 1.1 equivalents of **4b**. This strategy not only avoids the preparation of disilazanes but also circumvents the need for an excess amount of valuable amine substrates.⁹ With the practical method in hand, the author subsequently explored the substrate scope for the synthesis of diverse aminobenziodoxolones from primary amines. Simple aliphatic primary amines, such as *n*-butyl and allylamine, were suitable, furnishing **1c** and **1d** in high yields, respectively. The method also proved applicable to amines bearing functional groups such as methoxy (**1e**), hydroxy (**1f**, **1o**), *NH*-indolyl (**1g**), morpholine (**1h**), nitro (**1i**), tetrahydropyran (**1l**), and *N*-Boc-azetidine (**1m**) moieties, affording previously inaccessible compounds.^{2,9,13} Steric hindrance of amines had little effect on the ligand exchange, enabling the use of amines bearing α -secondary and tertiary carbon centers (**1j**–**o**), as well as a secondary amine (**1p**). Owing to the mild reaction conditions and inherent stability of the benziodoxolones, the method was further applicable to typically oxidation-sensitive aromatic amines.^{39,40} Various arylamines bearing electron-withdrawing groups such as bromo (**1r**, **1v**), trifluoromethyl (**1s**, **1w**), cyano (**1t**), and ethoxycarbonyl (**1u**) groups underwent smooth conversion to the corresponding aminobenziodoxolones. In contrast, more oxidizable electron-rich arylamines (**1x**, **1y**) than aniline were not compatible, resulting in the formation of complex mixtures containing azo compounds.^{1,17} Additionally, attempts to synthesize aminobenziodoxolones derived from *ortho*-substituted arylamine (**1z**) were also unsuccessful, affording complex mixtures including *o*-iodobenzoate and recovering a small amount of unreacted **3z**. Although several limitations remain, the author has established a general and practical method for the synthesis of aminobenziodoxolones using simple amines, including substrates that have been challenging to access by existing methods.^{2,9,13} The developed method considerably broadens the range of accessible aminobenziodoxolones, which are promising reagents in oxidative amination reactions.

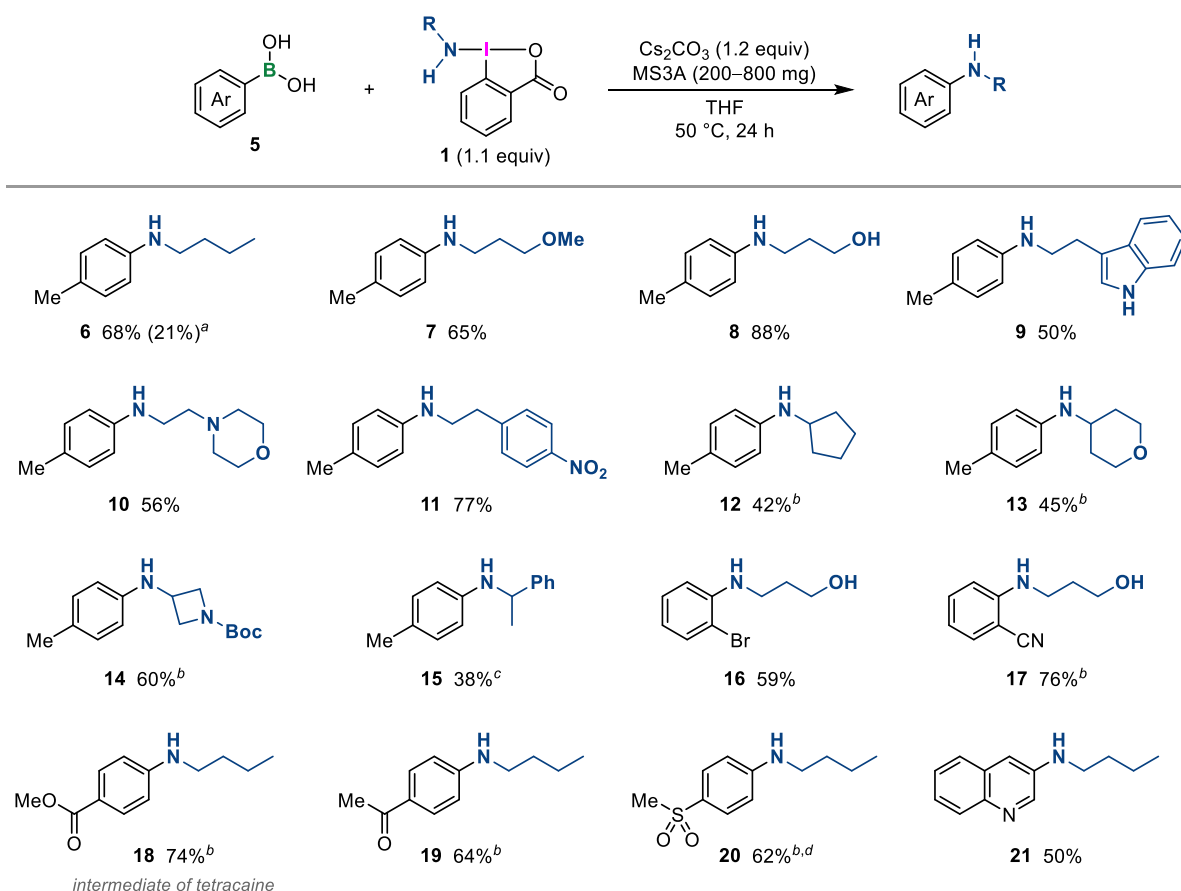


Scheme 2. Synthesis of aminobenziodoxolones using amines. Yields represent isolated yields. ^a Benzylamine (**4b**, 2 equiv) was used without NEt₃. ^b 1,4-Diazabicyclo[2.2.2]octane (DABCO) was used instead of NEt₃.

2-2-2. Amination of Arylboronic acids Using Aminobenziodoxolones

TM-free oxidative amination of arylboronic acid derivatives with electrophilic aminating reagents has been recognized as a valuable strategy for the synthesis of arylamines. However, existing methods have been predominantly limited to the synthesis of primary arylamines^{18–27}, largely due to the scarcity of suitable aminating reagents that enable efficient access to secondary amines.^{28–30} Although several protocols employing nitro(so) compounds have been reported, they typically require harsh reaction conditions, which limit their synthetic utility and functional group compatibility.^{31–35} In chapter 1, the author demonstrated that aminobenziodoxolones serve as suitable reagents for the oxidative amination of various arylboronic acid derivatives.⁹ Nevertheless, their application to secondary arylamine synthesis has remained limited due to the restricted availability of aminobenziodoxolones.

With the diverse range of reagents derived from primary amines now in hand, the author sought to explore their potential for secondary arylamine synthesis via oxidative amination of arylboronic acids, probably proceeds through the formation of a tetravalent borate complex with a B–N dative bond that is followed by 1,2-aryl migration (Scheme 3).⁹ The reaction of 4-methylphenylboronic acid (**5a**) with aminobenziodoxolone **1c** was carried out in THF at 50 °C in the presence of Cs₂CO₃ and molecular sieves 3A (MS3A) was found to furnish the desired secondary arylamine **6** in 68% yield. However, the corresponding boronic acid pinacol ester showed low reactivity to afford **6** in only 21% yield. A range of secondary arylamines were synthesized in good to high yields using reagents bearing functionalized amino groups, including methoxy, hydroxy, *NH*-indolyl, morpholino, and nitro moieties (**7–11**). Furthermore, amino groups possessing α -secondary carbon centers could also be successfully installed (**12–15**), whereas reagents derived from α -tertiary primary amine (**1o**) and secondary amine (**1p**) were unsuitable under the reaction conditions. The amination proved effective for arylboronic acids bearing



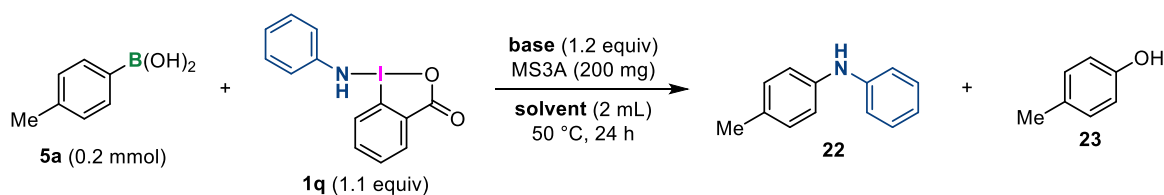
Scheme 3. The scope of amination of arylboronic acids with aminobenziodoxolones. Reactions were performed on a 0.2–0.4 mmol scale. ^a The corresponding pinacol boronic acid ester was used as a substrate. The yield was determined by ¹H NMR analysis of the crude product. ^b The reaction was conducted at 70 °C. ^c The reaction was conducted at 80 °C in 1,4-dioxane. ^d **1c** (1.5 equiv) was used.

electron-withdrawing substituents, such as bromo, cyano, carbonyl, and sulfonyl groups at either the *ortho*- or *para*-position (**16–20**), which are typically less reactive in electrophilic amination reactions.^{18–}

³⁰ This method was also successfully extended to heteroarylboronic acid, as exemplified by the amination of quinoline boronic acid to afford **21**.

Diarylamine synthesis via electrophilic amination of arylboronic acids has been quite limited, with existing methods requiring the use of hazardous arylazides²⁸ or nitro(so)arenes^{31,32,34} under harsh reaction conditions. It is noteworthy that arylamine-derived reagents **1q–w** were successfully applied to oxidative amination to provide the corresponding diarylamines. Following a brief optimization of the reaction conditions, the use of K₂CO₃ as a base in 1,4-dioxane proved to be effective for diarylamine synthesis (Table 3). This method enables the synthesis of a variety of unsymmetrical diarylamines with good functional group compatibility (Scheme 4), including bromo, trifluoromethyl, cyano, and ethoxycarbonyl groups (**22**, **24–28**). Sterically demanding diarylamine (**29**) and diarylamine bearing two different halogen substituents (**30**) could also be synthesized, which would be challenging to access via TM-catalyzed amination reactions.^{14,36–38} Furthermore, electron-deficient arylboronic acids could also be applied, albeit in relatively lower efficiency (**31**, **32**). This approach enables the TM-free synthesis of a diverse array of secondary arylamines under mild reaction conditions, offering a practical tool for accessing pharmaceutical intermediates, such as tetracaine (**18**) and flufenamic acid (**32**).^{39,40} For a complementary approach to the synthesis of arylamines, the arylation of amines with

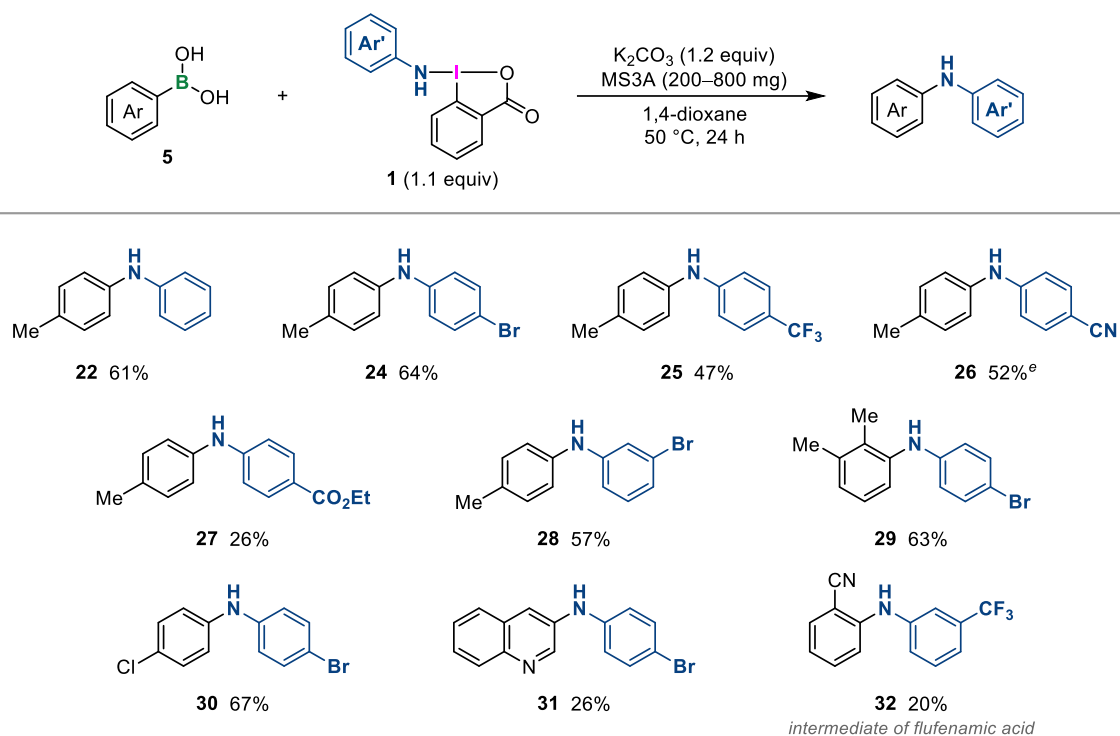
Table 3. Optimization of reaction conditions for the amination of boronic acid **5a** with **1q**.



entry	base	solvent	yield (%) ^a		recovery of 5a (%) ^a
			22	23	
1	Cs ₂ CO ₃	THF	50	<11	45
2	K ₂ CO ₃	THF	65	9	25
3	KOAc	THF	55	8	40
4	NEt ₃	THF	63	<10	0
5	K ₂ CO ₃	1,4-dioxane	70 (61)^b	n.d.	21
6	K ₂ CO ₃	toluene	33	n.d.	45
7	K ₂ CO ₃	MeCN	35	trace	40

^aDetermined by ¹H NMR analysis of the crude product. ^bIsolated yield.

diaryliodonium salts has been reported.^{41,42} A key feature of these methods is the synthesis of tertiary arylamines using secondary amines, which has not yet been achieved with the present method. In contrast, the present method uses readily available arylboronic acids, offering a broader scope in terms of aryl moieties.



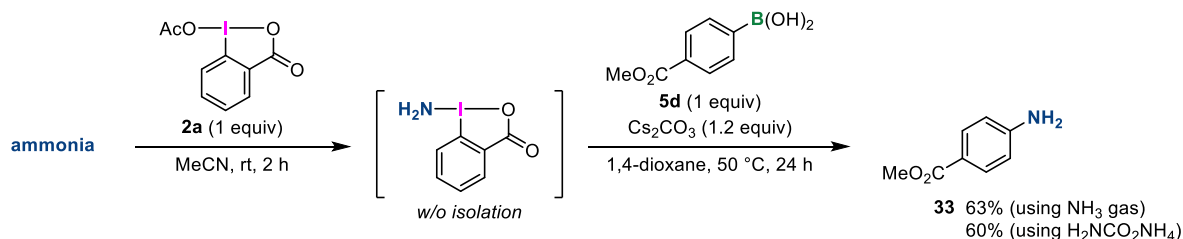
Scheme 4. The scope of amination of arylboronic acids with arylamine derived-aminobenziodoxolones. Reactions were performed on a 0.2–0.4 mmol scale. ^e KOtBu was used instead of K_2CO_3 .

2-2-3. One-pot Process for Coupling of Arylboronic Acids with Amines

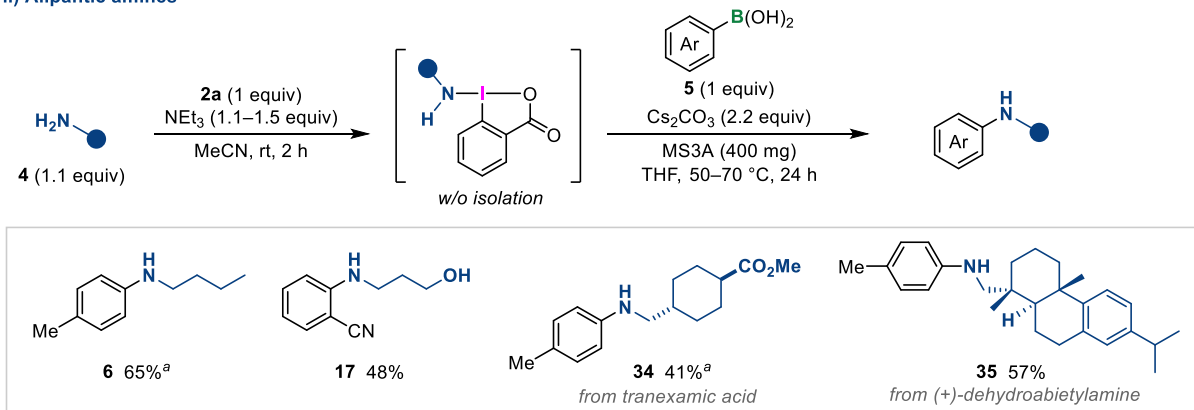
Building upon the highly efficient method for the preparation of aminobenziodoxolones from amines, the author next aimed to develop a direct oxidative amination of arylboronic acids using amines via the *in-situ* preparation of aminobenziodoxolones, offering a TM-free alternative to the Chan-Lam-Evans coupling (Scheme 5).^{43,44} Gaseous ammonia was first employed for the *in-situ* preparation of NH_2 -substituted benziodoxolone **1a**, which was subsequently reacted with arylboronic acid **5d** to afford the target primary amine **33** in 63% yield – comparable to the reaction using isolated **1a** (Scheme 5i).⁹ In addition, ammonium carbamate was also used in the one-pot process, affording **33** in comparable yield. Although the process requires the replacement of solvent and reaction atmosphere, the

transformation could be carried out through sequential one-pot operations. This protocol was further extended to the synthesis of secondary amines using primary amines (Scheme 5ii). In this manner, secondary arylamines **6** and **17** were obtained from 1.1 equivalents of the corresponding aliphatic primary amines with comparable efficiencies to those achieved with isolated reagents **1** (*cf.* Scheme 3). Notably, pharmaceutically relevant amines, such as tranexamic acid and dehydroabietylamine, also participated smoothly in the oxidative amination (**34**, **35**). When employing aliphatic amines, conducting the reaction by mixing all the reagents at once led to diminished yield. In contrast, reactions involving aniline derivatives proceeded efficiently upon single-step mixing of reagents, without the need for prior *in-situ* preparation of aminobenziodoxolones (Scheme 5iii). Notably, this operationally simple method was successfully applied to the gram-scale synthesis of **24**, further demonstrating its synthetic utility.

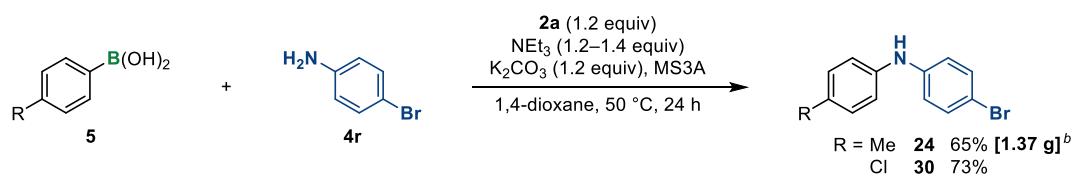
i) Ammonia



ii) Aliphatic amines



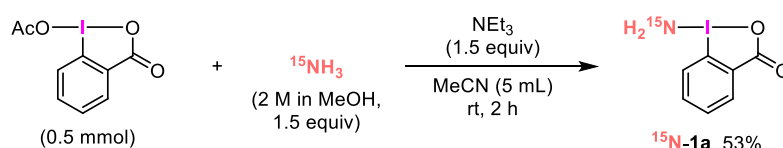
iii) Aromatic amines



Scheme 5. One-pot process for coupling of arylboronic acids with amines. ^a Both steps were performed in 1,4-dioxane. ^b The reaction was conducted in an 8 mmol scale.

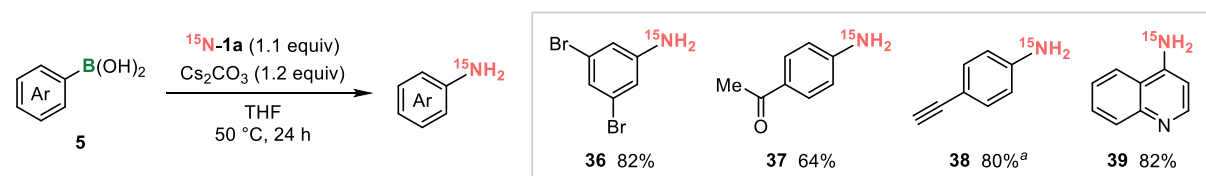
2-2-4. Synthesis of ^{15}N -labelled arylamines.

As an extension of the method for the synthesis of NH_2 -substituted benziodoxolone from ammonia, the author next focused on the preparation of ^{15}N -labelled analogue **^{15}N -1a**, which is a promising reagent for the synthesis of ^{15}N -labelled compounds. Such compounds are of considerable significance for detailed structural analysis and bioimaging studies of nitrogen-containing molecules in the field of organic chemistry and medicinal chemistry, owing to the favorable magnetic properties of the ^{15}N nucleus.^{45–47} Gratifyingly, the desired **^{15}N -1a** could be synthesized using a separately prepared methanolic solution of ammonia- ^{15}N (Scheme 6).⁴⁸

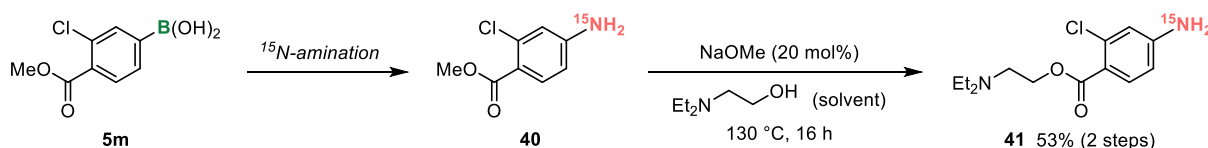


Scheme 6. Synthesis of ^{15}N -labelled aminobenziodoxolone.

The resulting **^{15}N -1a** was then applied to the oxidative amination of arylboronic acids or pinacol boronic acid esters (Scheme 7), furnishing ^{15}N -labelled aniline derivatives bearing bromo, acetyl, alkyne, and ester functionalities (**36–38**, **40**). Moreover, the method proved applicable to the synthesis of ^{15}N -labelled quinoline derivative **39**. Furthermore, ^{15}N -labelled chlorprocaine **41**, an analogue of a clinically used local anesthetic, was synthesized from **5m** via sequential ^{15}N -amination and transesterification. Conventionally, ^{15}N -labelled arylamines are synthesized by the Hofmann rearrangement of ^{15}N -benzamides^{49,50} or TM-catalyzed coupling reactions.^{51–53} The present method would offer a good alternative, featuring broad functional group tolerance under mild reaction conditions.



Synthesis of ^{15}N -chlorprocaine



Scheme 7. ^{15}N -labelled arylamine synthesis. ^a The corresponding pinacol boronic acid ester was used as a substrate.

2-3. Conclusion

In conclusion, the author has developed a versatile method for the synthesis of aminobenziodoxolones from simple amines. This protocol is widely applicable to ammonia, a variety of aliphatic and aromatic primary amines, and even secondary amines, substantially expanding the scope of synthetically accessible aminobenziodoxolones. The synthesized reagents were applied to the oxidative amination of arylboronic acids, enabling the efficient synthesis of pharmaceutically and synthetically valuable secondary amines under TM-free mild reaction conditions. Furthermore, a one-pot protocol integrating the *in-situ* preparation of aminobenziodoxolones and subsequent oxidative amination was established. As a further demonstration of the synthetic utility, ^{15}N -labelled arylamines were also synthesized using a ^{15}N -labelled aminating reagent.

2-4. Experimental Section

General Remarks

New compounds were characterized by ^1H NMR, $^{13}\text{C}\{^1\text{H}\}$ NMR, $^{19}\text{F}\{^1\text{H}\}$ NMR, $^{15}\text{N}\{^1\text{H}\}$ NMR, IR, MS, and HRMS. ^1H , $^{13}\text{C}\{^1\text{H}\}$, $^{19}\text{F}\{^1\text{H}\}$, $^{15}\text{N}\{^1\text{H}\}$ NMR spectra were recorded on a JEOL JMT-400/54/SS or JNM-ECZL400S spectrometers (^1H NMR, 400 MHz; $^{13}\text{C}\{^1\text{H}\}$ NMR, 100 MHz; $^{19}\text{F}\{^1\text{H}\}$ NMR, 376 MHz; $^{15}\text{N}\{^1\text{H}\}$ NMR, 41 MHz). ^1H NMR chemical shifts were determined relative to Me_4Si (0.0 ppm) as an internal standard in CDCl_3 or the signals of residual undeuterated dimethyl sulfoxide (2.49 ppm) in dimethyl sulfoxide- d_6 . $^{13}\text{C}\{^1\text{H}\}$ NMR chemical shifts were determined relative to CDCl_3 (77.00 ppm) or $(\text{CD}_3)_2\text{SO}$ (39.50 ppm). $^{19}\text{F}\{^1\text{H}\}$ NMR chemical shifts were determined relative to C_6F_6 (−164.9 ppm in CDCl_3 or −162.5 ppm in $(\text{CD}_3)_2\text{SO}$) as an external standard. $^{15}\text{N}\{^1\text{H}\}$ NMR chemical shifts were determined relative to nitromethane (380.2 ppm in both CDCl_3 and $(\text{CD}_3)_2\text{SO}$) as an external standard. The multiplicities are abbreviated as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad) and combinations thereof. Infrared spectra were recorded on a SHIMADZU IRAffinity-1 FT-IR Spectrometer. High-resolution mass spectra (HRMS) were obtained on JEOL JMS-700 (magnetic sector type mass spectrometer) and JMS-T100LP. Melting points were determined on a Stanford Research Systems MPA100 OptiMelt Automated Melting Point System. The X-ray diffraction data of the single crystal were collected on a two-dimensional X-ray detector (PILATUS 200K/R) equipped in Rigaku XtaLAB PRO diffractometer using thin multi-layer mirror monochromated Cu-K α radiation ($\lambda = 1.54187 \text{ \AA}$). Products were purified by chromatography on silica gel BW-300 (Fuji Silysia Chemical Ltd.) or Chromatorex NH (Fuji Silysia Chemical Ltd.). Analytical thin-layer chromatography

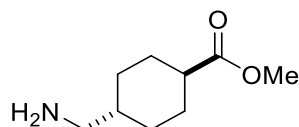
(TLC) was performed on pre-coated silica gel glass plates (Merck silica gel 60 F₂₅₄ and Fuji Silysia Chromatorex NH, 0.25 mm thickness). Compounds were visualized with UV lamp or treatment with an ethanolic solution of phosphomolybdic acid followed by heating.

Materials

Hypervalent iodine reagent **2** was prepared according to the reported procedure.⁵⁴⁾ Ammonia-¹⁵N methanol solution was prepared according to the reported procedure.⁴⁸⁾ Gaseous ammonia was purchased from TAIYO NIPPON SANSO CORPORATION (Purity: >99.999%) and used as obtained. Dehydrated acetonitrile and THF were used from a solvent purification system. Triethylamine was distilled over CaH₂ before use. All other solvents and reagents were purchased and used as obtained.

Preparation of primary amine

methyl *trans*-4-(aminomethyl)cyclohexane-1-carboxylate



A reaction flask equipped with a magnetic stirring bar was flame-dried under vacuum. After cooling to room temperature, the flask was charged with nitrogen gas, *trans*-4-(aminomethyl)cyclohexanecarboxylic acid (940 mg, 6.0 mmol, 1.0 equiv), and MeOH (4 mL). Then SOCl₂ (530 μ L, 7.2 mmol, 1.2 equiv) was added dropwise. After the mixture was stirred at room temperature for 12 h, the reaction mixture was concentrated under reduced pressure. To the residue, sat. NaHCO₃ aq. (40 mL) was added, and the mixture was extracted with EtOAc (3 $\times$ 40 mL). The combined organic layers were dried over Na₂SO₄, filtrated, and concentrated under reduced pressure to give the product as a colorless oil (331 mg, 1.93 mmol, 32% yield).

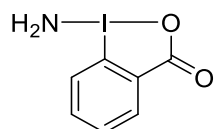
¹H NMR: (400 MHz, CDCl₃) δ 3.67 (s, 3H), 2.98 (br, 2H), 2.70–2.53 (m, 2H), 2.32–2.18 (m, 1H), 2.10–1.95 (m, 2H), 1.95–1.85 (m, 2H), 1.55–1.32 (m, 3H), 1.07–0.85 (m, 2H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 176.4, 51.4, 48.4, 43.4, 40.4, 29.7, 28.6; IR: (ATR) 2928, 2857, 1728, 1449, 1435, 1319, 1252, 1194, 1159, 1038, 1009, 895, 826, 766 cm⁻¹; HRMS (EI) *m/z*: [M]⁺ Calculated for C₉H₁₇NO₂ 171.1259; Found 171.1261

Synthesis of aminobenziodoxolones: experimental procedures and product data

General procedure I: A reaction flask equipped with a magnetic stirring bar was flame-dried under vacuum. After cooling to room temperature, the flask was charged with nitrogen gas, 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (1.0 equiv), MeCN, primary amine (1.0–1.1 equiv), and NEt₃ (1.0–1.5 equiv). The mixture was stirred at room temperature for 2 h. Then, the resulting precipitation was filtered and washed with MeCN or Et₂O and dried under vacuum to give the product.

General procedure II: A reaction flask equipped with a magnetic stirring bar was flame-dried under vacuum. After cooling to room temperature, the flask was charged with nitrogen gas, 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (1.0 equiv), MeCN, primary amine (1.1 equiv), and base (1.0–1.5 equiv). The mixture was stirred at room temperature for 2 h. Then, the reaction mixture was concentrated under reduced pressure, resulting in the formation of the crude solid, which was washed with MeCN or Et₂O and dried under vacuum to give the product.

1-amino-1,2-benziodoxol-3(1*H*)-one (1a)



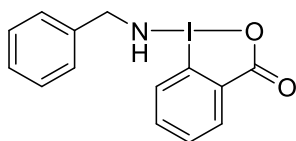
Using methanolic ammonia: A reaction flask equipped with a magnetic stirring bar was flame-dried under vacuum. After cooling to room temperature, the flask was charged with nitrogen gas, 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (153.2 mg, 0.5 mmol, 1.0 equiv), MeCN (5 mL), and ammonia methanol solution (2 M, 0.50 mL, 1.0 mmol, 2.0 equiv). The mixture was stirred at room temperature for 2 h. The precipitation was filtered, washed with CHCl₃, and dried under vacuum to give the product as a white solid (98.4 mg, 0.37 mmol, 75% yield).

Using gaseous ammonia: A reaction flask equipped with a magnetic stirring bar was flame-dried under vacuum. After cooling to room temperature, the flask was charged with nitrogen gas and 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (612 mg, 2.0 mmol, 1.0 equiv). The flask was vacuumed and refilled with gaseous ammonia (1 atm), and then MeCN (20 mL) was added. After the mixture was stirred at room temperature for 2 h, CHCl₃ (20 mL) and NEt₃ (1.4 mL) were added to the reaction mixture. The mixture was further stirred at room temperature for 10 min, resulting in the formation of precipitation, which was washed with CHCl₃ and dried under vacuum to give the product as a white solid (485 mg, 1.84 mmol, 92% yield).

Using ammonium carbamate: A reaction flask equipped with a magnetic stirring bar was flame-dried under vacuum. After cooling to room temperature, the flask was charged with nitrogen gas, 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (307 mg, 1.0 mmol, 1.0 equiv), ammonium carbamate (79.0 mg, 1.0 mmol, 1.0 equiv), and MeCN (10 mL). After the mixture was stirred at room temperature for 2 h, CHCl₃ (10 mL) and NEt₃ (0.7 mL) were added to the reaction mixture. The mixture was further stirred at room temperature for 10 min, resulting in the formation of precipitation, which was washed with CHCl₃ and dried under vacuum to give the product as a white solid (232 mg, 0.88 mmol, 88% yield).

¹H NMR: (400 MHz, DMSO-*d*₆) δ 8.05–7.95 (m, 2H), 7.90–7.78 (m, 1H), 7.68–7.57 (m, 1H), 4.67 (brs, 2H); ¹³C{¹H} NMR: (100 MHz, DMSO-*d*₆) δ 166.9, 133.4, 133.0, 130.9, 129.9, 125.6, 117.3

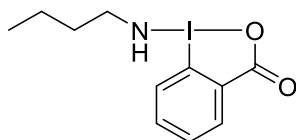
The analytical data for this compound were in excellent agreement with the reported data.⁹⁾

1-(benzylamino)-benziodoxol-3(1*H*)-one (1b)

According to the general procedure **I**, the reaction using 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (122.5 mg, 0.4 mmol, 1.0 equiv), MeCN (5 mL), benzylamine (47.4 mg, 0.44 mmol, 1.1 equiv), and NEt₃ (61.6 mg, 0.60 mmol, 1.5 equiv) was conducted. The precipitation was filtered, washed with MeCN, and dried under vacuum to give the product as a white solid (125.7 mg, 0.36 mmol, 89% yield).

¹H NMR: (400 MHz, DMSO-*d*₆) δ 8.04 (d, *J* = 7.6 Hz, 1H), 7.98 (d, *J* = 7.6 Hz, 1H), 7.82 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.41 (d, *J* = 7.6 Hz, 2H), 7.38–7.25 (m, 3H), 5.85 (t, *J* = 6.0 Hz, 1H), 4.46 (d, *J* = 6.0 Hz, 2H); ¹³C{¹H} NMR: (100 MHz, DMSO-*d*₆) δ 166.8, 140.7, 133.4, 133.1, 131.2, 130.0, 128.43, 128.39, 127.5, 125.7, 116.8, 54.5

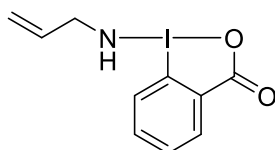
The analytical data for this compound were in excellent agreement with the reported data.⁹⁾

1-(butylamino)-benziodoxol-3(1*H*)-one (1c)

According to the general procedure **II**, the reaction using 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (1.224 g, 4.0 mmol, 1.0 equiv), MeCN (50 mL), *n*-butylamine (327.6 mg, 4.4 mmol, 1.1 equiv), and NEt₃ (831.8 μL, 6.0 mmol, 1.5 equiv) was conducted. The resulting solid was washed with Et₂O and dried under vacuum to give the product as a white solid (1.030 g, 3.23 mmol, 81% yield).

mp. 115.6 °C (decomposed); ¹H NMR: (400 MHz, CDCl₃) δ 8.29 (d, *J* = 7.6 Hz, 1H), 8.10 (d, *J* = 7.6 Hz, 1H), 7.77 (ddd, *J* = 7.6, 7.6, 1.6 Hz, 1H), 7.62 (dd, *J* = 7.6, 7.6 Hz, 1H), 4.93 (brs, 1H), 3.49–3.37 (m, 2H), 1.60 (tt, *J* = 7.2, 7.2 Hz, 2H), 1.42 (tq, *J* = 7.2, 7.2 Hz, 2H), 0.93 (t, *J* = 7.2 Hz, 3H);

¹³C{¹H} NMR: (100 MHz, DMSO-*d*₆) δ 166.8, 133.6, 133.2, 131.3, 130.0, 125.4, 116.9, 51.0, 34.4, 19.4, 13.8; IR: (ATR) 3163, 3055, 2949, 2932, 2862, 1599, 1584, 1560, 1477, 1456, 1433, 1334, 1300, 1258, 1244, 1159, 1142, 1115, 1040, 1026, 1011, 961, 907, 829, 812, 746 cm⁻¹; HRMS (FAB+) *m/z*: [M+H]⁺ Calculated for C₁₁H₁₅NO₂I 320.0148; Found 320.0152

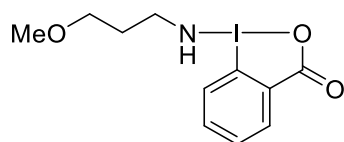
1-(allylamino)-1,2-benziodoxol-3(1*H*)-one (1d)

According to the general procedure **I**, the reaction using 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (122.6 mg, 0.4 mmol, 1.0 equiv), MeCN (4 mL), allylamine (26.0 mg, 0.44 mmol, 1.1 equiv), and NEt₃ (80 μ L, 0.6 mmol, 1.5 equiv) was conducted. The precipitation was filtered, washed with Et₂O, and dried under vacuum to give the product as a white solid (101.6 mg, 0.34 mmol, 84% yield).

¹H NMR: (400 MHz, DMSO-*d*₆) δ 8.10–7.97 (m, 2H), 7.90–7.80 (m, 1H), 7.64 (dd, *J* = 7.2, 7.2 Hz, 1H), 5.97–5.80 (m, 1H), 5.58 (t, *J* = 4.8 Hz, 1H), 5.32–5.22 (m, 1H), 5.22–5.10 (m, 1H), 4.02–3.90 (m, 2H); ¹³C{¹H} NMR: (100 MHz, DMSO-*d*₆) δ 166.8, 137.3, 133.4, 133.2, 131.2, 130.0, 125.5, 117.4, 116.9, 53.2

The analytical data for this compound were in excellent agreement with the reported data.⁹⁾

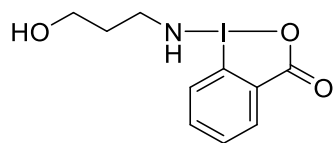
1-((3-methoxypropyl)amino)-benziodoxol-3(1*H*)-one (**1e**)



According to the general procedure **II**, the reaction using 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (122.7 mg, 0.4 mmol, 1.0 equiv), MeCN (5 mL), 3-methoxypropylamine (40.3 mg, 0.44 mmol, 1.1 equiv), and NEt₃ (58.2 mg, 0.60 mmol, 1.5 equiv) was conducted. The resulting solid was washed with Et₂O and dried under vacuum to give the product as a white solid (130.2 mg, 0.38 mmol, 97% yield).

mp. 93.5 °C (decomposed); ¹H NMR: (400 MHz, CDCl₃) δ 8.28 (d, *J* = 7.6 Hz, 1H), 8.10 (d, *J* = 7.6 Hz, 1H), 7.75 (ddd, *J* = 7.6, 7.6, 0.8 Hz, 1H), 7.60 (dd, *J* = 7.6, 7.6 Hz, 1H), 5.00 (br, 1H), 3.64–3.51 (m, 4H), 3.36 (s, 3H), 1.89 (tt, *J* = 6.0, 6.0 Hz, 2H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 168.9, 133.4, 132.8, 132.4, 130.2, 125.2, 116.5, 70.7, 58.8, 50.9, 33.1; IR: (ATR) 3167, 3059, 2955, 2934, 2913, 2874, 2855, 2814, 2797, 2158, 1603, 1585, 1564, 1477, 1454, 1433, 1377, 1334, 1296, 1258, 1238, 1209, 1177, 1152, 1121, 1111, 1080, 1042, 1011, 976, 957, 897, 880, 829, 808, 739 cm⁻¹; HRMS (FAB+) *m/z*: [M+H]⁺ Calculated for C₁₁H₁₅NO₃I 336.0097; Found 336.0090

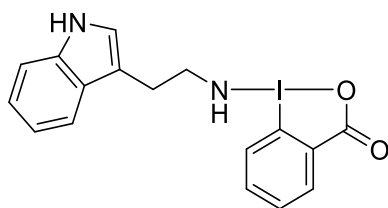
1-((3-hydroxypropyl)amino)-benziodoxol-3(1*H*)-one (**1f**)



According to the general procedure **II**, the reaction using 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (122.8 mg, 0.4 mmol, 1.0 equiv), MeCN (5 mL), 3-amino-1-propanol (34.1 mg, 0.44 mmol, 1.1 equiv), and NEt₃ (61.3 mg, 0.60 mmol, 1.5 equiv) was conducted. The resulting solid was washed with Et₂O and dried under vacuum to give the product as a white solid (121.5 mg, 0.38 mmol, 95% yield).

mp. 106.9 °C (decomposed); ^1H NMR: (400 MHz, $\text{DMSO-}d_6$) δ 8.06–7.98 (m, 2H), 7.84 (dd, $J = 7.2$, 7.2 Hz, 1H), 7.63 (dd, $J = 7.2$, 7.2 Hz, 1H), 5.47 (t, $J = 6.4$ Hz, 1H), 4.54 (brs, 1H), 3.50 (t, $J = 6.4$ Hz, 2H), 3.38 (t, $J = 6.4$ Hz, 2H), 1.64 (tt, $J = 6.4$, 6.4 Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, $\text{DMSO-}d_6$) δ 166.9, 133.6, 133.2, 131.3, 130.1, 125.5, 116.9, 58.2, 48.7, 35.5; IR: (ATR) 3175, 3086, 3075, 2941, 2924, 2870, 2853, 1603, 1585, 1560, 1466, 1435, 1398, 1337, 1315, 1298, 1236, 1182, 1150, 1080, 1057, 1034, 1011, 920, 897, 885, 829, 810, 746 cm^{-1} ; HRMS (FAB+) m/z : $[\text{M}+\text{H}]^+$ Calculated for $\text{C}_{10}\text{H}_{13}\text{NO}_3\text{I}$ 321.9940; Found 321.9938

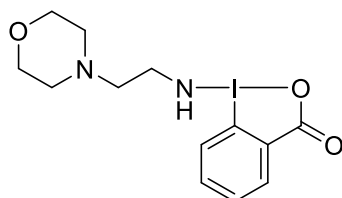
1-((2-(1*H*-indol-3-yl)ethyl)amino)-1,2-benziodoxol-3(1*H*)-one (1g)



According to the general procedure **I**, the reaction using 1-acetoxy-1,2-benziodoxol-3(1*H*)-one (153 mg, 0.5 mmol, 1.0 equiv), MeCN (10 mL), tryptamine (88.2 mg, 0.55 mmol, 1.1 equiv), and NEt_3 (100 μL , 0.75 mmol, 1.5 equiv) was conducted. The precipitation was filtered, washed with MeCN, and dried under vacuum to give the product as a white solid (182 mg, 0.45 mmol, 90% yield).

mp. 107.5 °C (decomposed); ^1H NMR: (400 MHz, $\text{DMSO-}d_6$) δ 10.91 (brs, 1H), 8.00–7.93 (m, 1H), 7.85 (d, $J = 8.4$ Hz, 1H), 7.68–7.61 (m, 1H), 7.61–7.50 (m, 2H), 7.36 (d, $J = 8.0$ Hz, 1H), 7.25–7.19 (m, 1H), 7.12–7.03 (m, 1H), 7.02–6.93 (m, 1H), 5.39 (t, $J = 6.8$ Hz, 1H), 3.64 (dt, $J = 6.8$, 6.8 Hz, 2H), 2.94 (t, $J = 6.8$ Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, $\text{DMSO-}d_6$) δ 166.8, 136.3, 133.3, 133.0, 131.2, 129.9, 127.2, 125.3, 123.5, 121.1, 118.38, 118.36, 117.2, 111.5, 111.1, 52.3, 28.7; IR: (ATR) 3300, 3235, 2918, 1595, 1557, 1435, 1335, 1296, 1234, 1182, 1098, 1007, 829, 756, 731 cm^{-1} ; HRMS (ESI+) m/z : $[\text{M}+\text{Na}]^+$ Calculated for $\text{C}_{17}\text{H}_{15}\text{N}_2\text{O}_2\text{NaI}$ 429.0076; Found 429.0061

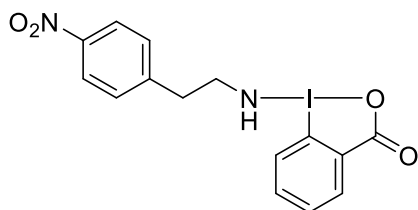
1-((2-morpholinoethyl)amino)-benziodoxol-3(1*H*)-one (1h)



According to the general procedure **II**, the reaction using 1-acetoxy-1,2-benziodoxol-3(1*H*)-one (122.8 mg, 0.4 mmol, 1.0 equiv), 1,4-diazabicyclo[2.2.2]octane (67.9 mg, 0.60 mmol, 1.5 equiv), MeCN (5 mL), and 4-(2-aminoethyl)morpholine (55.3 mg, 0.44 mmol, 1.1 equiv) was conducted. Then, volatiles were removed under reduced pressure. The resulting solid was washed with Et_2O and dried under vacuum to give the product as a white solid (142.6 mg, 0.38 mmol, 94% yield).

mp. 88.4 °C (decomposed); ^1H NMR: (400 MHz, $\text{DMSO}-d_6$) δ 8.08 (d, $J = 7.6$ Hz, 1H), 7.97 (d, $J = 7.6$ Hz, 1H), 7.81 (dd, $J = 7.6, 7.6$ Hz, 1H), 7.59 (dd, $J = 7.6, 7.6$ Hz, 1H), 5.30 (t, $J = 6.8$ Hz, 1H), 3.77–3.65 (m, 4H), 3.55–3.50 (m, 2H), 2.80–2.42 (m, 6H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, $\text{DMSO}-d_6$) δ 167.5, 133.9, 132.8, 131.1, 129.7, 125.9, 120.1, 66.5, 61.4, 53.2, 47.7; IR: (ATR) 3192, 2965, 2857, 2814, 2760, 1626, 1599, 1584, 1562, 1449, 1439, 1398, 1369, 1341, 1331, 1302, 1288, 1273, 1254, 1227, 1136, 1113, 1061, 1045, 1032, 1013, 937, 914, 856, 826, 814, 768, 737 cm^{-1} ; HRMS (FAB+) m/z : $[\text{M}+\text{H}]^+$ Calculated for $\text{C}_{13}\text{H}_{18}\text{N}_2\text{O}_3$ 377.0362; Found 377.0365

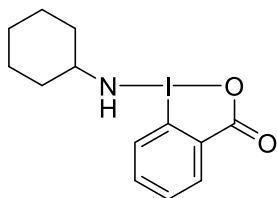
1-((4-nitrophenethyl)amino)-1,2-benziodoxol-3(1H)-one (1i)



According to the general procedure **I**, the reaction using 1-acetoxy-1,2-benziodoxol-3(1H)-one (307 mg, 1.0 mmol, 1.0 equiv), MeCN (10 mL), 2-(4-nitrophenyl)ethan-1-amine (183.6 mg, 1.1 mmol, 1.1 equiv), and NEt_3 (200 μL , 1.5 mmol, 1.5 equiv) was conducted. The precipitation was filtered, washed with MeCN, and dried under vacuum to give the product as a pale red solid (383 mg, 0.93 mmol, 93% yield).

mp. 141.6 °C (decomposed); ^1H NMR: (400 MHz, $\text{DMSO}-d_6$) δ 8.17 (d, $J = 8.8$ Hz, 2H), 8.03–7.93 (m, 1H), 7.70–7.50 (m, 5H), 5.47 (t, $J = 6.8$ Hz, 1H), 3.62 (dt, $J = 6.8, 6.8$ Hz, 2H), 2.95 (t, $J = 6.8$ Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, $\text{DMSO}-d_6$) δ 166.8, 147.9, 146.1, 133.4, 132.9, 131.2, 130.4, 130.0, 125.3, 123.4, 117.1, 52.0, 38.2; IR: (ATR) 3124, 1593, 1584, 1557, 1514, 1339, 1302, 1107, 1024, 1013, 829, 745 cm^{-1} ; HRMS (ESI+) m/z : $[\text{M}+\text{Na}]^+$ Calculated for $\text{C}_{15}\text{H}_{13}\text{N}_2\text{O}_4\text{Na}$ 434.9818; Found 434.9809

1-(cyclohexylamino)-1,2-benziodoxol-3(1H)-one (1j)



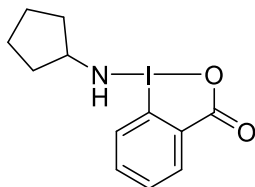
According to the general procedure **I**, the reaction using 1-acetoxy-1,2-benziodoxol-3(1H)-one (152 mg, 0.5 mmol, 1.0 equiv), MeCN (5 mL), cyclohexylamine (51.8 mg, 0.5 mmol, 1.0 equiv), and NEt_3 (70 μL , 0.5 mmol, 1.0 equiv) was conducted. The precipitation was filtered, washed with MeCN, and dried under vacuum to give the product as a white solid (149.5 mg, 0.43 mmol, 87% yield).

^1H NMR: (400 MHz, $\text{DMSO}-d_6$) δ 8.07 (d, $J = 8.4$ Hz, 1H), 8.03–7.97 (m, 1H), 7.88–7.79 (m, 1H), 7.77–7.58 (m, 1H), 5.54 (d, $J = 4.4$ Hz, 1H), 3.17–3.00 (m, 1H), 2.00–1.80 (m, 2H), 1.80–1.57 (m, 2H),

1.57–1.40 (m, 1H), 1.30–1.00 (m, 5H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, DMSO- d_6) δ 166.8, 133.6, 133.1, 131.1, 130.0, 125.3, 117.2, 58.2, 34.8, 25.2, 24.5

The analytical data for this compound were in excellent agreement with the reported data.⁹⁾

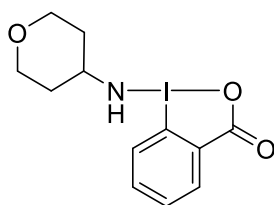
1-(cyclopentylamino)-benziodoxol-3(1H)-one (1k)



According to the general procedure **II**, the reaction using 1-acetoxy-1,2-benziodoxol-3-(1H)-one (122.5 mg, 0.4 mmol, 1.0 equiv), MeCN (5 mL), cyclopentylamine (38.0 mg, 0.44 mmol, 1.1 equiv), and NEt₃ (61.2 mg, 0.60 mmol, 1.5 equiv) was conducted. The resulting solid was washed with Et₂O and dried under vacuum to give the product as a white solid (118.6 mg, 0.36 mmol, 90% yield).

mp. 87.2 °C (decomposed); ^1H NMR: (400 MHz, DMSO- d_6) δ 8.04–7.98 (m, 2H), 7.84 (ddd, J = 7.2, 7.2, 1.2 Hz, 1H), 7.63 (dd, J = 7.2, 7.2 Hz, 1H), 5.64 (d, J = 4.0 Hz, 1H), 3.91–3.83 (m, 1H), 1.85–1.70 (m, 4H), 1.59–1.51 (m, 2H), 1.51–1.41 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, DMSO- d_6) δ 166.7, 133.6, 133.0, 131.2, 130.0, 125.3, 117.0, 60.9, 34.4, 23.5; IR: (ATR) 3161, 2955, 2930, 1678, 1601, 1584, 1562, 1454, 1433, 1335, 1314, 1288, 1240, 1171, 1157, 1123, 1024, 1011, 989, 827, 814, 745 cm^{-1} ; HRMS (FAB⁺) m/z : $[\text{M}+\text{H}]^+$ Calculated for C₁₂H₁₅NO₂I 332.0148; Found 332.0140

1-((tetrahydro-2H-pyran-4-yl)amino)-benziodoxol-3(1H)-one (1l)

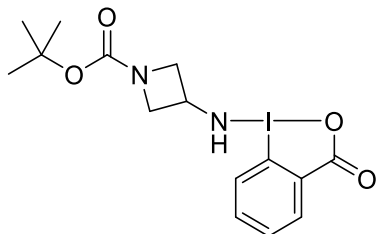


According to the general procedure **II**, the reaction using 1-acetoxy-1,2-benziodoxol-3-(1H)-one (310.0 mg, 1.0 mmol, 1.0 equiv), MeCN (5 mL), tetrahydro-2H-pyran-4-amine (120.5 mg, 1.1 mmol, 1.1 equiv), and NEt₃ (192 μL , 1.5 mmol, 1.5 equiv) was conducted. The resulting solid was washed with Et₂O and dried under vacuum to give the product as a white solid (343.7 mg, 0.99 mmol, 98% yield).

mp. 119.3 °C (decomposed); ^1H NMR: (400 MHz, DMSO- d_6) δ 8.08 (d, J = 7.2 Hz, 1H), 8.01 (d, J = 7.2 Hz, 1H), 7.84 (dd, J = 7.2, 7.2 Hz, 1H), 7.63 (dd, J = 7.2, 7.2 Hz, 1H), 5.62 (d, J = 4.8 Hz, 1H), 3.90–3.78 (m, 2H), 3.37–3.24 (m, 3H), 1.93–1.82 (m, 2H), 1.45–1.32 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, DMSO- d_6) δ 167.0, 133.6, 133.3, 131.3, 130.1, 125.5, 117.2, 65.8, 55.4, 35.1; IR: (ATR) 3157, 2968, 2949, 2940, 2918, 2847, 1599, 1584, 1562, 1466, 1437, 1366, 1337, 1298, 1283, 1244, 1231, 1169, 1144, 1128, 1115, 1088, 1072, 1024, 1011, 980, 962, 918, 866, 829, 820, 748 cm^{-1} ; HRMS

(FAB+) m/z : $[M+H]^+$ Calculated for $C_{12}H_{15}NO_3I$ 348.0097; Found 348.0091; Analysis Calculated for $C_{12}H_{14}NO_3I$: C, 41.52; H, 4.07; N, 4.03; I, 36.56; Found: C, 41.22; H, 3.92; N, 3.99; I, 36.63

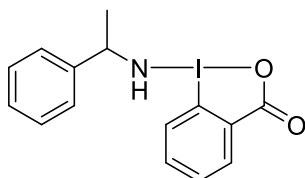
***tert*-butyl 3-((3-oxo-benziodaoxol-1(3*H*)-yl)amino)azetidine-1-carboxylate (1m)**



According to the general procedure **II**, the reaction using 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (122.6 mg, 0.4 mmol, 1.0 equiv), MeCN (5 mL), *tert*-butyl 3-aminoazetidine-1-carboxylate (74.8 mg, 0.44 mmol, 1.1 equiv), and NEt_3 (59.1 mg, 0.60 mmol, 1.5 equiv). The resulting solid was washed with Et_2O and dried under vacuum to give the product as a white solid (145.8 mg, 0.35 mmol, 87% yield).

mp. 117.0 °C (decomposed); 1H NMR: (400 MHz, $DMSO-d_6$) δ 8.04–7.97 (m, 2H), 7.86 (dd, $J = 7.6$, 7.6 Hz, 1H), 7.65 (dd, $J = 7.6$, 7.6 Hz, 1H), 5.96 (d, $J = 7.6$ Hz, 1H), 4.29–4.20 (m, 1H), 4.06–3.97 (m, 2H), 3.67–3.58 (m, 2H), 1.36 (s, 9H); $^{13}C\{^1H\}$ NMR: (100 MHz, $DMSO-d_6$) δ 167.0, 155.5, 133.5, 133.2, 131.3, 130.2, 125.3, 117.3, 78.7, 57.1 (br), 49.9, 28.0; IR: (ATR) 3202, 3192, 2976, 2934, 2880, 1697, 1655, 1593, 1585, 1560, 1476, 1454, 1425, 1371, 1364, 1339, 1300, 1285, 1248, 1152, 1140, 1113, 1053, 1028, 1011, 984, 974, 947, 860, 829, 800, 779, 762 cm^{-1} ; HRMS (FAB+) m/z : $[M+H]^+$ Calculated for $C_{15}H_{20}N_2O_4I$ 419.0468; Found 419.0473

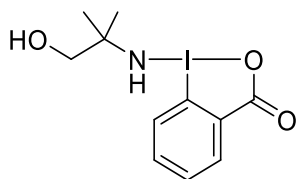
1-((1-phenylethyl)amino)-1,2-benziodoxol-3(1*H*)-one (1n)



According to the general procedure **I**, the reaction using 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (305 mg, 1.0 mmol, 1.0 equiv), MeCN (10 mL), 1-phenylethylamine (137.4 mg, 1.1 mmol, 1.1 equiv), and NEt_3 (200 μL , 1.5 mmol, 1.5 equiv) was conducted. The precipitation was filtered, washed with MeCN, and dried under vacuum to give the product as a white solid (284 mg, 0.77 mmol, 77% yield).

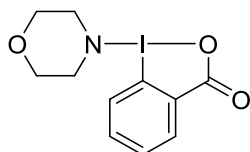
1H NMR: (400 MHz, $DMSO-d_6$) δ 8.12 (d, $J = 7.6$ Hz, 1H), 7.97 (dd, $J = 7.6$, 1.6 Hz, 1H), 7.87–7.79 (m, 1H), 7.66–7.56 (m, 1H), 7.45–7.38 (m, 2H), 7.35–7.27 (m, 2H), 7.27–7.20 (m, 1H), 5.95 (d, $J = 3.6$ Hz, 1H), 4.60–4.50 (m, 1H), 1.45 (d, $J = 7.2$ Hz, 3H); $^{13}C\{^1H\}$ NMR: (100 MHz, $DMSO-d_6$) 166.7, 144.5, 133.4, 133.1, 131.1, 130.0, 128.4, 127.6, 126.8, 125.8, 116.9, 58.4, 24.2

The analytical data for this compound were in excellent agreement with the reported data.⁴⁾

1-((1-hydroxy-2-methylpropan-2-yl)amino)-benziodoxol-3(1*H*)-one (1o)

According to the general procedure **II**, the reaction using 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (122.3 mg, 0.4 mmol, 1.0 equiv), MeCN (5 mL), 2-amino-2-methyl-1-propanol (39.1 mg, 0.44 mmol, 1.1 equiv), and NEt₃ (60.8 mg, 0.60 mmol, 1.5 equiv) was conducted. The resulting solid was washed with Et₂O and dried under vacuum to give the product as a white solid (114.2 mg, 0.34 mmol, 85% yield).

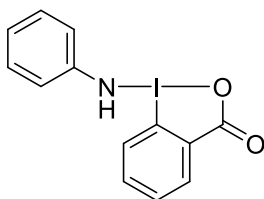
mp. 133.4 °C (decomposed); ¹H NMR: (400 MHz, DMSO-*d*₆) δ 8.15 (d, *J* = 7.6 Hz, 1H), 7.99 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.85 (ddd, *J* = 7.6, 7.6, 1.6 Hz, 1H), 7.61 (dd, *J* = 7.6, 7.6 Hz, 1H), 5.95 (t, *J* = 4.8 Hz, 1H), 5.47 (brs, 1H), 3.41–3.33 (m, 2H), 1.15 (s, 6H); ¹³C{¹H} NMR: (100 MHz, DMSO-*d*₆) δ 167.1, 133.7, 133.0, 131.1, 129.8, 125.0, 118.0, 70.9, 56.8, 24.6; IR: (ATR) 3381, 2976, 2918, 2872, 1672, 1616, 1524, 1477, 1454, 1406, 1364, 1321, 1308, 1298, 1265, 1244, 1155, 1136, 1112, 1042, 1009, 932, 920, 860, 808, 770, 752, 704 cm⁻¹; HRMS (FAB+) *m/z*: [M+H]⁺ Calculated for C₁₁H₁₅NO₃I 336.0097; Found 336.0105

1-morpholino-benziodoxol-3(1*H*)-one (1p)

According to the general procedure **II**, the reaction using 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (123.0 mg, 0.4 mmol, 1.0 equiv), MeCN (5 mL), morpholine (38.4 mg, 0.44 mmol, 1.1 equiv), and NEt₃ (61.8 mg, 0.60 mmol, 1.5 equiv) was conducted. The resulting solid was washed with Et₂O and dried under vacuum to give the product as a white solid (112.6 mg, 0.34 mmol, 85% yield).

¹H NMR: (400 MHz, DMSO-*d*₆) δ 8.21 (d, *J* = 7.6 Hz, 1H), 8.03 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.91 (ddd, *J* = 7.6, 7.6, 1.2 Hz, 1H), 7.64 (dd, *J* = 7.6, 7.6 Hz, 1H), 3.78–3.67 (m, 4H), 3.57–3.48 (m, 4H); ¹³C{¹H} NMR: (100 MHz, DMSO-*d*₆) δ 167.1, 133.7, 132.9, 131.6, 130.3, 125.8, 117.1, 68.8, 55.8

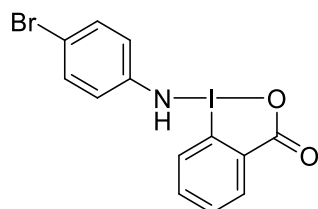
The analytical data for this compound were in excellent agreement with the reported data.³⁾

1-(phenylamino)-benziodoxol-3(1*H*)-one (1q)

According to the general procedure **II**, the reaction using 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (122.8 mg, 0.4 mmol, 1.0 equiv), MeCN (5 mL), aniline (42.8 mg, 0.44 mmol, 1.1 equiv), and NEt₃ (57.8 mg, 0.60 mmol, 1.5 equiv) was conducted. The resulting solid was washed with Et₂O and dried under vacuum to give the product as a pale yellow solid (123.3 mg, 0.36 mmol, 91% yield).

mp. 72.4 °C (decomposed); ¹H NMR: (400 MHz, DMSO-*d*₆) δ 8.12 (s, 1H), 8.05 (d, *J* = 7.2 Hz, 1H), 7.86–7.77 (m, 2H), 7.69 (dd, *J* = 7.2, 7.2 Hz, 1H), 7.18 (dd, *J* = 7.6, 7.6 Hz, 2H), 6.89 (d, *J* = 7.6 Hz, 2H), 6.78 (dd, *J* = 7.6, 7.6 Hz, 1H); ¹³C {¹H} NMR: (100 MHz, DMSO-*d*₆) δ 167.4, 148.2, 134.1, 133.0, 131.5, 130.6, 129.5, 125.7, 120.6, 119.5, 117.2; IR: (ATR) 3150, 3090, 3073, 3055, 3038, 3017, 2941, 2853, 1684, 1607, 1584, 1566, 1487, 1470, 1454, 1437, 1392, 1327, 1298, 1271, 1219, 1175, 1144, 1125, 1113, 1099, 1076, 1061, 1024, 1011, 903, 885, 826, 808, 741 cm⁻¹; HRMS (FAB+) *m/z*: [M+H]⁺ Calculated for C₁₃H₁₁NO₂I 339.9835; Found 339.9844

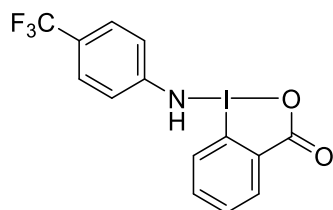
1-((4-bromophenyl)amino)-benziodoxol-3(1*H*)-one (1r)



According to the general procedure **II**, the reaction using 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (122.2 mg, 0.4 mmol, 1.0 equiv), MeCN (5 mL), 4-bromoaniline (77.6 mg, 0.44 mmol, 1.1 equiv), and NEt₃ (60.2 mg, 0.60 mmol, 1.5 equiv) was conducted. The resulting solid was washed with Et₂O and dried under vacuum to give the product as a pale yellow solid (149.1 mg, 0.36 mmol, 89% yield).

mp. 85.4 °C (decomposed); ¹H NMR: (400 MHz, DMSO-*d*₆) δ 8.18 (s, 1H), 8.05 (d, *J* = 8.0 Hz, 1H), 7.84 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.69 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.33 (d, *J* = 7.6 Hz, 2H), 6.86 (d, *J* = 7.6 Hz, 2H); ¹³C {¹H} NMR: (100 MHz, DMSO-*d*₆) δ 167.4, 147.7, 134.3, 132.8, 131.9, 131.5, 130.7, 125.6, 119.4, 119.2, 111.5; IR: (ATR) 3217, 3165, 3146, 1603, 1584, 1564, 1483, 1439, 1422, 1337, 1300, 1263, 1215, 1177, 1070, 1005, 831, 822, 745 cm⁻¹; HRMS (FAB+) *m/z*: [M]⁺ Calculated for C₁₃H₉BrNO₂I 416.8861; Found 416.8852

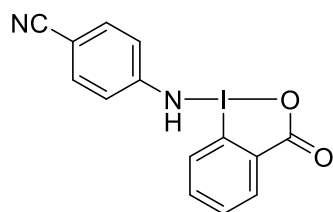
1-((4-(trifluoromethyl)phenyl)amino)-benziodoxol-3(1*H*)-one (1s)



According to the general procedure **II**, the reaction using 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (308.6 mg, 1.0 mmol, 1.0 equiv), MeCN (12.5 mL), 4-aminobenzotrifluoride (176.7 mg, 1.1 mmol, 1.1 equiv), and NEt₃ (160.1 mg, 1.5 mmol, 1.5 equiv) was conducted. The resulting solid was washed with Et₂O and dried under vacuum to give the product as a pale yellow solid (279.1 mg, 0.69 mmol, 69% yield).

mp. 145.1 °C (decomposed); ¹H NMR: (400 MHz, DMSO-*d*₆) δ 8.44 (s, 1H), 8.06 (d, *J* = 7.6 Hz, 1H), 7.83 (ddd, *J* = 7.6, 7.6, 1.2 Hz, 1H), 7.72–7.66 (m, 2H), 7.50 (d, *J* = 8.0 Hz, 2H), 7.02 (d, *J* = 8.0 Hz, 2H); ¹³C{¹H} NMR: (100 MHz, DMSO-*d*₆) δ 167.3, 151.8, 134.4, 132.7, 131.6, 130.7, 126.6 (q, *J*_{CF} = 3.8 Hz), 125.5, 124.6 (q, *J*_{CF} = 269.4 Hz), 119.9 (q, *J*_{CF} = 31.5 Hz), 119.4, 116.8; ¹⁹F{¹H} NMR (376 MHz, DMSO-*d*₆) δ -59.0; IR: (ATR) 3132, 3076, 3051, 1599, 1581, 1562, 1516, 1439, 1325, 1285, 1233, 1192, 1155, 1113, 1096, 1067, 1026, 1011, 988, 959, 939, 880, 831, 802, 743 cm⁻¹; HRMS (FAB+) *m/z*: [M+H]⁺ Calculated for C₁₄H₁₀F₃NO₂I 407.9708; Found 407.9704

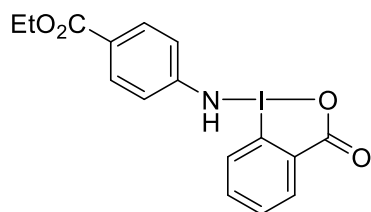
4-((3-oxo-benziodaoxol-1(3*H*)-yl)amino)benzonitrile (**1t**)



According to the general procedure **II**, the reaction using 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (123.0 mg, 0.4 mmol, 1.0 equiv), MeCN (5 mL), 4-aminobenzonitrile (52.8 mg, 0.44 mmol, 1.1 equiv), and NEt₃ (60.8 mg, 0.60 mmol, 1.5 equiv) was conducted. The resulting solid was washed with Et₂O and dried under vacuum to give the product as a pale yellow solid (103.1 mg, 0.28 mmol, 71% yield).

mp. 151.2 °C (decomposed); ¹H NMR: (400 MHz, DMSO-*d*₆) δ 8.59 (s, 1H), 8.06 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.84 (ddd, *J* = 7.6, 7.6, 1.6 Hz, 1H), 7.70 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.59 (d, *J* = 8.8 Hz, 2H), 6.99 (d, *J* = 8.8, 2H); ¹³C{¹H} NMR: (100 MHz, DMSO-*d*₆) δ 167.4, 152.7, 134.5, 133.8, 132.5, 131.6, 130.7, 125.5, 119.43, 119.42, 117.2, 101.0; IR: (ATR) 3136, 3123, 2214, 1678, 1597, 1585, 1564, 1503, 1437, 1337, 1306, 1277, 1233, 1169, 1148, 1123, 1013, 831, 797, 743, 716 cm⁻¹; HRMS (ESI-) *m/z*: [M-H]⁻ Calculated for C₁₄H₈N₂O₂I 362.9636; Found 362.9632

ethyl 4-((3-oxo-benziodaoxol-1(3*H*)-yl)amino)benzoate (**1u**)

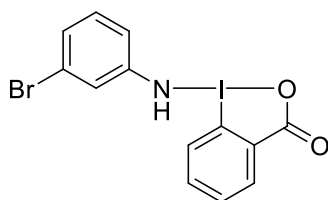


According to the general procedure **II**, the reaction using 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (309.1 mg, 1.0 mmol, 1.0 equiv), MeCN (12.5 mL), ethyl 4-aminobenzoate (183.6 mg, 1.1 mmol, 1.1 equiv),

and NEt_3 (161.9 mg, 1.5 mmol, 1.5 equiv) was conducted. The resulting solid was washed with Et_2O and dried under vacuum to give the product as a pale yellow solid (279.6 mg, 0.68 mmol, 68% yield).

mp. 120.2 °C (decomposed); ^1H NMR: (400 MHz, $\text{DMSO}-d_6$) δ 8.52 (s, 1H), 8.06 (d, $J = 7.6$ Hz, 1H), 7.83 (dd, $J = 7.6, 7.6$ Hz, 1H), 7.77 (d, $J = 8.0$ Hz, 2H), 7.74–7.63 (m, 2H), 6.95 (d, $J = 8.0$ Hz, 2H), 4.23 (q, $J = 7.2$ Hz, 2H), 1.27 (t, $J = 7.2$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, $\text{DMSO}-d_6$) δ 167.4, 165.3, 152.8, 134.4, 132.7, 131.6, 131.1, 130.7, 125.6, 121.0, 119.4, 116.4, 60.1, 14.3; IR: (ATR) 3119, 3075, 3042, 2984, 1701, 1688, 1595, 1560, 1508, 1479, 1437, 1364, 1339, 1269, 1234, 1175, 1105, 1026, 1013, 974, 959, 856, 831, 797, 764, 743 cm^{-1} ; HRMS (FAB+) m/z : $[\text{M}+\text{H}]^+$ Calculated for $\text{C}_{16}\text{H}_{15}\text{NO}_4\text{I}$ 412.0046; Found 412.0049

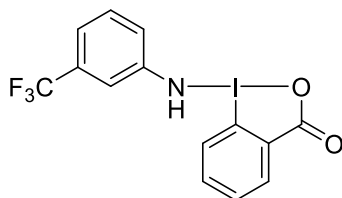
1-((3-bromophenyl)amino)-1,2-benziodoxol-3(1H)-one (1v)



According to the general procedure II, the reaction using 1-acetoxy-1,2-benziodoxol-3-(1H)-one (123.0 mg, 0.4 mmol, 1.0 equiv), MeCN (4 mL), 3-bromoaniline (76.8 mg, 0.44 mmol, 1.1 equiv), and NEt_3 (100 μL , 0.6 mmol, 1.5 equiv) was conducted. The resulting solid was washed with MeCN and dried under vacuum to give the product as a pale yellow solid (140.4 mg, 0.34 mmol, 84% yield).

mp. 96.5 °C (decomposed); ^1H NMR: (400 MHz, $\text{DMSO}-d_6$) δ 8.19 (brs, 1H), 8.13–8.02 (m, 1H), 7.90–7.82 (m, 1H), 7.82–7.74 (m, 1H), 7.74–7.65 (m, 1H), 7.20–7.06 (m, 2H), 6.98–6.92 (m, 1H), 6.92–6.84 (m, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, $\text{DMSO}-d_6$) δ 167.3, 150.1, 134.2, 132.7, 131.5, 131.2, 130.6, 125.5, 122.8, 122.1, 119.5, 119.4, 116.2; IR: (ATR) 3221, 1684, 1607, 1584, 1472, 1437, 1288, 1221, 1123, 1088, 1067, 991, 878, 829, 746 cm^{-1} ; HRMS (FAB+) m/z : $[\text{M}]^+$ Calculated for $\text{C}_{13}\text{H}_9\text{BrNO}_2\text{I}$ 416.8861; Found 416.8877

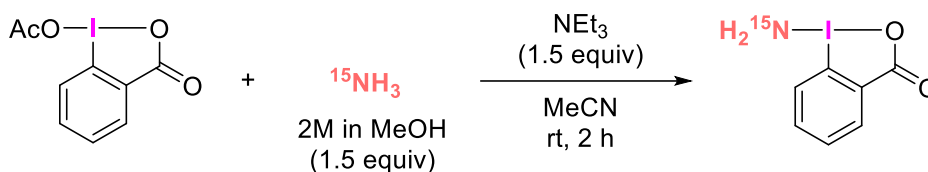
1-((3-(trifluoromethyl)phenyl)amino)-1,2-benziodoxol-3(1H)-one (1w)



According to the general procedure II, the reaction using 1-acetoxy-1,2-benziodoxol-3-(1H)-one (307 mg, 1.0 mmol, 1.0 equiv), MeCN (5 mL), 3-aminobenzotrifluoride (179.9 mg, 1.1 mmol, 1.1 equiv), and NEt_3 (170 μL , 1.1 mmol, 1.1 equiv) was conducted. The resulting solid was washed with MeCN and dried under vacuum to give the product as a pale yellow solid (301 mg, 0.74 mmol, 74% yield).

mp. 122.0 °C (decomposed); ^1H NMR: (400 MHz, $\text{DMSO-}d_6$) δ 8.34 (brs, 1H), 8.10–8.00 (m, 1H), 7.90–7.82 (m, 1H), 7.82–7.75 (m, 1H), 7.74–7.66 (m, 1H), 7.45–7.36 (m, 1H), 7.19 (s, 1H), 7.16–7.08 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, $\text{DMSO-}d_6$) δ 167.4, 149.2, 134.3, 132.7, 131.5, 130.64, 130.59, 130.0 (q, $J_{\text{CF}} = 31.4$ Hz), 125.5, 124.1 (q, $J_{\text{CF}} = 271.2$ Hz), 120.9, 119.5, 116.4 (q, $J_{\text{CF}} = 3.8$ Hz), 113.2 (q, $J_{\text{CF}} = 3.8$ Hz); $^{19}\text{F}\{^1\text{H}\}$ NMR: (376 MHz, $\text{DMSO-}d_6$) δ -60.7; IR: (ATR) 3090, 3051, 2841, 1597, 1585, 1564, 1464, 1441, 1329, 1302, 1233, 1159, 1111, 1072, 995, 900, 831, 748 cm^{-1} ; HRMS (FAB+) m/z : $[\text{M}]^+$ Calculated for $\text{C}_{14}\text{H}_9\text{F}_3\text{INO}_2$ 406.9630; Found 406.9625

1-(amino- ^{15}N)-1,2-benziodoxol-3-(1H)-one (^{15}N -1a)

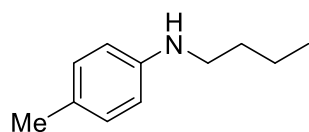


A reaction flask equipped with a magnetic stirring bar was flame-dried under vacuum. After cooling to room temperature, the flask was charged with nitrogen gas, 1-acetoxy-1,2-benziodoxol-3-(1H)-one (153.5 mg, 0.5 mmol, 1.0 equiv), MeCN (5 mL), ammonia- ^{15}N in methanol solution (2 M, 0.375 mL, 0.75 mmol, 1.5 equiv),⁴⁸⁾ and NEt_3 (100 μL , 0.75 mmol, 1.5 equiv). The mixture was stirred at room temperature for 2 h. The precipitation was filtered and washed with CHCl_3 and dried under vacuum to give the product as a white solid (69.8 mg, 0.26 mmol, 53% yield).

mp. 110.4 °C (decomposed); ^1H NMR: (400 MHz, $\text{DMSO-}d_6$) δ 8.05–7.95 (m, 2H), 7.88–7.78 (m, 1H), 7.63 (dd, $J = 7.2, 7.2$ Hz, 1H), 4.70 (d, $J_{\text{NH}} = 67.2$ Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, $\text{DMSO-}d_6$) δ 167.0, 133.5, 133.1, 130.9, 130.0, 125.6 (d, $J_{\text{CN}} = 1.6$ Hz), 117.4 (d, $J_{\text{CN}} = 4.2$ Hz); $^{15}\text{N}\{^1\text{H}\}$ NMR: (41 MHz, $\text{DMSO-}d_6$) δ 16.8; IR: (ATR) 3625, 3181, 3071, 1582, 1549, 1435, 1341, 1298, 1152, 1013, 829, 745 cm^{-1} ; HRMS (FAB+) m/z : $[\text{M}+\text{H}]^+$ Calculated for $\text{C}_7\text{H}_7^{15}\text{NO}_2\text{I}$ 264.9492; Found 264.9502

Oxidative amination of arylboronic acids: experimental procedures and product data

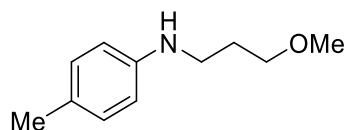
General procedure III: A reaction flask equipped with a magnetic stirring bar was charged with MS3A and flamed-dried under vacuum. After cooling down to room temperature, the flask was charged with nitrogen gas, arylboronic acid (1.0 equiv), aminobenziodoxolone **1** (1.1 equiv), base (1.2 equiv), and solvent. Then, the flask was sealed and placed in an aluminum block, which was preheated at indicated temperature. After the mixture was stirred at the temperature for 24 h, the reaction mixture was filtered by a pad of celite using CHCl_3 as an eluent. To the filtrate, sat. NaHCO_3 aq. was added, and the mixture was extracted with CHCl_3 (3 $\times$ 15 mL). The combined organic layers were dried over Na_2SO_4 , filtrated, and concentrated under reduced pressure to give the crude product. Purification by flash column chromatography on NH silica gel (hexane/EtOAc) gave the product.

N-butyl-4-methylaniline (6)

According to the general procedure **III**, the reaction using MS3A (407 mg), (4-methylphenyl)boronic acid (55.0 mg, 0.40 mmol, 1.0 equiv), aminobenziodoxolone **1c** (141.2 mg, 0.44 mmol, 1.1 equiv), Cs₂CO₃ (158.0 mg, 0.48 mmol, 1.2 equiv), and THF (4 mL) was conducted at 50 °C. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 99:1) gave the product as a pale yellow oil (44.2 mg, 0.27 mmol, 68% yield).

¹H NMR: (400 MHz, CDCl₃) δ 6.98 (d, *J* = 8.0 Hz, 2H), 6.53 (d, *J* = 8.0 Hz, 2H), 3.44 (brs, 1H), 3.08 (t, *J* = 7.2 Hz, 2H), 2.23 (s, 3H), 1.59 (tt, *J* = 8.0, 7.2 Hz, 2H), 1.42 (tq, *J* = 8.0, 7.2 Hz, 2H), 0.95 (t, *J* = 7.2 Hz, 3H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 146.3, 129.7, 126.3, 112.9, 44.0, 31.7, 20.35, 20.30, 13.9

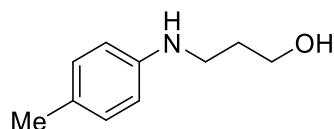
The analytical data for this compound were in excellent agreement with the reported data.⁵⁵⁾

N-(3-methoxypropyl)-4-methylaniline (7)

According to the general procedure **III**, the reaction using MS3A (610 mg), (4-methylphenyl)boronic acid (54.9 mg, 0.40 mmol, 1.0 equiv), aminobenziodoxolone **1e** (148.2 mg, 0.44 mmol, 1.1 equiv), Cs₂CO₃ (158.0 mg, 0.48 mmol, 1.2 equiv), and THF (4 mL) was conducted at 50 °C. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 95:5) gave the product as a pale yellow oil (46.7 mg, 0.26 mmol, 65% yield).

¹H NMR: (400 MHz, CDCl₃) δ 7.01–6.93 (m, 2H), 6.57–6.48 (m, 2H), 3.76 (brs, 1H), 3.50 (t, *J* = 6.4 Hz, 2H), 3.35 (s, 3H), 3.20 (t, *J* = 6.4 Hz, 2H), 2.23 (s, 3H), 1.87 (tt, *J* = 6.4, 6.4 Hz, 2H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 146.2, 129.7, 126.3, 112.9, 71.2, 58.7, 42.1, 29.4, 20.3

The analytical data for this compound were in excellent agreement with the reported data.⁵⁶⁾

3-(*p*-tolylamino)propan-1-ol (8)

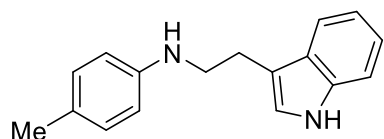
According to the general procedure **III**, the reaction using MS3A (207 mg), (4-methylphenyl)boronic acid (27.8 mg, 0.20 mmol, 1.0 equiv), aminobenziodoxolone **1f** (70.3 mg, 0.22 mmol, 1.1 equiv), Cs₂CO₃ (82.1 mg, 0.24 mmol, 1.2 equiv), and THF (1 mL) was conducted at 50 °C. Purification by

flash column chromatography on NH silica gel (hexane/EtOAc = 60:40) gave the product as a white solid (29.7 mg, 0.18 mmol, 88% yield).

^1H NMR: (400 MHz, CDCl_3) δ 7.00 (d, J = 8.0 Hz, 2H), 6.58 (d, J = 8.0 Hz, 2H), 3.81 (t, J = 6.4 Hz, 2H), 3.26 (t, J = 6.4 Hz, 2H), 2.74 (br, 1H), 2.24 (s, 3H), 1.87 (tt, J = 6.4, 6.4 Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 145.9, 129.7, 127.0, 113.5, 61.8, 42.5, 31.8, 20.4

The analytical data for this compound were in excellent agreement with the reported data.⁵⁷⁾

N-(2-(1*H*-indol-3-yl)ethyl)-4-methylaniline (**9**)

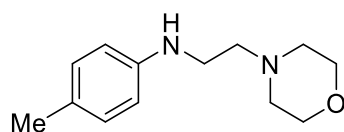


According to the general procedure **III**, the reaction using MS3A (217 mg, (4-methylphenyl)boronic acid (27.9 mg, 0.20 mmol, 1.0 equiv), aminobenziodoxolone **1g** (90.0 mg, 0.22 mmol, 1.1 equiv), Cs_2CO_3 (80.0 mg, 0.24 mmol, 1.2 equiv), and THF (2 mL) was conducted at 50 °C. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 7:3) gave the product as a white solid (25.7 mg, 0.10 mmol, 50% yield).

^1H NMR: (400 MHz, CDCl_3) δ 7.96 (brs, 1H), 7.62 (d, J = 8.0 Hz, 1H), 7.35 (d, J = 8.0 Hz, 1H), 7.25–7.16 (m, 1H), 7.16–7.08 (m, 1H), 7.06–6.90 (m, 3H), 6.55 (d, J = 8.4 Hz, 2H), 3.63 (brs, 1H), 3.45 (t, J = 6.8 Hz, 2H), 3.07 (t, J = 6.8 Hz, 2H), 2.23 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 145.9, 136.3, 129.7, 127.4, 126.5, 122.1, 122.0, 119.4, 118.8, 113.4, 113.2, 111.2, 44.3, 25.1, 20.4

The analytical data for this compound were in excellent agreement with the reported data.⁵⁸⁾

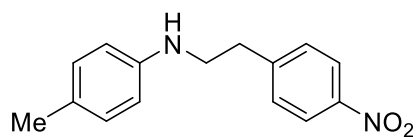
4-methyl-*N*-(2-morpholinoethyl)aniline (**10**)



According to the general procedure **III**, the reaction using MS3A (202 mg), (4-methylphenyl)boronic acid (27.7 mg, 0.20 mmol, 1.0 equiv), aminobenziodoxolone **1h** (83.1 mg, 0.22 mmol, 1.1 equiv), Cs_2CO_3 (80.2 mg, 0.24 mmol, 1.2 equiv), and THF (2 mL) was conducted at 50 °C. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 70:30) gave the product as a colorless oil (25.1 mg, 0.11 mmol, 56% yield).

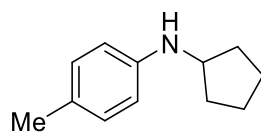
^1H NMR: (400 MHz, CDCl_3) δ 7.00 (d, J = 8.4 Hz, 2H), 6.57 (d, J = 8.4 Hz, 2H), 3.80–3.66 (m, 4H), 3.15 (t, J = 6.0 Hz, 2H), 2.62 (t, J = 6.0 Hz, 2H), 2.56–2.41 (m, 4H), 2.24 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 146.2, 129.7, 126.6, 113.1, 67.0, 57.2, 53.3, 40.3, 20.3

The analytical data for this compound were in excellent agreement with the reported data.⁵⁶⁾

4-methyl-*N*-(4-nitrophenethyl)aniline (11)

According to the general procedure **III**, the reaction using MS3A (412 mg), (4-methylphenyl)boronic acid (54.4 mg, 0.40 mmol, 1.0 equiv), aminobenziodoxolone **1i** (181.2 mg, 0.44 mmol, 1.1 equiv), Cs₂CO₃ (157.2 mg, 0.48 mmol, 1.2 equiv), and THF (4 mL) was conducted at 50 °C. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 8:2) gave the product as a yellow solid (79.2 mg, 0.31 mmol, 77% yield).

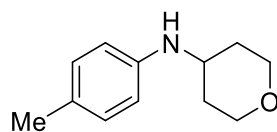
mp. 76.8–77.3 °C; TLC: *R_f* = 0.55 (NH, hexane/EtOAc = 7:3); ¹H NMR: (400 MHz, CDCl₃) δ 8.17 (d, *J* = 8.4 Hz, 2H), 7.37 (d, *J* = 8.4 Hz, 2H), 7.01 (d, *J* = 8.4 Hz, 2H), 6.55 (d, *J* = 8.4 Hz, 2H), 3.53 (brs, 1H), 3.44 (t, *J* = 6.8 Hz, 2H), 3.01 (t, *J* = 6.8 Hz, 2H), 2.25 (s, 3H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 147.4, 146.7, 145.1, 129.9, 129.6, 127.1, 123.8, 113.1, 44.8, 35.4, 20.4; IR: (ATR) 3381, 2932, 2914, 2862, 2845, 1599, 1510, 1474, 1342, 1319, 1304, 1288, 1246, 1184, 1094, 852, 814, 791 cm⁻¹; HRMS (EI) *m/z*: [M]⁺ Calculated for C₁₅H₁₆N₂O₂ 256.1212; Found 256.1213

***N*-cyclopentyl-4-methylaniline (12)**

According to the general procedure **III**, the reaction using MS3A (808 mg), (4-methylphenyl)boronic acid (55.2 mg, 0.40 mmol, 1.0 equiv), aminobenziodoxolone **1k** (146.7 mg, 0.44 mmol, 1.1 equiv), Cs₂CO₃ (158.2 mg, 0.48 mmol, 1.2 equiv), and THF (4 mL) was conducted at 70 °C. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 99:1) gave the product as a colorless oil (29.2 mg, 0.17 mmol, 42% yield).

¹H NMR: (400 MHz, CDCl₃) δ 6.97 (d, *J* = 8.4 Hz, 2H), 6.53 (d, *J* = 8.4 Hz, 2H), 3.76 (tt, *J* = 6.0, 6.0 Hz, 1H), 3.40 (br, 1H), 2.23 (s, 3H), 2.10–1.93 (m, 2H), 1.80–1.67 (m, 2H), 1.67–1.53 (m, 2H), 1.53–1.35 (m, 2H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 145.8, 129.6, 126.1, 113.4, 54.9, 33.6, 24.1, 20.3

The analytical data for this compound were in excellent agreement with the reported data.⁵⁶⁾

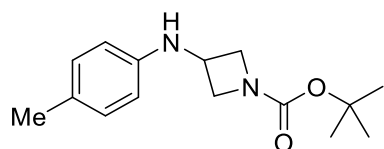
***N*-(*p*-tolyl)tetrahydro-2*H*-pyran-4-amine (13)**

According to the general procedure **III**, the reaction using MS3A (208 mg), (4-methylphenyl)boronic acid (27.1 mg, 0.20 mmol, 1.0 equiv), aminobenziodoxolone **1l** (76.8 mg, 0.22 mmol, 1.1 equiv), Cs₂CO₃ (80.8 mg, 0.24 mmol, 1.2 equiv), and THF (2 mL) was conducted at 70 °C. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 70:30) gave the product as a white solid (17.3 mg, 0.90 mmol, 45% yield).

¹H NMR: (400 MHz, CDCl₃) δ 6.99 (d, *J* = 8.4 Hz, 2H), 6.54 (d, *J* = 8.4 Hz, 2H), 4.14–3.97 (m, 2H), 3.53–3.25 (m, 4H), 2.24 (s, 3H), 2.14–1.97 (m, 2H), 1.50–1.40 (m, 2H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 144.3, 129.8, 126.8, 113.6, 66.9, 49.4, 33.6, 20.3

The analytical data for this compound were in excellent agreement with the reported data.⁵⁹⁾

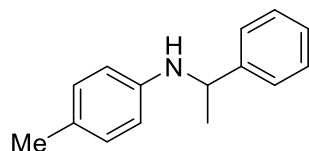
***tert*-butyl 3-(*p*-tolylamino)azetidine-1-carboxylate (**14**)**



According to the general procedure **III**, the reaction using MS3A (200 mg), (4-methylphenyl)boronic acid (27.2 mg, 0.20 mmol, 1.0 equiv), aminobenziodoxolone **1m** (91.4 mg, 0.22 mmol, 1.1 equiv), Cs₂CO₃ (78.7 mg, 0.24 mmol, 1.2 equiv), and THF (2 mL) was conducted at 70 °C. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 70:30) gave the product as a white solid (31.5 mg, 0.12 mmol, 60% yield).

mp. 118.2–119.5 °C; ¹H NMR: (400 MHz, CDCl₃) δ 7.01 (d, *J* = 8.4 Hz, 2H), 6.45 (d, *J* = 8.4 Hz, 2H), 4.28 (dd, *J* = 8.4, 8.4 Hz, 2H), 4.23–4.12 (m, 1H), 3.87 (br, 1H), 3.71 (dd, *J* = 8.4, 4.4 Hz, 2H), 2.25 (s, 3H), 1.44 (s, 9H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 156.2, 143.8, 129.9, 127.9, 113.3, 79.6, 57.0 (br), 43.5, 28.3, 20.4; IR: (ATR) 3381, 3250, 3051, 2970, 1674, 1584, 1557, 1528, 1474, 1433, 1416, 1364, 1321, 1298, 1263, 1246, 1217, 1180, 1155, 1146, 1063, 1026, 1013, 922, 833, 810, 772, 745 cm⁻¹; HRMS (FAB⁺) *m/z*: [M]⁺ Calculated for C₁₅H₂₂N₂O₂ 262.1681; Found 262.1679

4-methyl-*N*-(1-phenylethyl)aniline (15**)**

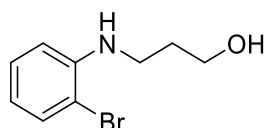


According to the general procedure **III**, the reaction using MS3A (816 mg), (4-methylphenyl)boronic acid (55.0 mg, 0.40 mmol, 1.0 equiv), aminobenziodoxolone **1n** (162.0 mg, 0.44 mmol, 1.1 equiv), Cs₂CO₃ (157.0 mg, 0.48 mmol, 1.2 equiv), and 1,4-dioxane (4 mL) was conducted at 80 °C. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 99:1) gave the product as a pale yellow oil (32.1 mg, 0.15 mmol, 38% yield).

^1H NMR: (400 MHz, CDCl_3) δ 7.40–7.34 (m, 2H), 7.34–7.27 (m, 2H), 7.24–7.17 (m, 1H), 6.89 (d, J = 8.8 Hz, 2H), 6.47–6.37 (m, 2H), 4.45 (q, J = 7.2 Hz, 1H), 3.90 (brs, 1H), 2.18 (s, 3H), 1.50 (d, J = 7.2 Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 145.4, 145.0, 129.6, 128.6, 126.8, 126.3, 125.8, 113.3, 53.6, 25.1, 20.3

The analytical data for this compound were in excellent agreement with the reported data.⁶⁰⁾

3-((2-bromophenyl)amino)propan-1-ol (16)

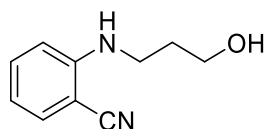


According to the general procedure **III**, the reaction using MS3A (603 mg), (2-bromophenyl)boronic acid (80.5 mg, 0.40 mmol, 1.0 equiv), aminobenziodoxolone **1f** (141.3 mg, 0.44 mmol, 1.1 equiv), Cs_2CO_3 (161.5 mg, 0.48 mmol, 1.2 equiv), and THF (4 mL) was conducted at 50 °C. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 8:2) gave the product as a colorless oil (54.5 mg, 0.24 mmol, 59% yield).

^1H NMR: (400 MHz, CDCl_3) δ 7.41 (dd, J = 8.4, 1.6 Hz, 1H), 7.24–7.10 (m, 1H), 6.66 (dd, J = 8.0, 1.6 Hz, 1H), 6.56 (ddd, J = 8.0, 8.0, 1.6 Hz, 1H), 4.51 (brs, 1H), 3.81 (t, J = 6.4 Hz, 2H), 3.30 (t, J = 6.4 Hz, 2H), 1.91 (tt, J = 6.4, 6.4 Hz, 2H), 1.84 (brs, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 145.0, 132.3, 128.5, 117.7, 111.3, 109.8, 61.1, 41.3, 31.6

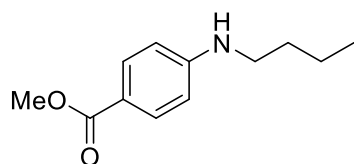
The analytical data for this compound were in excellent agreement with the reported data.⁶¹⁾

2-((3-hydroxypropyl)amino)benzonitrile (17)



According to the general procedure **III**, the reaction using MS3A (405 mg), (2-cyanophenyl)boronic acid (29.8 mg, 0.20 mmol, 1.0 equiv), aminobenziodoxolone **1f** (71.7 mg, 0.22 mmol, 1.1 equiv), Cs_2CO_3 (80.7 mg, 0.24 mmol, 1.2 equiv), and THF (2 mL) was conducted at 70 °C. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 7:3) gave the product as a colorless oil (26.8 mg, 0.15 mmol, 76% yield).

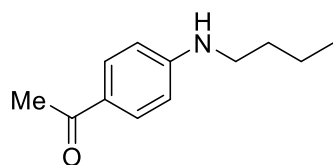
TLC: R_f = 0.30 (NH, hexane/EtOAc = 1:1); ^1H NMR: (400 MHz, CDCl_3) δ 7.47–7.30 (m, 2H), 6.75–6.60 (m, 2H), 4.94 (brs, 1H), 3.84 (t, J = 6.0 Hz, 2H), 3.37 (dt, J = 6.0, 6.0 Hz, 2H), 1.93 (tt, J = 6.0, 6.0 Hz, 2H), 1.67 (brs, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 150.5, 134.3, 132.7, 118.0, 116.3, 110.5, 95.6, 60.8, 40.8, 31.3; IR: (ATR) 3362, 2930, 2878, 2210, 1605, 1574, 1514, 1460, 1323, 1288, 1265, 1165, 1067, 1040, 947, 745 cm^{-1} ; HRMS (EI) m/z : $[\text{M}]^+$ Calculated for $\text{C}_{10}\text{H}_{12}\text{N}_2\text{O}$ 176.0950; Found 176.0944

methyl 4-(butylamino)benzoate (18)

According to the general procedure **III**, the reaction using MS3A (402 mg), (4-(methoxycarbonyl)phenyl)boronic acid (36.0 mg, 0.20 mmol, 1.0 equiv), aminobenziodoxolone **1c** (70.1 mg, 0.22 mmol, 1.1 equiv), Cs₂CO₃ (82.1 mg, 0.24 mmol, 1.2 equiv), and THF (2 mL) was conducted at 70 °C. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 9:1) gave the product as a white solid (30.7 mg, 0.15 mmol, 74% yield).

¹H NMR: (400 MHz, CDCl₃) δ 7.93–7.80 (m, 2H), 6.60–6.46 (m, 2H), 4.09 (brs, 1H), 3.84 (s, 3H), 3.26–3.04 (m, 2H), 1.61 (tt, *J* = 7.2, 7.2 Hz, 2H), 1.43 (tq, *J* = 7.2, 7.2 Hz, 2H), 0.96 (t, *J* = 7.2 Hz, 3H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 167.3, 152.1, 131.5, 117.9, 111.3, 51.4, 43.0, 31.4, 20.2, 13.8

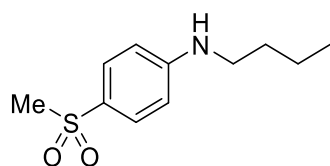
The analytical data for this compound were in excellent agreement with the reported data.⁶²⁾

1-(4-(butylamino)phenyl)ethan-1-one (19)

According to the general procedure **III**, the reaction using MS3A (410 mg), (4-acetylphenyl)boronic acid (32.8 mg, 0.20 mmol, 1.0 equiv), aminobenziodoxolone **1c** (70.6 mg, 0.22 mmol, 1.1 equiv), Cs₂CO₃ (81.0 mg, 0.24 mmol, 1.2 equiv), and THF (2 mL) was conducted at 70 °C. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 85:15) gave the product as a white solid (24.5 mg, 0.13 mmol, 64% yield).

¹H NMR: (400 MHz, CDCl₃) δ 7.82 (d, *J* = 8.8 Hz, 2H), 6.55 (d, *J* = 8.8 Hz, 2H), 4.17 (brs, 1H), 3.18 (dt, *J* = 6.4, 6.4 Hz, 2H), 2.50 (s, 3H), 1.70–1.55 (m, 2H), 1.44 (tq, *J* = 7.2, 7.2 Hz, 2H), 0.97 (t, *J* = 7.2 Hz, 3H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 196.3, 152.3, 130.8, 126.4, 111.2, 43.0, 31.3, 26.0, 20.2, 13.8

The analytical data for this compound were in excellent agreement with the reported data.⁶³⁾

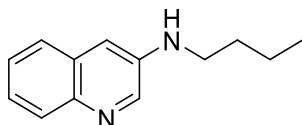
***N*-butyl-4-(methylsulfonyl)aniline (20)**

A reaction flask equipped with a magnetic stirring bar was charged with MS3A (807 mg) and flamed-dried under vacuum. After cooling down to room temperature, the flask was charged with nitrogen gas, (4-(methylsulfonyl)phenyl)boronic acid (80.6 mg, 0.40 mmol, 1.0 equiv), aminobenziodoxolone **1c** (191.9 mg, 0.60 mmol, 1.5 equiv), Cs₂CO₃ (158.2 mg, 0.48 mmol, 1.2 equiv), and THF (4 mL). The flask was sealed and placed in an aluminum block, which was preheated at 70 °C. After the mixture was stirred at 70 °C for 24 h, the reaction mixture was filtered by a pad of celite using acetone as an eluent. The filtrate was dried over Na₂SO₄, filtrated, and concentrated under reduced pressure to give the crude product. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 7:3) gave the product as a white solid (56.2 mg, 0.25 mmol, 62% yield).

¹H NMR: (400 MHz, CDCl₃) δ 7.68 (d, *J* = 8.8 Hz, 2H), 6.61 (d, *J* = 8.8 Hz, 2H), 4.26 (brs, 1H), 3.17 (dt, *J* = 7.2, 7.2 Hz, 2H), 3.00 (s, 3H), 1.70–1.55 (m, 2H), 1.44 (tq, *J* = 7.2, 7.2 Hz, 2H), 0.97 (t, *J* = 7.2 Hz, 3H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 152.4, 129.3, 126.9, 111.6, 45.1, 43.0, 31.2, 20.1, 13.8

The analytical data for this compound was in excellent agreement with the reported data.⁵³⁾

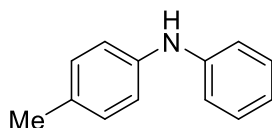
***N*-butylquinolin-3-amine (21)**



According to the general procedure **III**, the reaction using MS3A (210 mg), quinoline-3-boronic acid (34.6 mg, 0.20 mmol, 1.0 equiv), aminobenziodoxolone **1c** (71.4 mg, 0.22 mmol, 1.1 equiv), Cs₂CO₃ (80.6 mg, 0.24 mmol, 1.2 equiv), and THF (2 mL) was conducted at 50 °C. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 70:30) gave the product as a pale yellow oil (20.0 mg, 0.10 mmol, 50% yield).

¹H NMR: (400 MHz, CDCl₃) δ 8.42 (d, *J* = 2.4 Hz, 1H), 7.93 (dd, *J* = 7.8, 2.0 Hz, 1H), 7.63–7.59 (m, 1H), 7.44–7.36 (m, 2H), 7.00 (d, *J* = 2.4 Hz, 1H), 3.93 (brs, 1H), 3.24–3.18 (m, 2H), 1.72–1.65 (m, 2H), 1.49 (tq, *J* = 7.6, 7.6 Hz, 2H), 1.00 (t, *J* = 7.6 Hz, 3H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 143.4, 141.9, 141.7, 129.6, 128.9, 126.8, 125.8, 124.6, 109.7, 43.3, 31.2, 20.3, 13.8; IR: (ATR) 3275, 3258, 2955, 2928, 2860, 1609, 1574, 1516, 1487, 1472, 1416, 1389, 1366, 1350, 1283, 1258, 1219, 1190, 1142, 1082, 1016, 984, 947, 864, 839, 777, 745 cm⁻¹; HRMS (FAB+) *m/z*: [M+H]⁺ Calculated for C₁₃H₁₇N₂ 201.1392; Found 201.1397

4-methyl-*N*-phenylaniline (22)

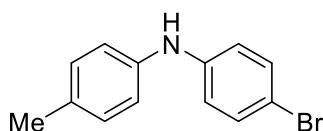


According to the general procedure **III**, the reaction using MS3A (211 mg), (4-methylphenyl)boronic acid (27.0 mg, 0.20 mmol, 1.0 equiv), aminobenziodoxolone **1q** (76.4 mg, 0.22 mmol, 1.1 equiv), K₂CO₃ (31.2 mg, 0.24 mmol, 1.2 equiv), and 1,4-dioxane (2 mL) was conducted at 50 °C. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 70:30) gave the product as a yellow oil (22.0 mg, 0.12 mmol, 61% yield).

¹H NMR: (400 MHz, CDCl₃) δ 7.23 (d, *J* = 7.2 Hz, 2H), 7.09 (d, *J* = 8.4 Hz, 2H), 7.02–6.98 (m, 4H), 6.88 (dd, *J* = 7.6, 7.6 Hz, 1H), 5.60 (brs, 1H), 2.30 (s, 3H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 143.9, 140.3, 130.9, 129.8, 129.3, 120.3, 118.9, 116.8, 20.6

The analytical data for this compound were in excellent agreement with the reported data.⁶⁴⁾

4-bromo-*N*-(*p*-tolyl)aniline (**24**)

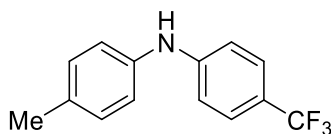


According to the general procedure **III**, the reaction using MS3A (201 mg), (4-methylphenyl)boronic acid (27.2 mg, 0.20 mmol, 1.0 equiv), aminobenziodoxolone **1r** (92.3 mg, 0.22 mmol, 1.1 equiv), K₂CO₃ (34.1 mg, 0.24 mmol, 1.2 equiv), and 1,4-dioxane (2 mL) was conducted at 50 °C. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 70:30) gave the product as a pale yellow oil (33.4 mg, 0.13 mmol, 64% yield).

¹H NMR: (400 MHz, CDCl₃) δ 7.31 (d, *J* = 8.0 Hz, 2H), 7.10 (d, *J* = 8.0 Hz, 2H), 6.98 (d, *J* = 8.0 Hz, 2H), 6.87 (d, *J* = 8.0 Hz, 2H), 5.58 (brs, 1H), 2.31 (s, 3H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 143.2, 139.5, 132.1, 131.6, 129.9, 119.3, 118.0, 111.7, 20.7

The analytical data for this compound were in excellent agreement with the reported data.⁶⁵⁾

4-methyl-*N*-(4-(trifluoromethyl)phenyl)aniline (**25**)



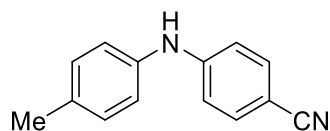
According to the general procedure **III**, the reaction using MS3A (212 mg), (4-methylphenyl)boronic acid (27.2 mg, 0.20 mmol, 1.0 equiv), aminobenziodoxolone **1s** (89.9 mg, 0.22 mmol, 1.1 equiv), K₂CO₃ (34.0 mg, 0.24 mmol, 1.2 equiv), and 1,4-dioxane (2 mL) was conducted at 50 °C. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 70:30) gave the product as a colorless oil (23.4 mg, 0.093 mmol, 47% yield).

¹H NMR: (400 MHz, CDCl₃) δ 7.45 (d, *J* = 8.4 Hz, 2H), 7.16 (d, *J* = 8.4 Hz, 2H), 7.08–7.04 (m, 2H), 6.97 (d, *J* = 8.4 Hz, 2H), 5.83 (brs, 1H), 2.35 (s, 3H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 147.5, 138.3,

133.0, 130.1, 126.6 (q, $J_{CF} = 3.8$ Hz), 124.7 (q, $J_{CF} = 269.4$ Hz), 121.01, 120.98 (q, $J_{CF} = 32.4$ Hz), 114.6, 20.8; $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -64.4

The analytical data for this compound were in excellent agreement with the reported data.⁶⁶⁾

4-(*p*-tolylamino)benzonitrile (26)

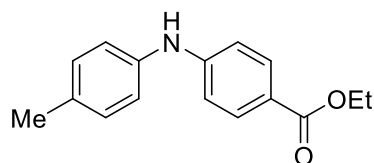


According to the general procedure **III**, the reaction using MS3A (402 mg), (4-methylphenyl)boronic acid (55.0 mg, 0.40 mmol, 1.0 equiv), aminobenziodoxolone **1t** (162.3 mg, 0.44 mmol, 1.1 equiv), KO t Bu (54.2 mg, 0.48 mmol, 1.2 equiv), and 1,4-dioxane (4 mL) was conducted at 50 °C. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 9:1) gave the product as a pale yellow solid (44.1 mg, 0.21 mmol, 52% yield).

^1H NMR: (400 MHz, CDCl_3) δ 7.50–7.40 (m, 2H), 7.17 (d, $J = 8.0$ Hz, 2H), 7.07 (d, $J = 8.0$ Hz, 2H), 6.93–6.85 (m, 2H), 5.98 (brs, 1H), 2.35 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 148.6, 137.1, 134.1, 133.7, 130.2, 122.1, 120.0, 114.3, 100.9, 20.9

The analytical data for this compound was in excellent agreement with the reported data.⁶⁷⁾

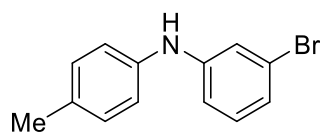
ethyl 4-(*p*-tolylamino)benzoate (27)



According to the general procedure **III**, the reaction using MS3A (416 mg), (4-methylphenyl)boronic acid (55.0 mg, 0.40 mmol, 1.0 equiv), aminobenziodoxolone **1u** (184.0 mg, 0.44 mmol, 1.1 equiv), K_2CO_3 (67.0 mg, 0.48 mmol, 1.2 equiv), and 1,4-dioxane (4 mL) was conducted at 50 °C. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 9:1) gave the product as a pale red solid (26.1 mg, 0.10 mmol, 26% yield).

^1H NMR: (400 MHz, CDCl_3) δ 7.90 (d, $J = 8.0$ Hz, 2H), 7.15 (d, $J = 8.0$ Hz, 2H), 7.08 (d, $J = 8.0$ Hz, 2H), 6.92 (d, $J = 8.0$ Hz, 2H), 5.95 (brs, 1H), 4.33 (q, $J = 7.2$ Hz, 2H), 2.34 (s, 3H), 1.37 (t, $J = 7.2$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 166.6, 148.6, 138.1, 133.0, 131.4, 130.0, 121.2, 120.8, 113.9, 60.4, 20.8, 14.4

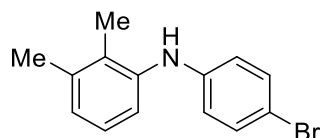
The analytical data for this compound was in excellent agreement with the reported data.⁶⁸⁾

3-bromo-*N*-(*p*-tolyl)aniline (28)

According to the general procedure **III**, the reaction using MS3A (405 mg), (4-methylphenyl)boronic acid (54.0 mg, 0.40 mmol, 1.0 equiv), aminobenziodoxolone **1v** (190.4 mg, 0.44 mmol, 1.1 equiv), K₂CO₃ (69.0 mg, 0.48 mmol, 1.2 equiv), and 1,4-dioxane (4 mL) was conducted at 50 °C. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 95:5) gave the product as a yellow oil (59.9 mg, 0.23 mmol, 57% yield).

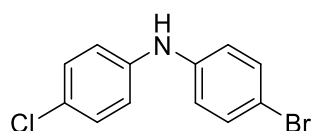
¹H NMR: (400 MHz, CDCl₃) δ 7.17–7.08 (m, 3H), 7.06 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.03–6.97 (m, 2H), 6.97–6.92 (m, 1H), 6.88–6.82 (m, 1H), 5.59 (brs, 1H), 2.31 (s, 3H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 145.8, 139.0, 132.1, 130.5, 130.0, 123.1, 122.6, 120.1, 118.6, 114.7, 20.7

The analytical data for this compound was in excellent agreement with the reported data.⁶⁸⁾

***N*-(4-bromophenyl)-2,3-dimethylaniline (29)**

According to the general procedure **III**, the reaction using MS3A (210 mg), (2,3-dimethylphenyl)boronic acid (30.1 mg, 0.20 mmol, 1.0 equiv), aminobenziodoxolone **1r** (92.7 mg, 0.22 mmol, 1.1 equiv), K₂CO₃ (35.0 mg, 0.24 mmol, 1.2 equiv), and 1,4-dioxane (2 mL) was conducted at 50 °C. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 9:1) gave the product as a yellow oil (34.9 mg, 0.13 mmol, 63% yield).

TLC: *R_f* = 0.80 (NH, hexane/EtOAc = 7:3); ¹H NMR: (400 MHz, CDCl₃) δ 7.33–7.26 (m, 2H), 7.10–7.02 (m, 2H), 6.97–6.90 (m, 1H), 6.72–6.63 (m, 2H), 5.35 (brs, 1H), 2.31 (s, 3H), 2.13 (s, 3H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 144.3, 140.1, 138.1, 132.0, 129.5, 126.1, 125.4, 119.6, 117.6, 111.2, 20.6, 13.7; IR: (ATR) 3391, 2914, 1580, 1485, 1472, 1383, 1306, 1234, 1175, 1067, 1001, 814, 775, 750 cm⁻¹; HRMS (EI) *m/z*: [*M*]⁺ Calculated for C₁₄H₁₄BrN 275.0310; Found 275.0302

4-bromo-*N*-(4-chlorophenyl)aniline (30)

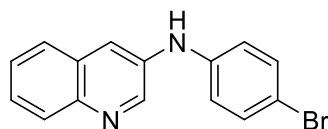
According to the general procedure **III**, the reaction using MS3A (405 mg), (4-chlorophenyl)boronic acid (63.1 mg, 0.40 mmol, 1.0 equiv), aminobenziodoxolone **1r** (183.7 mg, 0.44 mmol, 1.1 equiv),

K₂CO₃ (66.3 mg, 0.48 mmol, 1.2 equiv), and 1,4-dioxane (4 mL) was conducted at 50 °C. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 9:1) gave the product as an orange solid (75.2 mg, 0.27 mmol, 67% yield).

¹H NMR: (400 MHz, CDCl₃) δ 7.35 (d, *J* = 8.8 Hz, 2H), 7.21 (d, *J* = 8.8 Hz, 2H), 6.96 (d, *J* = 8.8 Hz, 2H), 6.90 (d, *J* = 8.8 Hz, 2H), 5.64 (brs, 1H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 141.9, 141.1, 132.3, 129.4, 126.2, 119.3, 113.2 (one sp² signal was not observed because of overlapping)

The analytical data for this compound was in excellent agreement with the reported data.⁶⁹⁾

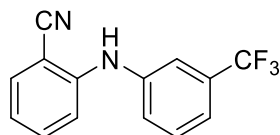
N-(4-bromophenyl)quinolin-3-amine (31)



According to the general procedure **III**, the reaction using MS3A (407 mg), quinolin-3-ylboronic acid (69.0 mg, 0.40 mmol, 1.0 equiv), aminobenziodoxolone **1r** (183.8 mg, 0.44 mmol, 1.1 equiv), K₂CO₃ (66.6 mg, 0.48 mmol, 1.2 equiv), and 1,4-dioxane (4 mL) was conducted at 50 °C. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 8:2) gave the product as a pale red solid (31.0 mg, 0.10 mmol, 26% yield).

mp. 149.5–151.0 °C; TLC: *R*_f = 0.25 (NH, hexane/EtOAc = 7:3); ¹H NMR: (400 MHz, CDCl₃) δ 8.68 (d, *J* = 2.8 Hz, 1H), 8.01 (d, *J* = 8.4 Hz, 1H), 7.71 (d, *J* = 2.8 Hz, 1H), 7.65 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.58–7.52 (m, 1H), 7.52–7.46 (m, 1H), 7.46–7.40 (m, 2H), 7.10–7.00 (m, 2H), 5.97 (brs, 1H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 145.1, 143.9, 141.1, 136.3, 132.5, 129.1, 128.6, 127.3, 126.9, 126.5, 119.8, 117.8, 114.2; IR: (ATR) 3279, 3049, 1607, 1595, 1582, 1489, 1462, 1429, 1364, 1339, 1312, 1294, 1279, 1254, 1175, 1074, 1003, 986, 899, 860, 814, 785, 752 cm⁻¹; HRMS (CI) *m/z*: [M+H]⁺ Calculated for C₁₅H₁₂BrN₂ 299.0184; Found 299.0189

2-((3-(trifluoromethyl)phenyl)amino)benzonitrile (32)



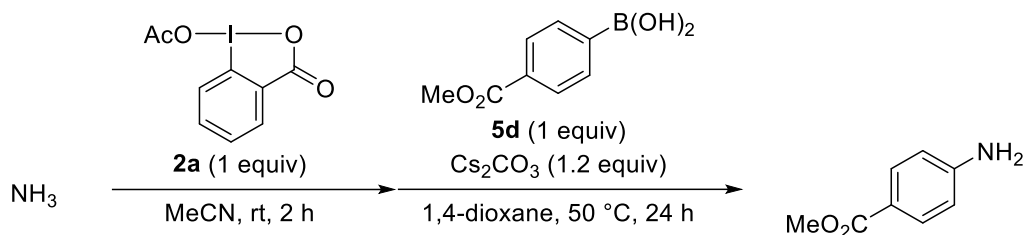
According to the general procedure **III**, the reaction using MS3A (420 mg), (2-cyanophenyl)boronic acid (59.7 mg, 0.40 mmol, 1.0 equiv), aminobenziodoxolone **1w** (195.7 mg, 0.48 mmol, 1.2 equiv), K₂CO₃ (67.3 mg, 0.48 mmol, 1.2 equiv), and 1,4-dioxane (4 mL) was conducted at 50 °C. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 9:1) gave the product as a pale yellow solid (20.6 mg, 0.079 mmol, 20% yield).

¹H NMR: (400 MHz, CDCl₃) δ 7.56 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.52–7.39 (m, 3H), 7.39–7.30 (m, 2H), 7.30–7.25 (m, 1H), 7.00–6.91 (m, 1H), 6.42 (brs, 1H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 146.0,

140.9, 134.1, 133.3, 132.1 (q, $J_{CF} = 32.4$ Hz), 130.2, 123.8 (q, $J_{CF} = 271.3$ Hz), 123.7, 120.6, 120.2 (q, $J_{CF} = 3.8$ Hz), 117.19, 117.17 (q, $J_{CF} = 0.8$ Hz), 115.0, 99.9; $^{19}\text{F}\{^1\text{H}\}$ NMR: (376 MHz, CDCl_3) δ -65.9
The analytical data for this compound was in excellent agreement with the reported data.³⁴⁾

One-pot process for coupling of arylboronic acids with amines

methyl 4-aminobenzoate (33)



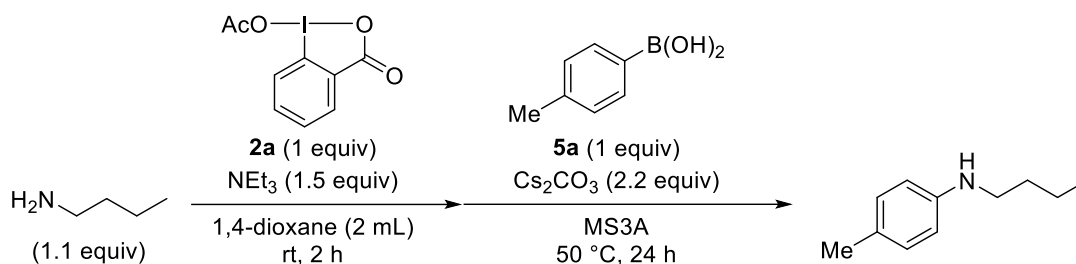
Using gaseous ammonia: A heat-gun-dried reaction flask containing a magnetic stir bar was charged with 1-acetoxy-1,2-benziodoxol-3-(1H)-one (308 mg, 1.0 mmol, 1.0 equiv). The flask was refilled with gaseous ammonia (1 atm), and MeCN (10 mL) was added. After the mixture was stirred at room temperature for 2 h, the reaction mixture was concentrated under reduced pressure. Then, the flask was refilled with nitrogen gas, and (4-(methoxycarbonyl)phenyl)boronic acid (181.0 mg, 1.0 mmol, 1.0 equiv), Cs_2CO_3 (390.0 mg, 1.2 mmol, 1.2 equiv), and 1,4-dioxane (10 mL) were added. The flask was sealed and placed in an aluminum block, which was preheated at 50 °C. After the mixture was stirred at 50 °C for 24 h, sat. NaHCO_3 aq. was added, and the mixture was extracted with CHCl_3 (3×30 mL). The combined organic layers were dried over Na_2SO_4 , filtrated, and concentrated under reduced pressure to give the crude product. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 7:3) gave the product as a white solid (94.9 mg, 0.63 mmol, 63% yield).

Using ammonium carbamate: A reaction flask equipped with a magnetic stirring bar was flame-dried under vacuum. After cooling to room temperature, the flask was charged with nitrogen gas, 1-acetoxy-1,2-benziodoxol-3-(1H)-one (307 mg, 1.0 mmol, 1.0 equiv), ammonium carbamate (79.0 mg, 1.0 mmol, 1.0 equiv), and MeCN (10 mL). After the mixture was stirred at room temperature for 2 h, the reaction mixture was concentrated under reduced pressure. Then, the flask was refilled with nitrogen gas, and (4-(methoxycarbonyl)phenyl)boronic acid (181 mg, 1.0 mmol, 1.0 equiv), Cs_2CO_3 (392 mg, 1.2 mmol, 1.2 equiv), and 1,4-dioxane (10 mL) were added. The flask was sealed and placed in an aluminum block, which was preheated at 50 °C. After the mixture was stirred at 50 °C for 24 h, sat. NaHCO_3 aq. was added, and the mixture was extracted with CHCl_3 (3×30 mL). The combined organic layers were dried over Na_2SO_4 , filtrated, and concentrated under reduced pressure to give the crude product. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 7:3) gave the product as a white solid (90.2 mg, 0.60 mmol, 60% yield).

^1H NMR: (400 MHz, CDCl_3) δ 7.90–7.80 (m, 2H), 6.69–6.60 (m, 2H), 4.06 (brs, 2H), 3.85 (s, 3H);
 $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 167.1, 150.8, 131.6, 119.7, 113.8, 51.6

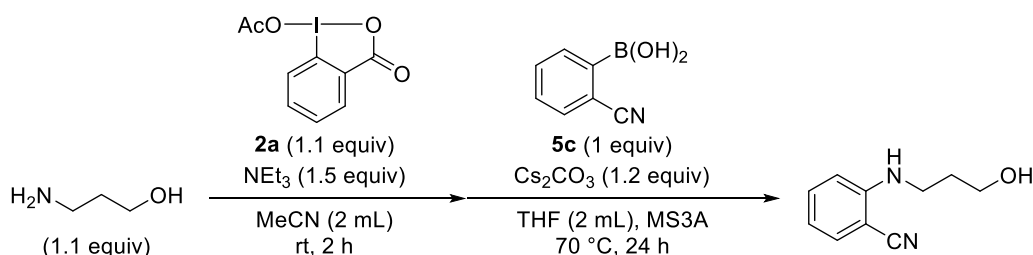
The analytical data for this compound were in excellent agreement with the reported data.⁹⁾

N-butyl-4-methylaniline (6)



A reaction flask equipped with a magnetic stirring bar was flame-dried under vacuum. After cooling to room temperature, the flask was charged with nitrogen gas, 1-acetoxyl-2-benziodoxol-3-(1*H*)-one (61.5 mg, 0.2 mmol, 1.0 equiv), 1,4-dioxane (2 mL), *n*-butylamine (16.0 mg, 0.22 mmol, 1.1 equiv), and NEt_3 (40 μL , 0.30 mmol, 1.5 equiv). After the mixture was stirred at room temperature for 2 h, (4-methylphenyl)boronic acid (27.5 mg, 0.20 mmol, 1.0 equiv), Cs_2CO_3 (147.4 mg, 0.44 mmol, 2.2 equiv), and dry MS3A (394 mg) were added. Then, the flask was sealed and placed in an aluminum block, which was preheated at 50 °C. After the mixture was stirred at 50 °C for 24 h, the reaction mixture was filtered by a pad of celite using CHCl_3 as an eluent. To the filtrate, sat. NaHCO_3 aq. was added, and the mixture was extracted with CHCl_3 (3 $\times$ 15 mL). The combined organic layers were dried over Na_2SO_4 , filtrated, and concentrated under reduced pressure to give the crude product. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 99:1) gave the product as a colorless oil (21.2 mg, 0.13 mmol, 65% yield).

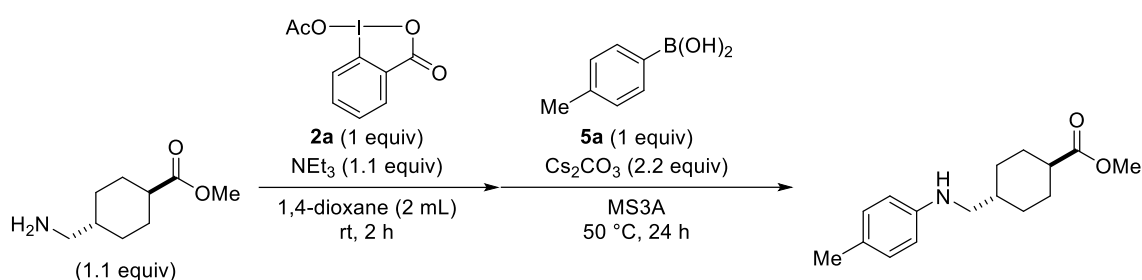
2-((3-hydroxypropyl)amino)benzonitrile (17)



A reaction flask equipped with a magnetic stirring bar was flame-dried under vacuum. After cooling to room temperature, the flask was charged with nitrogen gas, 1-acetoxyl-2-benziodoxol-3-(1*H*)-one (65.3 mg, 0.22 mmol, 1.1 equiv), MeCN (2 mL), 3-aminopropan-1-ol (17.6 mg, 0.22 mmol, 1.1 equiv), and NEt_3 (30 μL , 0.22 mmol, 1.1 equiv). After the mixture was stirred at room temperature for 2 h, the reaction mixture was concentrated under reduced pressure. Then, the flask was refilled with nitrogen

gas, and (2-cyanophenyl)boronic acid (30.0 mg, 0.2 mmol, 1.0 equiv), Cs₂CO₃ (144.0 mg, 0.44 mmol, 2.2 equiv), dry MS3A (408 mg), and THF (2 mL) were added. The flask was sealed and placed in an aluminum block, which was preheated at 70 °C. After the mixture was stirred at 70 °C for 24 h, the reaction mixture was filtered by a pad of celite using CHCl₃ as an eluent. To the filtrate, sat. NaHCO₃ aq. was added, and the mixture was extracted with CHCl₃ (3 × 15 mL). The combined organic layers were dried over Na₂SO₄, filtrated, and concentrated under reduced pressure to give the crude product. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 7:3) gave the product as a colorless oil (16.9 mg, 0.096 mmol, 48% yield).

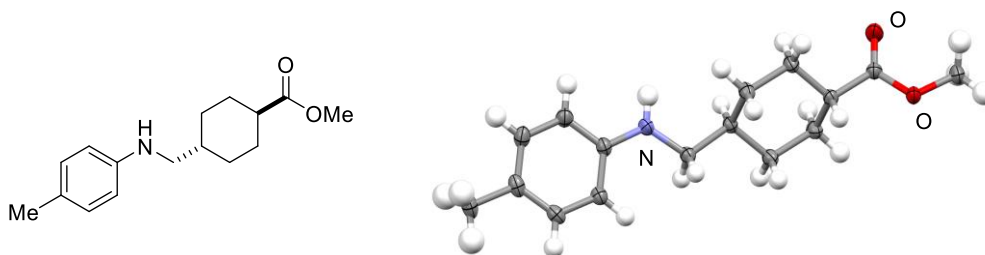
methyl *trans*-4-((*p*-tolylamino)methyl)cyclohexane-1-carboxylate (34)



A reaction flask equipped with a magnetic stirring bar was flame-dried under vacuum. After cooling to room temperature, the flask was charged with nitrogen gas, 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (62.0 mg, 0.2 mmol, 1.0 equiv), 1,4-dioxane (2 mL), *trans*-methyl 4-(aminomethyl)cyclohexanecarboxylate (38.3 mg, 0.22 mmol, 1.1 equiv), and NEt₃ (30 μL, 0.22 mmol, 1.1 equiv). After the mixture was stirred at room temperature for 2 h, (4-methylphenyl)boronic acid (27.7 mg, 0.20 mmol, 1.0 equiv), Cs₂CO₃ (144.2 mg, 0.44 mmol, 2.2 equiv), and dry MS3A (410 mg) were added. Then, the flask was sealed and placed in an aluminum block, which was preheated at 50 °C. After the mixture was stirred at 50 °C for 24 h, the reaction mixture was filtered by a pad of celite using CHCl₃ as an eluent. To the filtrate, sat. NaHCO₃ aq. was added, and the mixture was extracted with CHCl₃ (3 × 15 mL). The combined organic layers were dried over Na₂SO₄, filtrated, and concentrated under reduced pressure to give the crude product. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 9:1) gave the product as a white solid (21.4 mg, 0.081 mmol, 41% yield). Recrystallization from hexane/CH₂Cl₂ gave single crystals suitable for X-ray analysis.

mp. 97.1–98.7 °C; TLC: *R_f* = 0.75 (NH, hexane/EtOAc = 7:3); ¹H NMR: (400 MHz, CDCl₃) δ 6.98 (d, *J* = 8.4 Hz, 2H), 6.52 (d, *J* = 8.4 Hz, 2H), 3.66 (s, 3H), 3.56 (brs, 1H), 2.95 (d, *J* = 6.4 Hz, 2H), 2.37–2.17 (m, 4H), 2.09–1.85 (m, 4H), 1.70–1.52 (m, 1H), 1.52–1.33 (m, 2H), 1.10–0.92 (m, 2H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 176.4, 146.1, 129.7, 126.3, 112.8, 51.5, 50.6, 43.3, 36.9, 30.2, 28.6, 20.3; IR: (ATR) 3404, 2949, 2934, 2849, 1722, 1616, 1522, 1474, 1450, 1435, 1319, 1265, 1248, 1213, 1192,

1171, 1150, 1130, 1078, 1036, 1009, 961, 870, 762 cm^{-1} ; HRMS (EI) m/z : $[M]^+$ Calculated for $\text{C}_{16}\text{H}_{23}\text{NO}_2$ 261.1729; Found 261.1728

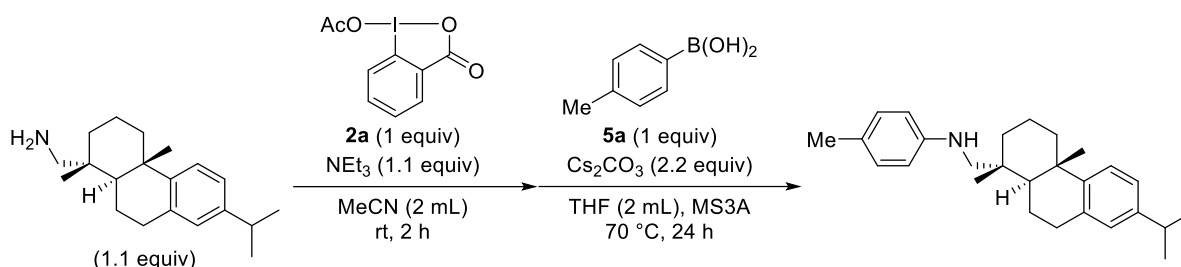


The structure of **34** was determined by X-ray structural analysis. CCDC 2471676 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

CCDC number	2471676
Empirical formula	$\text{C}_{16}\text{H}_{23}\text{NO}_2$
Formula weight	261.35
Temperature/K	123.15
Crystal system	monoclinic
Space group	$P2_1/c$
$a/\text{\AA}$	6.78020(10)
$b/\text{\AA}$	9.48310(10)
$c/\text{\AA}$	22.5161(3)
$\alpha/^\circ$	90
$\beta/^\circ$	90.7410(10)
$\gamma/^\circ$	90
Volume/ $\text{\AA}^3$	1447.60(3)
Z	4
$\rho_{\text{calc}}/\text{g cm}^{-3}$	1.199
μ/mm^{-1}	0.617
$F(000)$	568.0
Crystal size/ mm^3	$0.184 \times 0.163 \times 0.133$
Radiation	$\text{Cu K}\alpha$ ($\lambda = 1.54184$)
2θ range for data collection/ $^\circ$	7.854 to 153.286
Index ranges	$-8 \leq h \leq 8, -11 \leq k \leq 11, -28 \leq l \leq 21$
Reflections collected	17188

Independent reflections	2983 [$R_{\text{int}} = 0.0400$, $R_{\text{sigma}} = 0.0274$]
Data/restraints/parameters	2983/0/174
Goodness-of-fit on F^2	1.072
Final R indexes [$I > 2\sigma(I)$]	$R_1 = 0.0397$, $wR_2 = 0.1116$
Final R indexes [all data]	$R_1 = 0.0430$, $wR_2 = 0.1147$
Largest diff. peak/hole / $e \text{ \AA}^{-3}$	0.21/-0.22

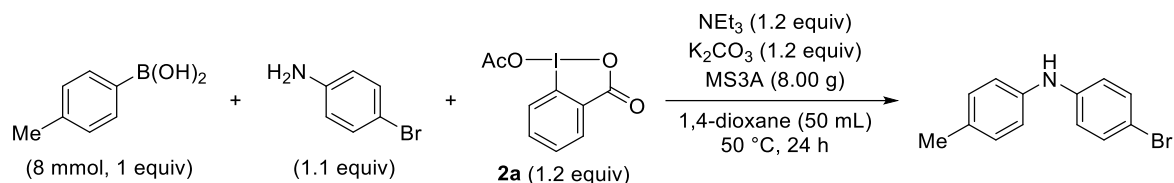
***N*-(((1*R*,4*aS*,10*aR*)-7-isopropyl-1,4*a*-dimethyl-1,2,3,4,4*a*,9,10,10*a*-octahydrophenanthren-1-yl)methyl)-4-methylaniline (35)**



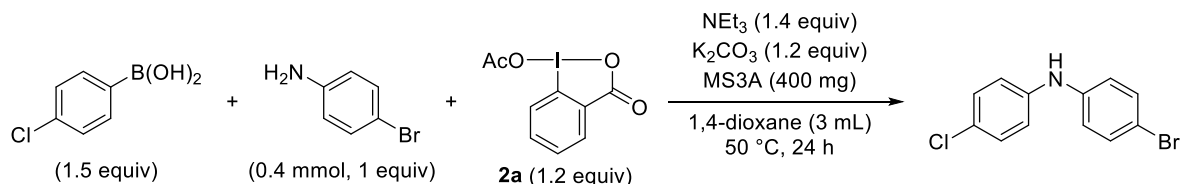
A reaction flask equipped with a magnetic stirring bar was flame-dried under vacuum. After cooling to room temperature, the flask was charged with nitrogen gas, 1-acetoxyl-1,2-benziodoxol-3-(1*H*)-one (62.0 mg, 0.2 mmol, 1.0 equiv), MeCN (2 mL), dehydroabietylamine (63.5 mg, 0.22 mmol, 1.1 equiv), and NEt₃ (30 μ L, 0.22 mmol, 1.1 equiv). After the mixture was stirred at room temperature for 2 h, the reaction mixture was concentrated under reduced pressure. Then, the flask was refilled with nitrogen gas, and (4-methylphenyl)boronic acid (28.0 mg, 0.20 mmol, 1.0 equiv), Cs₂CO₃ (145.0 mg, 0.44 mmol, 2.2 equiv), dry MS3A (420 mg), and THF (2 mL) were added. The flask was sealed and placed in an aluminum block, which was preheated at 70 °C. After the mixture was stirred at 70 °C for 24 h, the reaction mixture was filtered by a pad of celite using CHCl₃ as an eluent. To the filtrate, sat. NaHCO₃ aq. was added, and the mixture was extracted with CHCl₃ (3 $\times$ 15 mL). The combined organic layers were dried over Na₂SO₄, filtrated, and concentrated under reduced pressure to give the crude product. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 99:1) gave the product as a colorless oil (42.9 mg, 0.11 mmol, 57% yield).

¹H NMR: (400 MHz, CDCl₃) δ 7.19 (d, $J = 8.0$ Hz, 1H), 7.00 (dd, $J = 8.0, 2.0$ Hz, 1H), 6.96 (d, $J = 8.8$ Hz, 2H), 6.93–6.85 (m, 1H), 6.60–6.43 (m, 2H), 3.46 (brs, 1H), 3.02 (d, $J = 12.0$ Hz, 1H), 2.96–2.70 (m, 4H), 2.37–2.24 (m, 1H), 2.22 (s, 3H), 1.90–1.55 (m, 5H), 1.50–1.30 (m, 3H), 1.30–1.10 (m, 9H), 1.00 (s, 3H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 147.3, 146.7, 145.6, 134.7, 129.7, 126.8, 125.9, 124.2, 123.8, 112.7, 55.2, 45.2, 38.4, 37.43, 37.40, 36.2, 33.4, 30.1, 25.3, 24.0, 20.3, 19.3, 18.8, 18.7

The analytical data for this compound was in excellent agreement with the reported data.³⁰⁾

4-bromo-*N*-(*p*-tolyl)aniline (24)

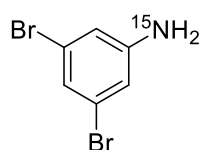
A reaction flask equipped with a magnetic stirring bar was charged with MS3A (8.00 g) and flamed-dried under vacuum. After cooling down to room temperature, the flask was charged with nitrogen gas, (4-methylphenyl)boronic acid (1.09 g, 8 mmol, 1.0 equiv), 4-bromoaniline (1.51 g, 8.8 mmol, 1.1 equiv), K₂CO₃ (1.33 g 9.6 mmol, 1.2 equiv), 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (2.94 g, 9.6 mmol, 1.2 equiv), 1,4-dioxane (50 mL), NEt₃ (1.35 mL, 9.6 mmol, 1.2 equiv). The flask was sealed and placed in an aluminum block, which was preheated at 50 °C. After the mixture was stirred at 50 °C for 24 h, the reaction mixture was concentrated under reduced pressure to remove 1,4-dioxane and then filtered by a pad of celite using CHCl₃ as an eluent. To the filtrate, sat. NaHCO₃ aq. was added, and the mixture was extracted with CHCl₃ (3 × 40 mL). The combined organic layers were dried over Na₂SO₄, filtrated, and concentrated under reduced pressure to give the crude product. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 95:5) gave the product as an orange solid (1.37 g, 5.23 mmol, 65% yield).

4-bromo-*N*-(4-chlorophenyl)aniline (30)

A reaction flask equipped with a magnetic stirring bar was charged with MS3A (406 mg) and flamed-dried under vacuum. After cooling down to room temperature, the flask was charged with nitrogen gas, (4-chlorophenyl)boronic acid (93.9 mg, 0.6 mmol, 1.5 equiv), 4-bromoaniline (69.0 mg, 0.4 mmol, 1.0 equiv), K₂CO₃ (67.6 mg 0.48 mmol, 1.2 equiv), 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (147.6 mg, 0.48 mmol, 1.2 equiv), 1,4-dioxane (3 mL), NEt₃ (80 μL, 0.56 mmol, 1.4 equiv). The flask was sealed and placed in an aluminum block, which was preheated at 50 °C. After the mixture was stirred at 50 °C for 24 h, the reaction mixture was filtered by a pad of celite using CHCl₃ as an eluent. To the filtrate, sat. NaHCO₃ aq. was added, and the mixture was extracted with CHCl₃ (3 × 20 mL). The combined organic layers were dried over Na₂SO₄, filtrated, and concentrated under reduced pressure to give the crude product. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 9:1) gave the product as a yellow solid (82.5 mg, 0.29 mmol, 73% yield).

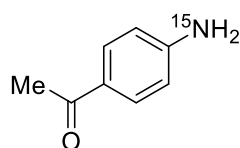
¹⁵N-labelled arylamine synthesis

General procedure IV: An oven-dried reaction vial containing a magnetic stir bar was charged with arylboronic acid or ester (1.0 equiv), ¹⁵N-**1a** (1.1 equiv), Cs₂CO₃ (1.2 equiv), and THF (2 mL). Then, the vial was purged with nitrogen gas, sealed, and placed in an aluminum block, which was preheated at 50 °C. After the mixture was stirred at 50 °C for 24 h, sat. NaHCO₃ aq. was added, and the mixture was extracted with CHCl₃ (3 × 15 mL). The combined organic layers were dried over Na₂SO₄, filtrated, and concentrated under reduced pressure to give the crude product. Purification by flash column chromatography on NH silica gel (hexane/EtOAc) gave the product.

3,5-dibromoaniline-¹⁵N (36)

According to the general procedure **IV**, the reaction using (3,5-dibromophenyl)boronic acid (112.3 mg, 0.40 mmol, 1.0 equiv), ¹⁵N-**1a** (117.0 mg, 0.44 mmol, 1.1 equiv), Cs₂CO₃ (158.0 mg, 0.48 mmol, 1.2 equiv), and THF (2 mL) was conducted at 50 °C. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 9:1) gave the product as a white solid (82.4 mg, 0.33 mmol, 82% yield).

mp. 54.8–55.3 °C; TLC: *R_f* = 0.50 (NH, hexane/EtOAc = 7:3); ¹H NMR: (400 MHz, CDCl₃) δ 7.02 (t, *J* = 1.6 Hz, 1H), 6.74 (dd, *J* = 1.6, 1.6 Hz, 2H), 3.77 (d, *J_{NH}* = 81.6 Hz, 2H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 148.6 (d, *J_{CN}* = 12.4 Hz), 123.6, 123.3 (d, *J_{CN}* = 1.9 Hz), 116.4 (d, *J_{CN}* = 3.4 Hz); ¹⁵N{¹H} NMR: (41 MHz, CDCl₃) δ 58.7; IR: (ATR) 3408, 3285, 3183, 3078, 1618, 1582, 1557, 1441, 1420, 1298, 1263, 1103, 1076, 986, 903, 851, 829, 743 cm⁻¹; HRMS (EI) *m/z*: [M]⁺ Calculated for C₆H₃Br₂¹⁵N 249.8759; Found 249.8758

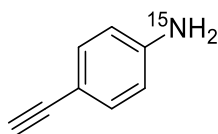
1-(4-(amino-¹⁵N)phenyl)ethan-1-one (37)

According to the general procedure **IV**, the reaction using (4-acetylphenyl)boronic acid (66.2 mg, 0.40 mmol, 1.0 equiv), ¹⁵N-**1a** (116.8 mg, 0.44 mmol, 1.1 equiv), Cs₂CO₃ (157.1 mg, 0.48 mmol, 1.2 equiv), and THF (2 mL) was conducted at 50 °C. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 7:3) gave the product as a white solid (34.7 mg, 0.26 mmol, 64% yield).

mp. 105.2–106.5 °C; TLC: *R_f* = 0.20 (NH, hexane/EtOAc = 7:3); ¹H NMR: (400 MHz, CDCl₃) δ 7.81 (d, *J* = 8.8 Hz, 2H), 6.72–6.59 (m, 2H), 4.15 (d, *J_{NH}* = 84.0 Hz, 2H), 2.51 (s, 3H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 196.5, 151.0 (d, *J_{CN}* = 12.8 Hz), 130.8 (d, *J_{CN}* = 1.4 Hz), 127.8, 113.7 (d, *J_{CN}* = 2.9 Hz),

26.1; $^{15}\text{N}\{^1\text{H}\}$ NMR: (41 MHz, CDCl_3) δ 63.9; IR: (ATR) 3379, 3316, 3210, 1649, 1634, 1586, 1562, 1435, 1358, 1279, 1177, 959, 835, 818 cm^{-1} ; HRMS (EI) m/z : $[\text{M}]^+$ Calculated for $\text{C}_8\text{H}_9^{15}\text{NO}$ 136.0654; Found 136.0659

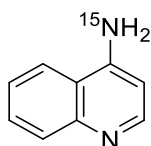
4-ethynylaniline- ^{15}N (38)



According to the general procedure **IV**, the reaction using 2-(4-ethynylphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (91.8 mg, 0.40 mmol, 1.0 equiv), ^{15}N -**1a** (116.6 mg, 0.44 mmol, 1.1 equiv), Cs_2CO_3 (157.4 mg, 0.48 mmol, 1.2 equiv), and THF (2 mL) was conducted at 50 °C. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 9:1) gave the product as a pale yellow solid (38.0 mg, 0.32 mmol, 80% yield).

mp. 99.0–100.2 °C; TLC: R_f = 0.33 (NH, hexane/EtOAc = 7:3); ^1H NMR: (400 MHz, CDCl_3) δ 7.30 (d, J = 8.4 Hz, 2H), 6.70–6.53 (m, 2H), 3.81 (d, J_{NH} = 80.8 Hz, 2H), 2.96 (s, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 147.0 (d, J_{CN} = 11.4 Hz), 133.5 (d, J_{CN} = 1.5 Hz), 114.6 (d, J_{CN} = 2.9 Hz), 111.3, 84.4, 74.9; $^{15}\text{N}\{^1\text{H}\}$ NMR: (41 MHz, CDCl_3) δ 60.0; IR: (ATR) 3474, 3381, 3306, 3258, 2097, 1609, 1560, 1510, 1290, 1177, 1061, 827 cm^{-1} ; HRMS (EI) m/z : $[\text{M}]^+$ Calculated for $\text{C}_8\text{H}_7^{15}\text{N}$ 118.0549; Found 118.0547

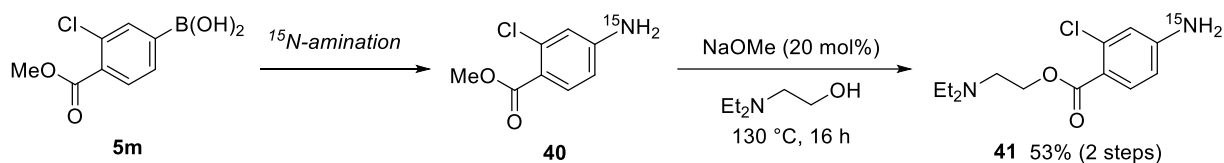
quinolin-4-amine- ^{15}N (39)



According to the general procedure **IV**, the reaction using quinolin-4-ylboronic acid (69.4 mg, 0.40 mmol, 1.0 equiv), ^{15}N -**1a** (116.6 mg, 0.44 mmol, 1.1 equiv), Cs_2CO_3 (158.0 mg, 0.48 mmol, 1.2 equiv), and THF (2 mL) was conducted at 50 °C. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 4:6) gave the product as a pale yellow solid (47.7 mg, 0.33 mmol, 82% yield).

mp. 151.5–152.7 °C; TLC: R_f = 0.38 (NH, EtOAc); ^1H NMR: (400 MHz, CDCl_3) δ 8.54 (d, J = 5.2 Hz, 1H), 8.01 (d, J = 8.4 Hz, 1H), 7.77 (d, J = 8.4 Hz, 1H), 7.72–7.61 (m, 1H), 7.52–7.40 (m, 1H), 6.60 (dd, J = 5.2, 2.0 Hz, 1H), 4.81 (d, J_{NH} = 85.6 Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 150.7 (d, J_{CN} = 2.4 Hz), 149.5 (d, J_{CN} = 13.8 Hz), 148.8, 129.9, 129.3, 124.8, 120.1 (d, J_{CN} = 1.9 Hz), 118.7 (d, J_{CN} = 1.5 Hz), 103.7 (d, J_{CN} = 1.9 Hz); $^{15}\text{N}\{^1\text{H}\}$ NMR: (41 MHz, CDCl_3) δ 61.5; IR: (ATR) 3383, 3318, 3198, 1641, 1618, 1578, 1566, 1512, 1468, 1443, 1402, 1366, 1287, 1215, 1121, 1020, 881, 858, 827, 754 cm^{-1} ; HRMS (EI) m/z : $[\text{M}]^+$ Calculated for $\text{C}_9\text{H}_8\text{N}^{15}\text{N}$ 145.0658; Found 145.0657

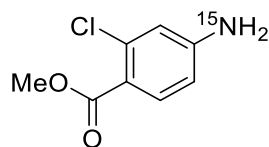
Synthesis of ^{15}N -chlorprocaine



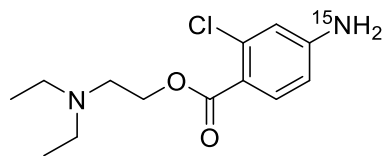
^{15}N -amination: According to the general procedure **IV**, the reaction using (3-chloro-4-(methoxycarbonyl)phenyl)boronic acid (86.0 mg, 0.40 mmol, 1.0 equiv), ^{15}N -**1a** (116.7 mg, 0.44 mmol, 1.1 equiv), Cs_2CO_3 (156.4 mg, 0.48 mmol, 1.2 equiv), and THF (2 mL) was conducted at 50 °C. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 7:3) gave **40** as a white solid (61.5 mg, 0.33 mmol, 82% yield).

Transesterification: A reaction flask equipped with a magnetic stirring bar was charged with MS3A and flamed-dried under vacuum. After cooling down to room temperature, the flask was charged with nitrogen gas, NaOMe (3.2 mg, 0.06 mmol, 0.2 equiv), **40** (56.0 mg, 0.3 mmol, 1.0 equiv), and 2-(diethylamino)ethanol (1 mL). Then, the flask was sealed and placed in an aluminum block, which was preheated at 135 °C. After the mixture was stirred at 135 °C for 16 h, water was added, and the mixture was extracted with CHCl_3 (3 $\times$ 20 mL). The combined organic layers were washed by brine, dried over Na_2SO_4 , filtrated, and concentrated under reduced pressure to give the crude product. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 6:4) gave **41** as a colorless oil (52.1 mg, 0.19 mmol, 64% yield, 53% yield in 2 steps).

methyl 4-(amino- ^{15}N)-2-chlorobenzoate (**40**)



mp. 108.6–109.8 °C; TLC: R_f = 0.20 (NH, hexane/EtOAc = 7:3); ^1H NMR: (400 MHz, CDCl_3) δ 7.78 (d, J = 8.8 Hz, 1H), 6.70 (dd, J = 2.0, 2.0 Hz, 1H), 6.52 (ddd, J = 8.8, 2.0, 2.0 Hz, 1H), 4.09 (d, J_{NH} = 84.4 Hz, 2H), 3.86 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 165.6, 150.5 (d, J_{CN} = 13.8 Hz), 136.2 (d, J_{CN} = 1.9 Hz), 133.8 (d, J_{CN} = 1.4 Hz), 118.0, 116.3 (d, J_{CN} = 2.9 Hz), 112.3 (d, J_{CN} = 2.4 Hz), 51.8; $^{15}\text{N}\{^1\text{H}\}$ NMR: (41 MHz, CDCl_3) δ 63.0; IR: (ATR) 3414, 3327, 3213, 2953, 1699, 1626, 1591, 1549, 1499, 1429, 1325, 1244, 1184, 1119, 1042, 905, 852, 831, 772 cm^{-1} ; HRMS (EI) m/z : $[\text{M}]^+$ Calculated for $\text{C}_8\text{H}_8\text{Cl}^{15}\text{NO}_2$ 186.0214; Found 186.0209

2-(diethylamino)ethyl 4-(amino-¹⁵N)-2-chlorobenzoate (41)

TLC: R_f = 0.38 (NH, hexane/EtOAc = 1:1); ^1H NMR: (400 MHz, CDCl_3) δ 7.76 (d, J = 8.8 Hz, 1H), 6.67 (dd, J = 2.0, 2.0 Hz, 1H), 6.50 (ddd, J = 8.8, 2.0, 2.0 Hz, 1H), 4.34 (t, J = 6.4 Hz, 2H), 4.18 (d, J_{NH} = 84.4 Hz, 2H), 2.83 (t, J = 6.4 Hz, 2H), 2.62 (q, J = 7.2 Hz, 4H), 1.05 (t, J = 7.2 Hz, 6H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 165.1, 150.6 (d, J_{CN} = 13.3 Hz), 136.1 (d, J_{CN} = 1.5 Hz), 133.7 (d, J_{CN} = 1.4 Hz), 117.8, 116.2 (d, J_{CN} = 3.4 Hz), 112.2 (d, J_{CN} = 2.9 Hz), 63.0, 51.0, 47.6, 11.9; $^{15}\text{N}\{^1\text{H}\}$ NMR: (41 MHz, CDCl_3) δ 63.6; IR: (ATR) 3362, 2968, 2814, 1701, 1593, 1501, 1321, 1258, 1242, 1038, 907, 849, 770 cm^{-1} ; HRMS (CI) m/z : $[\text{M}+\text{H}]^+$ Calculated for $\text{C}_{13}\text{H}_{20}\text{ClN}^{15}\text{NO}_2$ 272.1184; Found 272.1191

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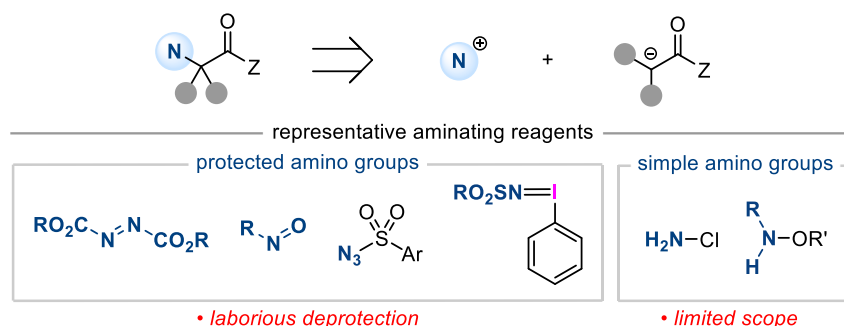
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Chapter 3

Oxidative α -Amination and Aziridination of β -Ketoesters Using Aminobenziodoxolones

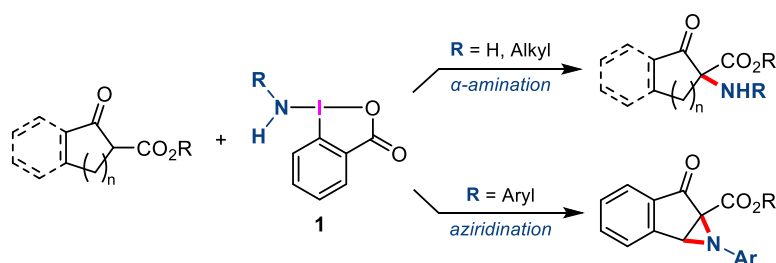
3-1. Introduction

α -Amino carbonyl compounds serve as valuable synthetic intermediates for a wide range of nitrogen-containing organic molecules and represent highly attractive structural motifs in pharmaceuticals.^{1,2} The most straightforward approach for their synthesis is the α -amination of readily available carbonyl compounds. Traditionally, such transformations have relied on the nucleophilic α -amination of α -halogenated or otherwise electrophilically activated carbonyl compounds.^{3–6} Meanwhile, methods for electrophilic α -amination of enamines and metal (Li, Si, Sn, etc.) enolates have also been developed as a promising alternative approaches (Scheme 1).^{7–9} Readily available 1,3-dicarbonyl compounds have also been recognized as useful enolate nucleophiles because of their facile enolization, allowing their direct use in electrophilic amination. For such reactions, typical electrophilic aminating reagents include azodicarboxylates, nitroso compounds, azides, and iminoiodanes. However, as referred in the general introduction, methods employing these reagents often require laborious deprotection steps to convert the installed amino functionalities into free NH_2 or other amino groups.^{7,10,11} Although, aiming at the direct introduction of simple and unprotected amino groups ($-\text{NH}_2$, $-\text{NHR}$), several approaches using chloramine and hydroxylamine derivatives as aminating reagents have been reported,^{12–17} most of these methods focus on the synthesis of primary amines, with only limited examples achieving secondary amine synthesis.^{18–20} The development of versatile electrophilic aminating reagents capable of installing various amino groups, therefore, remains a challenging task for the efficient synthesis of diverse α -amino carbonyl compounds.



Scheme 1. Electrophilic α -amination of carbonyl compounds

Hypervalent iodine(III) reagents containing N–I bonds are also promising candidates for the electrophilic α -amination of carbonyl compounds due to the high leaving ability of the iodine(III) moiety.^{21–33} Recently, Marques and co-workers reported the synthesis of aminoiodanes derived from benzylic amines and demonstrated their application to the α -amination of indanone-based β -ketoesters.³⁴ Nevertheless, the scope of transferable amino groups remains limited to benzylic amines because of the restricted generality of the available aminoiodanes. As described in chapter 1 and 2, versatile methods for the synthesis of various aminobenziodoxolones **1** have been developed directly using simple amines, including ammonia and primary amines,^{35,36} thereby dramatically expanding the scope of accessible aminoiodanes.³⁷ To expand the synthetic utility of these reagents in oxidative amination reactions, the author explored their reactivity toward β -ketoesters as nucleophiles. Herein, the author reports two distinct types of oxidative amination reactions of β -ketoesters with aminobenziodoxolones: a versatile α -amination and aziridination, both providing efficient access to structurally unique α -amino carbonyl compounds (Scheme 2).



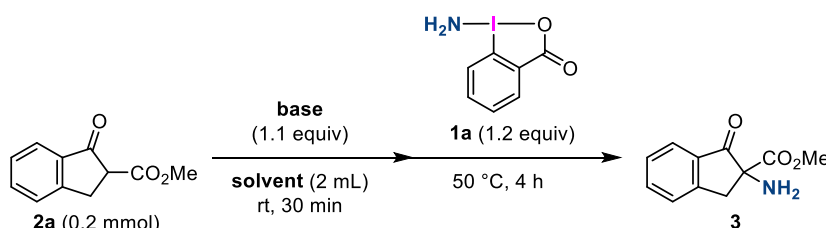
Scheme 2. Oxidative amination of β -ketoesters using aminobenziodoxolones

3-2. Results and Discussion

3-2-1. Optimization of Reaction Conditions

The author first investigated the installation of an NH₂ group by the α -amination of β -ketoester **2a** using aminobenziodoxolone **1a** (Table 1). The reaction was conducted in the presence of K₂CO₃ as a base in *N,N*-dimethylformamide (DMF) at 50 °C, affording the desired α -amino- β -ketoester **3** in 80% yield (entry 1). In the absence of a base, the reaction proceeded with significantly lower efficiency (entry 2), indicating that a base is essential for promoting the amination. The reaction also proceeded at room temperature albeit with a slightly reduced yield (entry 3). A brief screening of solvents revealed that DMF was the most suitable medium for this transformation (entries 4–6). The use of Cs₂CO₃ as a base also effectively promotes the amination, affording **3** in a yield comparable to that obtained with K₂CO₃ (entry 7). Based on these results, inexpensive K₂CO₃ in DMF under mild heating conditions was selected as the optimized conditions (entry 1). Notably, this represents the first example of the synthesis of a primary α -amino- β -ketoester using a hypervalent iodine reagent, conducted under mild conditions with a simple operation.

Table 1. Optimization of reaction conditions for α -amination of β -ketoester **2a**



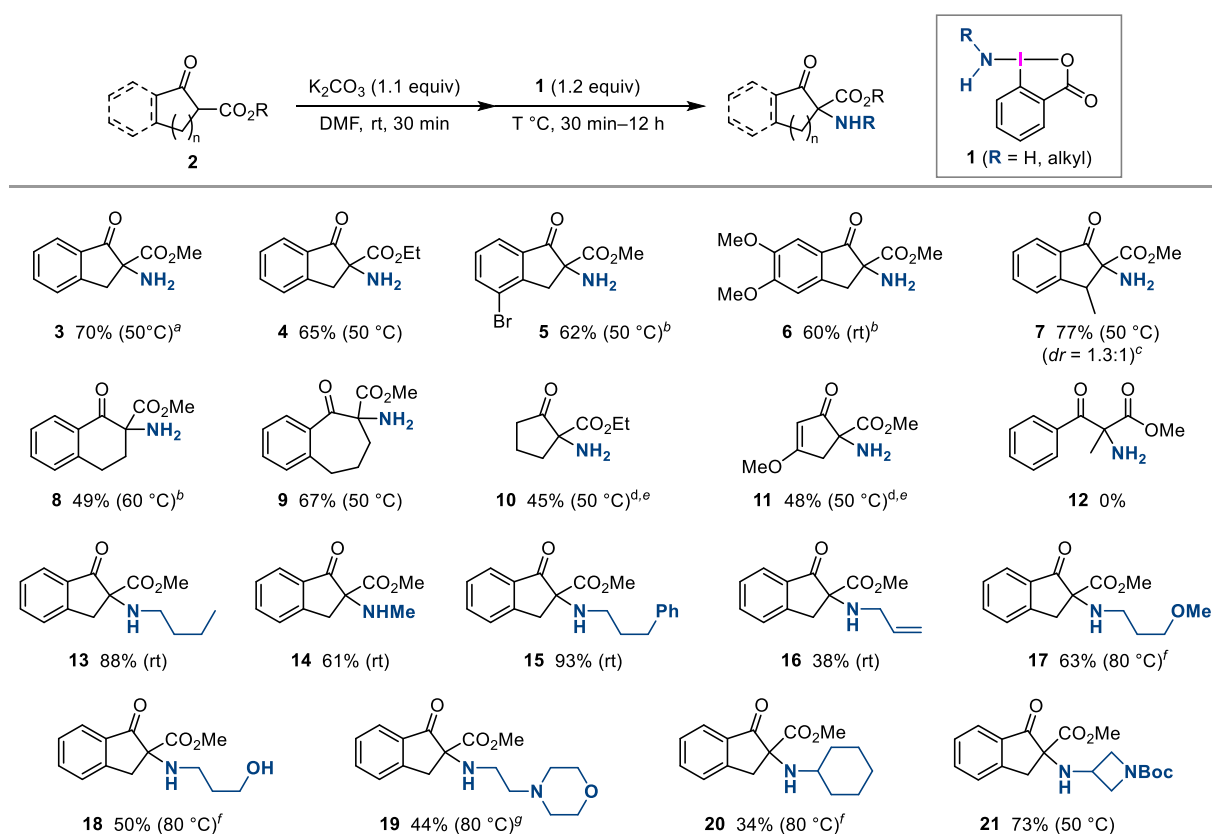
entry	base	solvent	yield (%) ^a
1	K ₂ CO ₃	DMF	80
2	none	DMF	20
3 ^b	K ₂ CO ₃	DMF	64
4	K ₂ CO ₃	THF	55
5	K ₂ CO ₃	1,4-dioxane	26
6	K ₂ CO ₃	MeCN	70
7	Cs ₂ CO ₃	DMF	83

^aDetermined by ¹H NMR analysis. ^b room temperature.

3-2-2. Scope for α -Amination of β -Ketoesters.

With the optimized reaction conditions in hand, the generality of the α -amination was next examined (Scheme 3). The corresponding ethyl ester of the indanone-derived β -ketoester also

underwent the reaction to give **4**. Substrates bearing bromo and methoxy substituents on the aryl ring were efficiently aminated to afford **5** and **6**, respectively. The steric hindrance of a 3-methyl substituent had little influence on the reactivity, furnishing **7** as a mixture of diastereomers (*dr* = 1.3:1). Beyond the indanone scaffold, the introduction of an NH₂ group into tetralone- and benzosuberone-based β -ketoesters was also successful (**8**, **9**). In addition, monocyclic substrates were also applicable to the amination, affording **10** and **11**; notably, compound **11** corresponds to the racemic aza-analogue of (+)-kjellmanianone, a biologically active natural product.^{38–40} In these cases, the use of Cs₂CO₃ as a base improved the product yields. However, the reaction with an acyclic β -ketoester resulted in a complex mixture, and only small amount of the substrate was recovered (**12**).



Scheme 3. Scope for α -Amination of β -Ketoesters ^a The reaction was conducted on a 2 mmol scale. ^b MS3A (200 mg) was added. ^c Determined by ¹H NMR analysis of the crude product. ^d Cs₂CO₃ was used instead of K₂CO₃. ^e Yields of the isolated products after benzoyl protection. ^f **1** (2 equiv) was used. ^g **1** (1.5 equiv) was used.

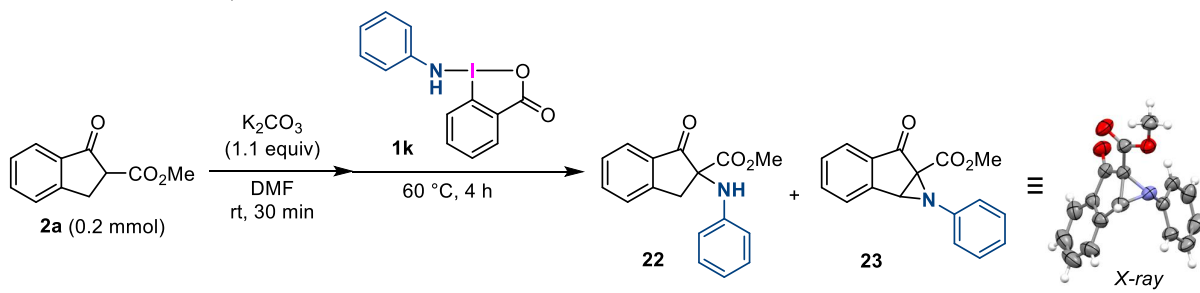
The scope of installable amino groups was further examined using aliphatic primary amine-derived aminobenziodoxolones **1**. The reaction enabled the synthesis of a range of *N*-alkyl α -amino- β -ketoesters (**13–21**), incorporating both simple and functionalized alkylamino groups. The transformation exhibited good functional group tolerance, accommodating oxidatively labile allyl (**16**), methoxy (**17**), hydroxy

(**18**), and morpholino (**19**) groups. Moreover, sterically hindered amino groups bearing α -secondary carbon centers could also be installed (**20**, **21**). However, attempts at amination using secondary amine-derived aminobenziodoxolones were unsuccessful. Nevertheless, the present method substantially broadens the scope of electrophilic α -amination reactions, providing access to α -amino carbonyl compounds that are difficult to synthesize by existing methods.^{20,34}

3-2-3. Aziridination of β -Ketoesters with Arylamine-Derived Aminobenziodoxolones

During the exploration of the reaction scope using an aniline-derived aminobenziodoxolone **1k**, the author unexpectedly observed the formation of aziridine **23** as the major product, accompanied by a smaller amount of the α -aminated product **22** (Table 2, entry 1). When two equivalents of **1k** were employed, the yield of **23** increased to 60% (entry 2). Given that this aziridine formation proceeds through a formal double C(sp³)-H amination, which theoretically requires two equivalents of oxidant, it is reasonable to assume that one equivalent of **1k** is consumed as a simple oxidant. To reduce the amount of **1k** required, the author briefly screened other hypervalent iodine oxidants that could serve as substitutes for aminobenziodoxolones. As a result, the use of one equivalent of commercially available PhI(OAc)₂ in combination with **1k** proved effective, selectively affording aziridine **23** in good yield (entry 3). This transformation represents a rare example of aziridination proceeding via a formal C(sp³)-H amination,⁴¹ despite the existence of numerous aziridination methods.⁴² Moreover, aziridines bearing fused-ring scaffolds like **23** are unique and valuable synthetic intermediates.^{43–47}

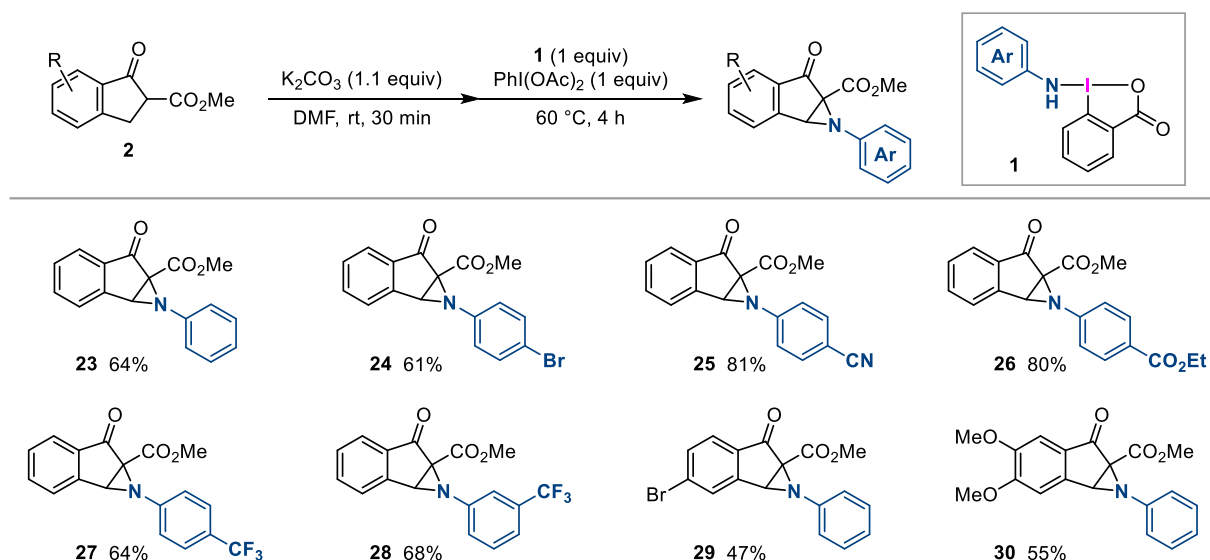
Table 2. Aziridination of β -Ketoester with Aniline-Derived Aminobenziodoxolone **1k**



entry	aminating reagent (oxidant)	yield (%) ^a	
		22	23
1	1k (1 equiv)	9	31
2	1k (2 equiv)	12	60
3	1k (1 equiv) + PhI(OAc) ₂ (1 equiv)	3	64 (64) ^b

^aDetermined by ¹H NMR analysis. ^bIsolated yield.

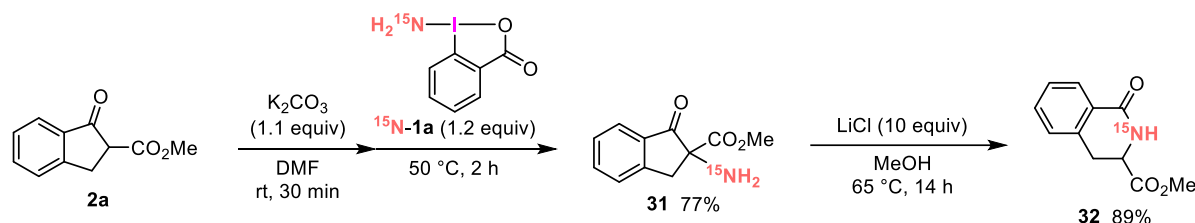
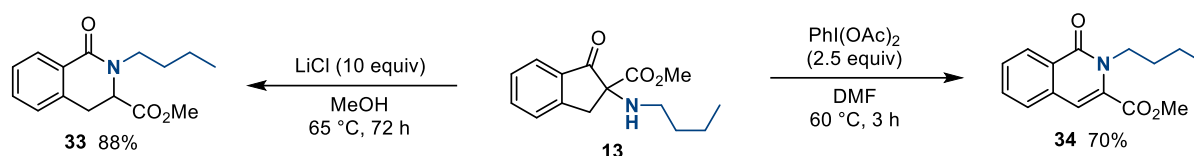
The author then examined the scope of this aziridination (Scheme 4). In addition to simple aniline, a variety of arylamines bearing substituents such as bromo, cyano, ethoxycarbonyl, and trifluoromethyl groups were also compatible with this aziridination (**24–30**). Regarding the scope of β -ketoesters, substrates derived from tetralone or cyclopentanone were not compatible under the current conditions.



Scheme 4. Synthesis of aziridines

3-2-4. Synthetic Applications

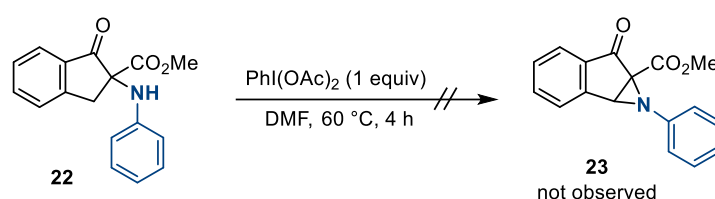
The synthetic utility of the developed α -amination reaction was further demonstrated by the synthesis of ^{15}N -labelled compounds (Scheme 5A). The ^{15}N -labelled compound **31** was successfully synthesized using aminobenziodoxolone ^{15}N -**1a**. Treatment of **31** with LiCl in MeOH induced a retro-Dieckmann reaction followed by intramolecular amidation, affording dihydroisoquinolone **32**,^{33,48} a valuable synthetic intermediate of ^{15}N -labelled analogue of biologically active molecules.^{49–52} Similarly, the *N*-alkyl α -aminated product **13** was converted to dihydroisoquinolinone **33** (Scheme 5B). Furthermore, isoquinolinone **34** was synthesized via oxidative rearrangement with $PhI(OAc)_2$.⁵³ These two-step transformations for the synthesis of aza-heterocyclic compounds represent a formal nitrogen insertion into β -ketoesters, a process of considerable interest in modern organic and medicinal chemistry.^{33,47,54–60}

A) Synthesis of ^{15}N -labelled compoundsB) Transformations of the α -aminated product to aza-heterocycles

Scheme 5. Synthetic Applications

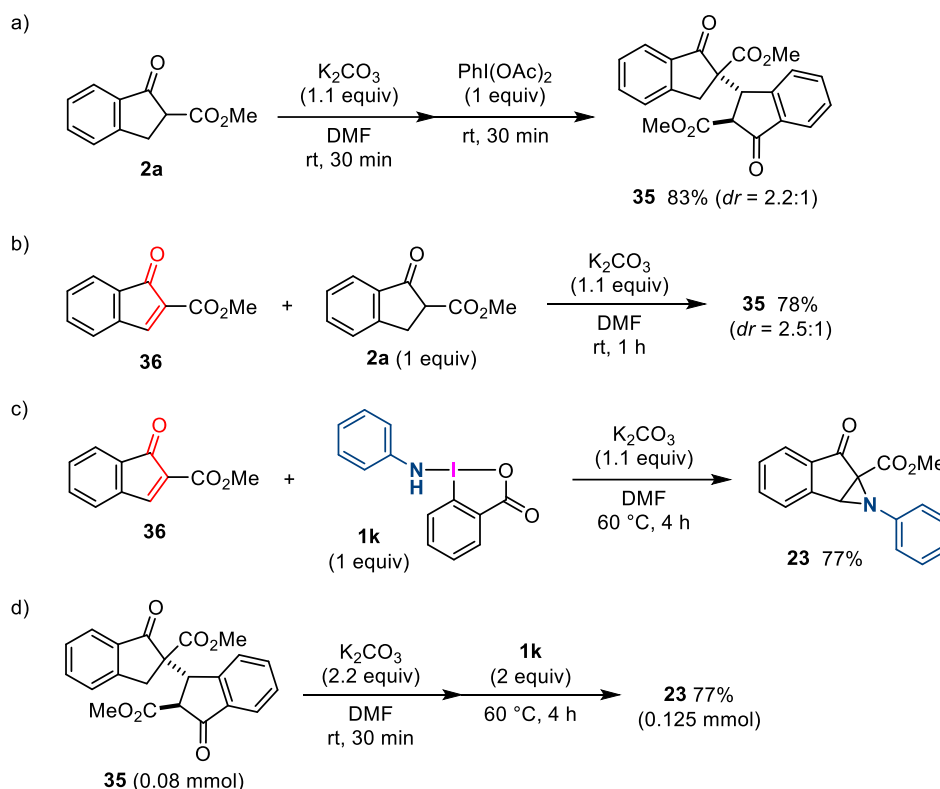
3-2-5. Mechanistic investigations for aziridination

According to previous reports,^{17,34} the α -amination reaction likely proceeds via an $\text{S}_{\text{N}}2$ -type electrophilic amination mechanism. In contrast, the mechanism of the aziridination is quite particularly intriguing; therefore, several mechanistic investigations were conducted. In the reaction of β -ketoester **2a** with aminobenziodoxolone **1k**, the α -aminated product **22** was observed along with aziridine **23** (Table 2), suggesting that **22** might serve as an intermediate in the aziridination. To examine the possibility that oxidation of **22** with $\text{PhI}(\text{OAc})_2$ leads to the formation of **23**, **22** was treated with $\text{PhI}(\text{OAc})_2$; however, no formation of **23** was observed, thereby ruling out this pathway (Scheme 6).

Scheme 6. The reaction of α -amino- β -ketoester **22** with $\text{PhI}(\text{OAc})_2$

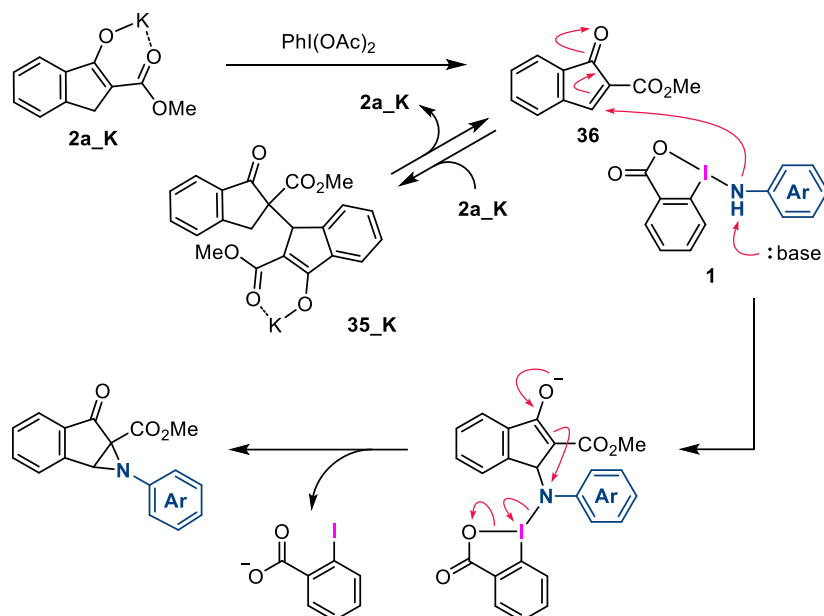
To further investigate the role of $\text{PhI}(\text{OAc})_2$, β -ketoester **2a** was reacted with $\text{PhI}(\text{OAc})_2$, affording **35** in 83% yield (Scheme 7a). This result suggests the in situ formation of α,β -unsaturated ketoester **36**, which is subsequently trapped by the enolate of **2a**. To confirm this, separately prepared **36** was reacted with **2a**, furnishing **35** (Scheme 7b). These results strongly support the in situ generation of **36** as an intermediate, although it was not directly observed in the reaction mixture. Indeed, **36** smoothly reacted

with the iodine reagent **1k** to provide aziridine **23** in high yield (Scheme 7c).^{41,61} Furthermore, treatment of **35** with a base, followed by reaction with **1k**, also produced **23** (Scheme 7d), indicating that **35** undergoes reverse reaction to regenerate **36** and **2a** under the reaction conditions.



Scheme 7. Mechanistic Experiments. Yields were determined by 1H NMR analysis of the crude product.

Based on the experimental results, a proposed reaction pathway for the aziridination is shown in Scheme 8. The enolate of β -ketoester (**2a_K**) initially reacts with $PhI(OAc)_2$, likely via the formation of an enolonium intermediate,^{62–64} to give α,β -unsaturated ketoester **36**, which reversibly reacts with **2a_K** to form **35_K**. Subsequently, **36** undergoes aziridination with aminobenziodoxolone **1** through an addition–elimination pathway. The dual nucleophilic and electrophilic character of aminobenziodoxolones is crucial for facilitating this transformation. As described in Table 2, the reaction using only iodine reagent **1k** also led to aziridination (entry 2), suggesting that **1k** can serve as an oxidant to convert **2a** into **36**. This transformation is likely initiated by the formation of enolonium species via a facile ligand exchange between **1k** and enolate **2a_K**, facilitated by the labile aniline ligand.



Scheme 8. Proposed Reaction Pathway for Aziridination

3-3. Conclusion

In conclusion, two distinct oxidative amination reactions of β -ketoesters, α -amination and aziridination, were successfully achieved using aminobenziodoxolones. Both NH_2 -substituted and alkylamine-derived iodine reagents enabled α -amination, providing a variety of α -amino- β -ketoesters, including compounds not accessible by existing electrophilic amination methods. The synthetic utility of the method was highlighted by the elaboration of the products into aza-heterocyclic compounds, including ^{15}N -labelled derivatives. In contrast, arylamine-derived iodine reagents promoted aziridination, offering straightforward access to unique fused aziridines.

3-4. Experimental Section

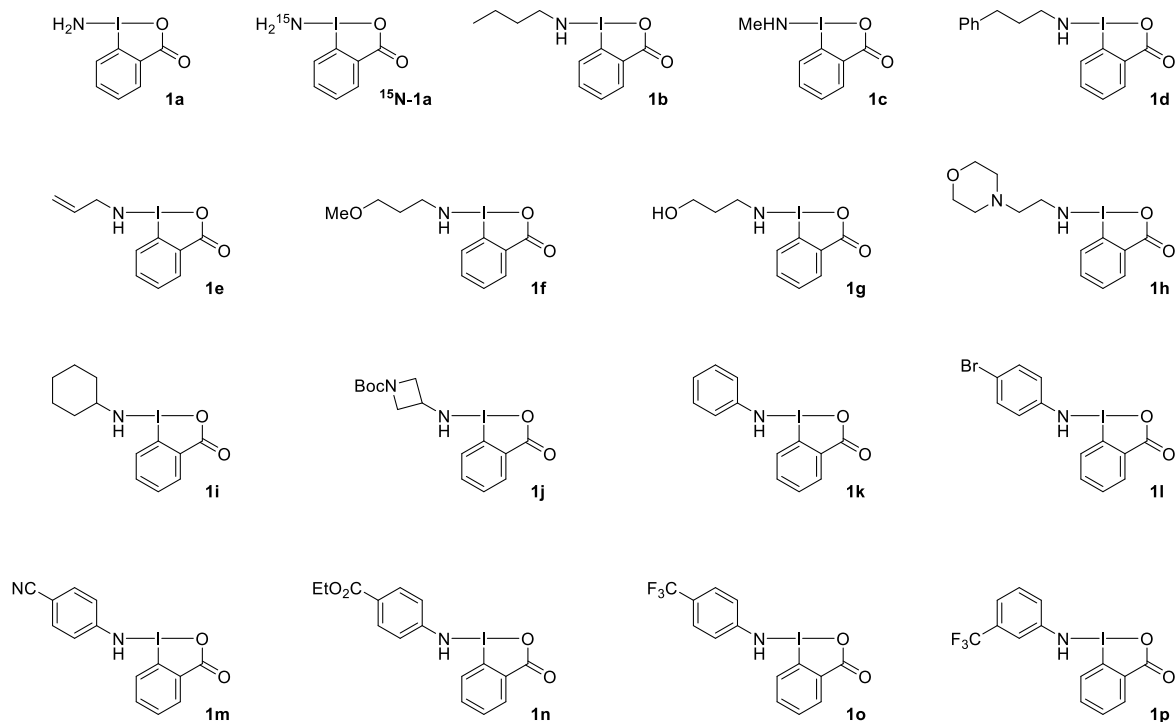
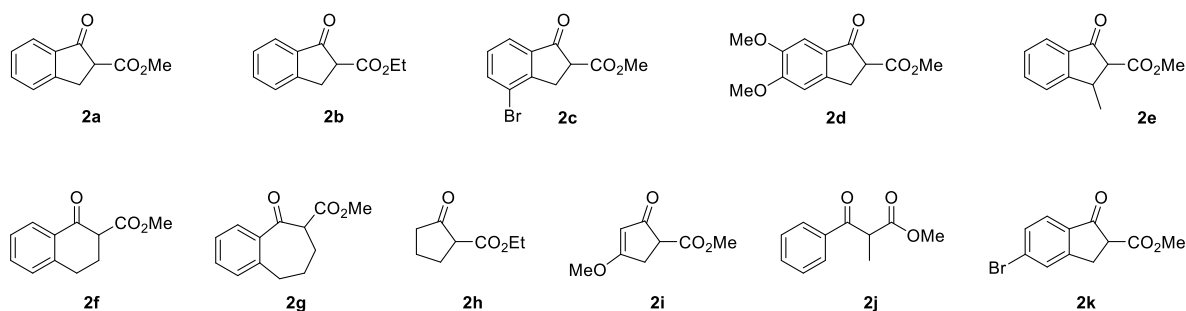
General Remarks

New compounds were characterized by ^1H NMR, $^{13}\text{C}\{^1\text{H}\}$ NMR, $^{19}\text{F}\{^1\text{H}\}$ NMR, $^{15}\text{N}\{^1\text{H}\}$ NMR, IR, MS, and HRMS. ^1H , $^{13}\text{C}\{^1\text{H}\}$, $^{19}\text{F}\{^1\text{H}\}$, $^{15}\text{N}\{^1\text{H}\}$ NMR spectra were recorded on a JEOL JMT-400/54/SS or JNM-ECZL400S spectrometers (^1H NMR, 400 MHz; $^{13}\text{C}\{^1\text{H}\}$ NMR, 100 MHz; $^{19}\text{F}\{^1\text{H}\}$ NMR, 376 MHz; $^{15}\text{N}\{^1\text{H}\}$ NMR, 41 MHz). ^1H NMR chemical shifts were determined relative to Me_4Si (0.0 ppm) as an internal standard in CDCl_3 or the signals of residual undeuterated dimethyl sulfoxide

(2.49 ppm) in dimethyl sulfoxide-*d*₆. ¹³C{¹H} NMR chemical shifts were determined relative to CDCl₃ (77.00 ppm) or (CD₃)₂SO (39.50 ppm). ¹⁹F{¹H} NMR chemical shifts were determined relative to C₆F₆ (−164.9 ppm in CDCl₃) as an external standard. ¹⁵N{¹H} NMR chemical shifts were determined relative to nitromethane (380.2 ppm in CDCl₃) as an external standard. The multiplicities are abbreviated as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad) and combinations thereof. Infrared spectra were recorded on a SHIMADZU IRAffinity-1 FT-IR Spectrometer. High-resolution mass spectra (HRMS) were obtained on JEOL JMS-700 (magnetic sector type mass spectrometer) and JMS-T100LP. Melting points were determined on a Stanford Research Systems MPA100 OptiMelt Automated Melting Point System. The X-ray diffraction data of the single crystal were collected on a two-dimensional X-ray detector (PILATUS 200K/R) equipped in Rigaku XtaLAB PRO diffractometer using thin multi-layer mirror monochromated Cu-Kα radiation (λ = 1.54187 Å). Products were purified by chromatography on silica gel BW-300 (Fuji Silysia Chemical Ltd.) or Chromatorex NH (Fuji Silysia Chemical Ltd.). Analytical thin-layer chromatography (TLC) was performed on pre-coated silica gel glass plates (Merck silica gel 60 F₂₅₄ and Fuji Silysia Chromatorex NH, 0.25 mm thickness). Compounds were visualized with UV lamp or treatment with an ethanolic solution of phosphomolybdic acid followed by heating.

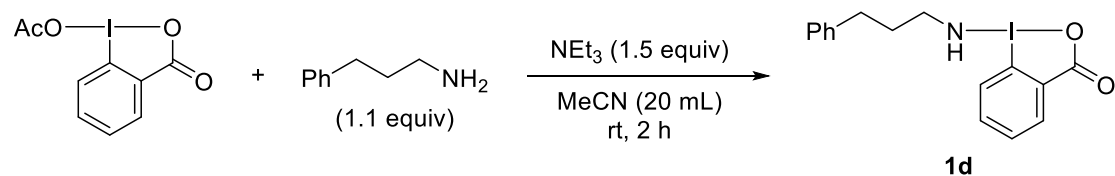
Materials

Hypervalent iodine reagents **1a–c**, **1e–p** and ¹⁵N-**1a** were prepared according to the reported procedure.^{35,36} β-Ketoesters **2a–g**, **2i–k** were prepared according to the reported procedure.^{34, 66–70} α,β-Unsaturated ketoester **36** was prepared according to the reported procedure.⁷¹ DMF was stored in the presence of MS4A. Dehydrated acetonitrile and THF were used from a solvent purification system. Triethylamine was distilled over CaH₂ before use. All other solvents and reagents were purchased and used as obtained.

**Figure S1.** List of iodine reagents**Figure S2.** List of substrates

Preparation of a hypervalent iodine reagent

1-((3-phenylpropyl)amino)-benziodoxol-3(1*H*)-one (**1d**)



To a solution of 1-acetoxy-1,2-benziodoxol-3(1*H*)-one (613.1 mg, 2.0 mmol, 1.0 equiv) in MeCN (20 mL), 3-phenylpropylamine (305.9 mg, 2.2 mmol, 1.1 equiv) and triethylamine (313.5 mg, 3.1 mmol, 1.5 equiv) was added. The mixture was stirred at room temperature for 2 h. Then, volatiles were

removed under reduced pressure. The resulting solid was washed with Et₂O and dried under vacuum to give the product as a white solid (595.0 mg, 78% yield).

mp: 121.5 °C (decomposed); ¹H NMR: (400 MHz, DMSO-*d*₆) δ 8.01 (d, *J* = 7.6 Hz, 2H), 7.84 (ddd, *J* = 7.6, 7.6, 1.6 Hz, 1H), 7.63 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.32–7.14 (m, 5H), 5.52 (t, *J* = 6.4 Hz, 1H), 3.39–3.29 (m, 2H), 2.67 (t, *J* = 7.6 Hz, 2H), 1.80 (tt, *J* = 7.6, 7.6 Hz, 2H); ¹³C {¹H} NMR: (100 MHz, DMSO-*d*₆) δ 166.9, 141.6, 133.5, 133.2, 131.3, 130.1, 128.3, 125.8, 125.4, 116.9, 50.8, 34.1, 32.2 (one sp² signal was not observed because of overlapping); IR: (ATR) 3196, 3061, 2959, 2940, 1599, 1582, 1331, 829, 752, 719 cm⁻¹; HRMS (FAB) *m/z*: [M+H]⁺ Calculated for C₁₆H₁₇NO₂I 382.0299; Found 382.0313

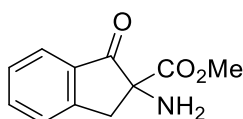
α-Amination of β-ketoesters: experimental procedures and product data

General procedure I: A reaction flask charged with a magnetic stirring bar was flame-dried under vacuum. After cooling down to room temperature, β-ketoester **2** (0.20–0.30 mmol, 1.0 equiv), K₂CO₃ (0.22–0.33 mmol, 1.1 equiv), and DMF (2–3 mL) were added. The mixture was stirred at room temperature for 30 min, and hypervalent iodine reagent **1** (0.24–0.60 mmol, 1.2–2.0 equiv) was added. Then, the flask was placed in an aluminum block, which was preheated at indicated temperature. After the mixture was stirred at indicated temperature for indicated time, sat. NaHCO₃ aq. was added, and the mixture was extracted with AcOEt (2 × 15 mL). The organic solution was washed three times with brine. The combined organic layers were dried over Na₂SO₄, filtrated, and concentrated under reduced pressure to give the crude product. Purification by flash column chromatography on (NH) silica gel (hexane/EtOAc) gave the product.

General procedure II: A reaction flask charged with a magnetic stirring bar and MS3A (200 mg) were flame-dried under vacuum. After cooling down to room temperature, β-ketoester **2** (0.20 mmol, 1.0 equiv), K₂CO₃ (0.22 mmol, 1.1 equiv), and DMF (2 mL) were added. The mixture was stirred at room temperature for 30 min, and hypervalent iodine reagent **1** (0.24 mmol, 1.2 equiv) was added. Then, the flask was placed in an aluminum block, which was preheated at indicated temperature. After the mixture was stirred at indicated temperature for indicated time, the reaction mixture was filtered by a

pad of celite using AcOEt as an eluent. To the filtrate, sat. NaHCO_3 aq. was added, and the mixture was extracted with AcOEt (2×15 mL). The organic solution was washed three times with brine. The combined organic layers were dried over Na_2SO_4 , filtrated, and concentrated under reduced pressure to give the crude product. Purification by flash column chromatography on (NH) silica gel (hexane/EtOAc) gave the product.

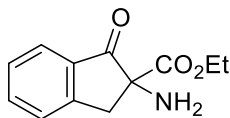
methyl 2-amino-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (3)



A reaction flask charged with a magnetic stirring bar was flame-dried under vacuum. After cooling down to room temperature, methyl 1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**2a**, 379.7 mg, 2.0 mmol, 1.0 equiv), K_2CO_3 (304.8 mg, 2.2 mmol, 1.1 equiv), and DMF (20 mL) were added. The mixture was stirred at room temperature for 30 min, and hypervalent iodine reagent **1a** (631.7 mg, 2.4 mmol, 1.2 equiv) was added. Then, the flask was placed in an aluminum block, which was preheated at 50 °C. After the mixture was stirred at 50 °C for 4 h, sat. NaHCO_3 aq. was added, and the mixture was extracted with AcOEt (3×30 mL). The organic solution was washed three times with brine. The combined organic layers were dried over Na_2SO_4 , filtrated, and concentrated under reduced pressure to give the crude product. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 70:30) gave the product as a colorless oil (285.7 mg, 70% yield).

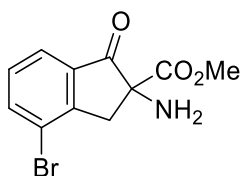
^1H NMR: (400 MHz, CDCl_3) δ 7.81 (d, $J = 7.6$ Hz, 1H), 7.66 (ddd, $J = 7.6, 7.6, 1.2$ Hz, 1H), 7.49 (d, $J = 7.6$ Hz, 1H), 7.43 (dd, $J = 7.6, 7.6$ Hz, 1H), 3.75–3.65 (m, 1H), 3.69 (s, 3H), 3.09 (d, $J = 17.2$ Hz, 1H), 2.16 (brs, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 202.1, 172.9, 152.4, 135.8, 133.9, 128.0, 126.4, 125.2, 67.0, 53.0, 41.2

The analytical data for this compound was in excellent agreement with the reported data.⁷²⁾

ethyl 2-amino-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (4)

According to the general procedure **I**, the reaction using ethyl 1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**2b**, 41.3 mg, 0.20 mmol, 1.0 equiv), K₂CO₃ (30.5 mg, 0.22 mmol, 1.1 equiv), DMF (2 mL), and hypervalent iodine reagent **1a** (63.9 mg, 0.24 mmol, 1.2 equiv) was conducted at 50 °C for 4 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 70:30) gave the product as an orange viscous liquid (28.9 mg, 65% yield).

¹H NMR: (400 MHz, CDCl₃) δ 7.81 (d, *J* = 7.4 Hz, 1H), 7.66 (dd, *J* = 7.4, 7.4 Hz, 1H), 7.49 (d, *J* = 7.4 Hz, 1H), 7.43 (dd, *J* = 7.4, 7.4 Hz, 1H), 4.22–4.10 (m, 2H), 3.71 (d, *J* = 17.2 Hz, 1H), 3.08 (d, *J* = 17.2 Hz, 1H), 2.14 (br, 2H), 1.17 (t, *J* = 7.0 Hz, 3H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 202.3, 172.4, 152.5, 135.7, 134.0, 128.0, 126.4, 125.2, 67.1, 62.0, 41.2, 14.0; IR: (ATR) 3372, 2982, 2934, 2907, 1738, 1713, 1186, 746 cm⁻¹; HRMS (EI) *m/z*: [M]⁺ Calculated for C₁₂H₁₃NO₃ 219.0890; Found 219.0898

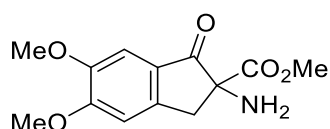
methyl 2-amino-4-bromo-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (5)

According to the general procedure **II**, the reaction using MS3A (200 mg), methyl 4-bromo-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**2c**, 53.9 mg, 0.20 mmol, 1.0 equiv), K₂CO₃ (30.3 mg, 0.22 mmol, 1.1 equiv), DMF (2 mL), and hypervalent iodine reagent **1a** (64.2 mg, 0.24 mmol, 1.2 equiv) was conducted at 50 °C for 4 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 80:20) gave the product as a pale yellow solid (35.4 mg, 62% yield).

mp: 74.4–77.1 °C; ¹H NMR: (400 MHz, CDCl₃) δ 7.83 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.77 (d, *J* = 7.6 Hz, 1H), 7.34 (dd, *J* = 7.6, 7.6 Hz, 1H), 3.71 (s, 3H), 3.63 (d, *J* = 17.6 Hz, 1H), 3.02 (d, *J* = 17.6 Hz, 1H),

2.17 (br, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 201.4, 172.6, 152.2, 138.5, 136.0, 129.8, 124.1, 121.9, 66.9, 53.1, 42.3; IR: (ATR) 3389, 3374, 3358, 3308, 3026, 2957, 2922, 1738, 1715, 1248, 1192, 1180, 1128, 1047, 945, 775, 748 cm^{-1} ; HRMS (CI) m/z : $[\text{M}+\text{H}]^+$ Calculated for $\text{C}_{11}\text{H}_{11}\text{BrNO}_3$ 283.9917; Found 283.9925

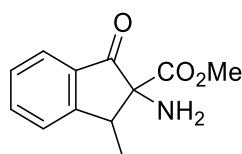
methyl 2-amino-5,6-dimethoxy-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (6)



According to the general procedure **II**, the reaction using MS3A (200 mg), methyl 5,6-dimethoxy-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**2d**, 50.3 mg, 0.20 mmol, 1.0 equiv), K_2CO_3 (30.9 mg, 0.22 mmol, 1.1 equiv), DMF (2 mL), and hypervalent iodine reagent **1a** (63.8 mg, 0.24 mmol, 1.2 equiv) was conducted at room temperature for 12 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 80:20) gave the product as an orange viscous liquid (32.1 mg, 60% yield).

^1H NMR: (400 MHz, CDCl_3) δ 7.20 (s, 1H), 6.90 (s, 1H), 3.99 (s, 3H), 3.92 (s, 3H), 3.70 (s, 3H), 3.62 (d, J = 17.2 Hz, 1H), 3.00 (d, J = 17.2 Hz, 1H), 2.00 (brs, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 200.5, 173.2, 156.4, 149.8, 148.2, 126.5, 107.2, 105.2, 67.5, 56.3, 56.1, 53.0, 40.9; IR: (ATR) 3370, 3011, 2953, 2837, 1740, 1697, 1587, 1501, 1315, 1271, 1217, 1198, 1111, 1016, 862, 727 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ Calculated for $\text{C}_{13}\text{H}_{16}\text{NO}_5$ 266.1023; Found 266.1025

methyl 2-amino-1-methyl-3-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (7)

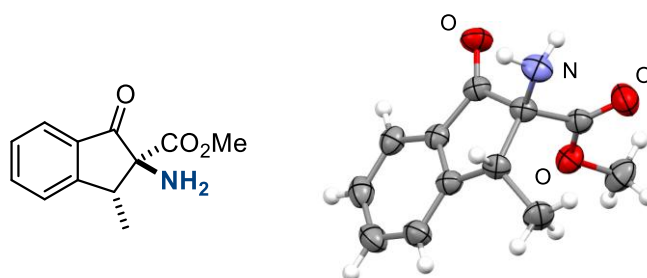


According to the general procedure **I**, the reaction using methyl 1-methyl-3-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**2e**, 41.5 mg, 0.20 mmol, 1.0 equiv), K_2CO_3 (31.0 mg, 0.22 mmol, 1.1 equiv), DMF (2 mL), and hypervalent iodine reagent **1a** (63.0 mg, 0.24 mmol, 1.2 equiv) was conducted at

50 °C for 4 h. The crude product was analyzed by ^1H NMR spectroscopy (*syn/anti* = 1.3:1). Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 70:30) gave the product as colorless oil (*syn* isomer, 11.8 mg), pale yellow oil (mixture of diastereomer, 11.8 mg), and pale yellow solid (*anti* isomer, 10.0 mg) (77% combined yield of diastereomers). Recrystallization of *anti* isomer from hexane/ CHCl_3 gave single crystals suitable for X-ray analysis.

***syn* isomer:** ^1H NMR: (400 MHz, CDCl_3) δ 7.79 (d, J = 8.0 Hz, 1H), 7.67 (ddd, J = 7.6, 7.6, 1.2 Hz, 1H), 7.52 (dd, J = 7.6, 0.8 Hz, 1H), 7.47–7.39 (m, 1H), 3.77 (q, J = 7.2 Hz, 1H), 3.69 (s, 3H), 1.97 (brs, 2H), 1.35 (d, J = 7.2 Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 202.2, 173.3, 158.3, 135.9, 133.2, 128.0, 125.3, 124.9, 69.8, 53.0, 42.8, 15.5; IR: (ATR) 3377, 2955, 1738, 1709, 1605, 1587, 1466, 1290, 1244, 1215, 1184, 1063, 966, 901, 760 cm^{-1} ; HRMS (EI) m/z : $[\text{M}]^+$ Calculated for $\text{C}_{12}\text{H}_{13}\text{NO}_3$ 219.0890; Found 219.0893

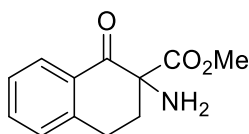
***anti* isomer:** mp: 96.0–98.3 °C; ^1H NMR: (400 MHz, CDCl_3) δ 7.79 (d, J = 7.6 Hz, 1H), 7.72–7.63 (m, 1H), 7.48 (d, J = 7.6 Hz, 1H), 7.44 (dd, J = 7.6, 7.6 Hz, 1H), 3.62 (s, 3H), 3.36 (q, J = 7.6 Hz, 1H), 2.13 (br, 2H), 1.41 (d, J = 7.6 Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) 202.1, 172.2, 155.8, 135.8, 134.6, 128.0, 124.5, 124.4, 72.4, 52.4, 47.2, 13.8; IR: (ATR) 3399, 3326, 2957, 1742, 1709, 1603, 1583, 1431, 1294, 1207, 1157, 1119, 1080, 930, 787, 754 cm^{-1} ; HRMS (EI) m/z : $[\text{M}]^+$ Calculated for $\text{C}_{12}\text{H}_{13}\text{NO}_3$ 219.0890; Found 219.0901



The structure of ***anti*-7** was determined by X-ray structural analysis. CCDC 2498273 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

CCDC number	2498273
Empirical formula	$\text{C}_{12}\text{H}_{13}\text{NO}_3$

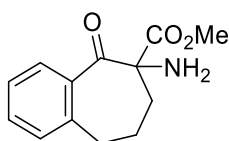
Formula weight	219.23
Temperature/K	123
Crystal system	triclinic
Space group	P-1
a/Å	6.5394(5)
b/Å	8.9122(8)
c/Å	10.3982(8)
$\alpha/^\circ$	75.045(7)
$\beta/^\circ$	76.366(7)
$\gamma/^\circ$	76.548(7)
Volume/Å ³	559.38(8)
Z	2
$\rho_{\text{calc}}/\text{g}/\text{cm}^3$	1.302
μ/mm^{-1}	0.777
F(000)	232.0
Crystal size/mm ³	0.199 × 0.157 × 0.137
Radiation	Cu K α (λ = 1.54184)
2 Θ range for data collection/ $^\circ$	8.96 to 154.688
Index ranges	-8 ≤ h ≤ 8, -11 ≤ k ≤ 11, -13 ≤ l ≤ 13
Reflections collected	11231
Independent reflections	2266 [R_{int} = 0.1915, R_{sigma} = 0.0825]
Data/restraints/parameters	2266/0/154
Goodness-of-fit on F ²	1.166
Final R indexes [$I \geq 2\sigma(I)$]	R_1 = 0.0869, wR_2 = 0.2481
Final R indexes [all data]	R_1 = 0.0972, wR_2 = 0.2890
Largest diff. peak/hole / e Å ⁻³	0.39/-0.37

methyl 2-amino-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (8)

According to the general procedure **II**, the reaction using MS3A (200 mg), methyl 1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (**2f**, 39.9 mg, 0.20 mmol, 1.0 equiv), K₂CO₃ (31.1 mg, 0.23 mmol, 1.1 equiv), DMF (2 mL), and hypervalent iodine reagent **1a** (63.9 mg, 0.24 mmol, 1.2 equiv) was conducted at 60 °C for 6 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 80:20) gave the product as an orange viscous liquid (21.0 mg, 49% yield).

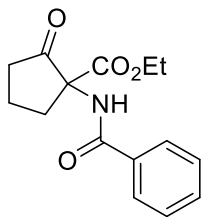
¹H NMR: (400 MHz, CDCl₃) δ 8.08 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.50 (ddd, *J* = 7.6, 7.6, 1.6 Hz, 1H), 7.34 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.25 (d, *J* = 7.6 Hz, 1H), 3.71 (s, 3H), 3.14–2.95 (m, 2H), 2.62 (ddd, *J* = 13.6, 6.0, 4.8 Hz, 1H), 2.40–1.80 (m, 3H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 194.5, 173.6, 143.4, 133.9, 130.8, 128.8, 128.2, 126.9, 64.7, 52.8, 34.3, 25.6; IR: (ATR) 3381, 2953, 1732, 1682, 1599, 1238, 1198, 741 cm⁻¹; HRMS (MALDI, positive, DCTB) *m/z*: [M+Na]⁺ Calculated for C₁₂H₁₃NO₃Na 242.0788; Found 242.0788

methyl 6-amino-5-oxo-6,7,8,9-tetrahydro-5H-benzo[7]annulene-6-carboxylate (9)



According to the general procedure **I**, the reaction using methyl 5-oxo-6,7,8,9-tetrahydro-5H-benzo[7]annulene-6-carboxylate (**2g**, 42.7 mg, 0.20 mmol, 1.0 equiv), K₂CO₃ (30.5 mg, 0.22 mmol, 1.1 equiv), DMF (2 mL), and hypervalent iodine reagent **1a** (62.9 mg, 0.24 mmol, 1.2 equiv) was conducted at 50 °C for 4 h. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 90:10) gave the product as an orange viscous liquid (30.6 mg, 67% yield).

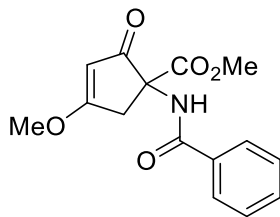
¹H NMR: (400 MHz, CDCl₃) δ 7.47–7.38 (m, 2H), 7.30 (ddd, *J* = 7.6, 7.6, 0.8 Hz, 1H), 7.16 (dd, *J* = 7.6, 0.8 Hz, 1H), 3.67 (s, 3H), 3.00 (ddd, *J* = 14.8, 9.6, 5.2 Hz, 1H), 2.85 (ddd, *J* = 14.8, 5.2, 5.2 Hz, 1H), 2.38–2.28 (m, 1H), 2.10–1.76 (m, 5H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 206.2, 173.8, 138.9, 138.5, 131.8, 129.0, 128.5, 126.6, 68.5, 52.7, 33.2, 32.4, 21.9; IR: (ATR) 3377, 3316, 2951, 2866, 1740, 1684, 1213, 964, 764, 741 cm⁻¹; HRMS (DART) *m/z*: [M+H]⁺ Calculated for C₁₃H₁₆NO₃ 234.1125; Found 234.1126

ethyl 1-benzamido-2-oxocyclopentane-1-carboxylate (10)

A reaction flask charged with a magnetic stirring bar was flame-dried under vacuum. After cooling down to room temperature, ethyl 2-oxocyclopentane-1-carboxylate (**2h**, 32.0 mg, 0.20 mmol, 1.0 equiv), Cs₂CO₃ (73.0 mg, 0.22 mmol, 1.1 equiv), and DMF (2 mL) were added. The mixture was stirred at room temperature for 30 min, and hypervalent iodine reagent **1a** (63.8 mg, 0.24 mmol, 1.2 equiv) was added. Then, the flask was placed in an aluminum block, which was preheated at 50 °C. After the mixture was stirred at 50 °C for 4 h, sat. NaHCO₃ aq. was added, and the mixture was extracted with AcOEt (2 × 15 mL). The organic solution was washed three times with brine. The combined organic layers were dried over Na₂SO₄, filtrated, and concentrated under reduced pressure. To the residue, CHCl₃ (2 mL), benzoyl chloride (37.0 mg, 0.26 mmol, 1.3 equiv), and triethylamine (61.0 mg, 0.60 mmol, 3.0 equiv) were added, and the mixture was stirred at room temperature for 12 h. Sat. NaHCO₃ aq. was added to the reaction mixture, and the mixture was extracted with CHCl₃ (3 × 15 mL). The combined organic layers were dried over Na₂SO₄, filtrated, and concentrated under reduced pressure to give the crude product. Purification by flash column chromatography on silica gel (hexane/EtOAc = 80:20) gave the product as a colorless oil (25.0 mg, 45% yield).

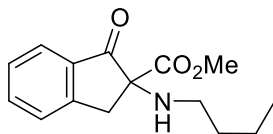
¹H NMR: (400 MHz, CDCl₃) δ 7.83–7.78 (m, 2H), 7.56–7.50 (m, 1H), 7.50–7.41 (m, 3H), 4.36–4.22 (m, 2H), 2.86 (dt, *J* = 19.2, 9.6 Hz, 1H), 2.74–2.63 (m, 1H), 2.62–2.47 (m, 2H), 2.34–2.13 (m, 2H), 1.30 (dd, *J* = 7.2, 7.2 Hz, 3H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 210.5, 169.8, 165.9, 132.9, 132.0, 128.6, 127.1, 67.5, 62.9, 36.7, 34.0, 19.2, 13.9

The analytical data for this compound was in excellent agreement with the reported data.⁷³⁾

methyl 1-benzamido-4-methoxy-2-oxocyclopent-3-ene-1-carboxylate (11)

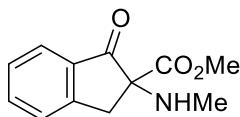
A reaction flask charged with a magnetic stirring bar was flame-dried under vacuum. After cooling down to room temperature, methyl 4-methoxy-2-oxocyclopent-3-ene-1-carboxylate (**2i**, 34.3 mg, 0.20 mmol, 1.0 equiv), Cs₂CO₃ (72.0 mg, 0.22 mmol, 1.1 equiv), and DMF (2 mL) were added. The mixture was stirred at room temperature for 30 min, and hypervalent iodine reagent **1a** (63.8 mg, 0.24 mmol, 1.2 equiv) was added. Then, the flask was placed in an aluminum block, which was preheated at 50 °C. After the mixture was stirred at 50 °C for 4 h, sat. NaHCO₃ aq. was added, and the mixture was extracted with AcOEt (2 × 15 mL). The organic solution was washed three times with brine. The combined organic layers were dried over Na₂SO₄, filtrated, and concentrated under reduced pressure. To the residue, CHCl₃ (2 mL), benzoyl chloride (36.4 mg, 0.26 mmol, 1.3 equiv), and triethylamine (60.6 mg, 0.60 mmol, 3.0 equiv) were added, and the mixture was stirred at room temperature for 12 h. Sat. NaHCO₃ aq. was added to the reaction mixture, and the mixture was extracted with CHCl₃ (3 × 15 mL). The combined organic layers were dried over Na₂SO₄, filtrated, and concentrated under reduced pressure to give the crude product. Purification by flash column chromatography on silica gel (hexane/EtOAc = 60:40) gave the product as a white solid (27.4 mg, 48% yield).

mp: 162.8–164.3 °C; ¹H NMR: (400 MHz, CDCl₃) δ 7.87–7.79 (m, 2H), 7.57–7.50 (m, 1H), 7.49–7.41 (m, 2H), 7.31 (brs, 1H), 5.44 (s, 1H), 3.97 (s, 3H), 3.78 (s, 3H), 3.51 (dd, *J* = 17.6, 0.8 Hz, 1H), 3.10 (dd, *J* = 17.6, 1.2 Hz, 1H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 196.5, 190.8, 168.9, 167.4, 133.0, 132.1, 128.6, 127.2, 101.2, 67.3, 59.2, 53.7, 40.4; IR: (ATR) 3300, 1742, 1715, 1636, 1587, 1578, 1531, 1487, 1412, 1368, 1314, 1252, 1180, 1165, 995, 843, 721 cm⁻¹; HRMS (CI) *m/z*: [M+H]⁺ Calculated for C₁₅H₁₆NO₅ 290.1023; Found 290.1023

methyl 2-(butylamino)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (13)

According to the general procedure **I**, the reaction using methyl 1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**2a**, 38.1 mg, 0.20 mmol, 1.0 equiv), K₂CO₃ (31.5 mg, 0.23 mmol, 1.1 equiv), DMF (2 mL), and hypervalent iodine reagent **1b** (77.0 mg, 0.24 mmol, 1.2 equiv) was conducted at room temperature for 2 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 80:20) gave the product as an orange viscous liquid (46.0 mg, 88% yield).

¹H NMR: (400 MHz, CDCl₃) δ 7.77 (d, *J* = 7.6 Hz, 1H), 7.64 (ddd, *J* = 7.6, 7.6, 0.8 Hz, 1H), 7.50 (d, *J* = 7.6 Hz, 1H), 7.40 (dd, *J* = 7.6, 7.6 Hz, 1H), 3.77 (d, *J* = 17.2 Hz, 1H), 3.70 (s, 3H), 3.19 (d, *J* = 17.2 Hz, 1H), 2.60–2.48 (m, 3H), 1.53–1.46 (m, 2H), 1.40–1.31 (m, 2H), 0.90 (t, *J* = 7.2 Hz, 3H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 201.5, 171.1, 153.0, 135.8, 134.2, 127.9, 126.4, 125.0, 72.9, 52.9, 44.0, 36.9, 32.6, 20.3, 13.9; IR: (ATR) 2955, 2930, 2860, 1744, 1713, 1198, 750 cm⁻¹; HRMS (CI) *m/z*: [M+H]⁺ Calculated for C₁₅H₂₀NO₃ 262.1438; Found 262.1434

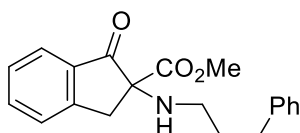
methyl 2-(methylamino)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (14)

According to the general procedure **I**, the reaction using methyl 1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**2a**, 38.0 mg, 0.20 mmol, 1.0 equiv), K₂CO₃ (30.5 mg, 0.22 mmol, 1.1 equiv), DMF (2 mL), and hypervalent iodine reagent **1c** (67.2 mg, 0.25 mmol, 1.2 equiv) was conducted at room temperature for 4 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 60:40) gave the product as an orange viscous liquid (26.7 mg, 61% yield).

¹H NMR: (400 MHz, CDCl₃) δ 7.77 (d, *J* = 7.6 Hz, 1H), 7.64 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.51 (d, *J* = 7.6 Hz, 1H), 7.41 (dd, *J* = 7.6, 7.6 Hz, 1H), 3.74 (d, *J* = 17.2 Hz, 1H), 3.70 (s, 3H), 3.20 (d, *J* = 17.2 Hz, 1H), 2.40 (s, 3H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 201.4, 171.0, 152.9, 135.8, 134.3, 127.9, 126.5,

125.0, 73.1, 52.9, 36.4, 30.9; IR: (ATR) 3341, 2953, 2884, 2805, 1742, 1709, 1209, 1196, 1169, 1152, 1028, 914, 748, 708 cm^{-1} ; HRMS (CI) m/z : $[\text{M}+\text{H}]^+$ Calculated for $\text{C}_{12}\text{H}_{14}\text{NO}_3$ 220.0968; Found 220.0973

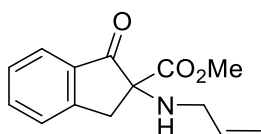
methyl 1-oxo-2-((3-phenylpropyl)amino)-2,3-dihydro-1*H*-indene-2-carboxylate (15)



According to the general procedure **I**, the reaction using methyl 1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**2a**, 37.7 mg, 0.20 mmol, 1.0 equiv), K_2CO_3 (31.8 mg, 0.23 mmol, 1.1 equiv), DMF (2 mL), and hypervalent iodine reagent **1d** (92.0 mg, 0.24 mmol, 1.2 equiv) was conducted at room temperature for 4 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 80:20) gave the product as an orange viscous liquid (59.4 mg, 93% yield).

^1H NMR: (400 MHz, CDCl_3) δ 7.77 (d, J = 7.6 Hz, 1H), 7.64 (ddd, J = 7.6, 7.6, 1.2 Hz, 1H), 7.49 (dd, J = 7.6, 0.8 Hz, 1H), 7.40 (dd, J = 7.6, 7.6 Hz, 1H), 7.32–7.22 (m, 2H), 7.20–7.12 (m, 3H), 3.75 (d, J = 16.8 Hz, 1H), 3.68 (s, 3H), 3.15 (d, J = 16.8 Hz, 1H), 2.73–2.44 (m, 5H), 1.92–1.78 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 201.3, 171.1, 153.0, 141.8, 135.8, 134.2, 128.4, 128.3, 127.9, 126.4, 125.8, 125.0, 72.9, 52.9, 43.8, 37.0, 33.3, 32.1; IR: (ATR) 3024, 2949, 2934, 2857, 1742, 1713, 1196, 1177, 746 cm^{-1} ; HRMS (CI) m/z : $[\text{M}+\text{H}]^+$ Calculated for $\text{C}_{20}\text{H}_{22}\text{NO}_3$ 324.1594; Found 324.1590

methyl 2-(allylamino)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (16)

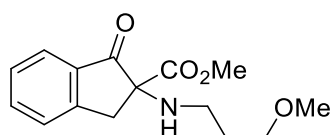


According to the general procedure **I**, the reaction using methyl 1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**2a**, 37.6 mg, 0.20 mmol, 1.0 equiv), K_2CO_3 (32.0 mg, 0.23 mmol, 1.1 equiv), DMF (2 mL), and hypervalent iodine reagent **1e** (73.9 mg, 0.24 mmol, 1.2 equiv) was conducted at room temperature for 4 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 80:20) gave the

product as an orange viscous liquid (18.4 mg, 38% yield).

^1H NMR: (400 MHz, CDCl_3) δ 7.78 (d, $J = 7.6$ Hz, 1H), 7.65 (ddd, $J = 7.6, 7.6, 1.2$ Hz, 1H), 7.50 (d, $J = 7.6$, 1H), 7.41 (dd, $J = 7.6, 7.6$ Hz, 1H), 5.90 (dddd, $J = 17.2, 10.4, 6.0, 6.0$ Hz, 1H), 5.21 (dd, $J = 17.2, 1.6$ Hz, 1H), 5.09 (dd, $J = 10.4, 1.6$ Hz, 1H), 3.78 (d, $J = 17.2$ Hz, 1H), 3.71 (s, 3H), 3.31–3.17 (m, 3H), 2.63 (br, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 201.1, 171.0, 152.9, 136.0, 135.9, 134.2, 127.9, 126.4, 125.0, 116.5, 72.6, 52.9, 47.2, 37.1; IR: (ATR) 2953, 2845, 2158, 1742, 1713, 1198, 748 cm^{-1} ; HRMS (CI) m/z : $[\text{M}+\text{H}]^+$ Calculated for $\text{C}_{14}\text{H}_{16}\text{NO}_3$ 246.1125; Found 246.1123

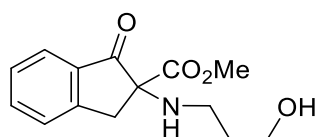
methyl 2-((3-methoxypropyl)amino)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (17)



According to the general procedure **I**, the reaction using methyl 1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**2a**, 57.5 mg, 0.30 mmol, 1.0 equiv), K_2CO_3 (45.7 mg, 0.33 mmol, 1.0 equiv), DMF (3 mL), and hypervalent iodine reagent **1f** (167.4 mg, 0.60 mmol, 2.0 equiv) was conducted at 80 $^\circ\text{C}$ for 30 min. Purification by flash column chromatography on silica gel (hexane/EtOAc = 60:40) gave the product as an orange viscous liquid (41.7 mg, 63% yield).

^1H NMR: (400 MHz, CDCl_3) δ 7.77 (d, $J = 7.6$ Hz, 1H), 7.64 (ddd, $J = 7.6, 7.6, 0.8$ Hz, 1H), 7.50 (d, $J = 7.6$ Hz, 1H), 7.40 (dd, $J = 7.6, 7.6$ Hz, 1H), 3.76 (d, $J = 16.8$ Hz, 1H), 3.70 (s, 3H), 3.45 (t, $J = 6.0$ Hz, 2H), 3.31 (s, 3H), 3.19 (d, $J = 16.8$ Hz, 1H), 2.74–2.65 (m, 1H), 2.65–2.50 (m, 1H), 1.77 (ddt, $J = 6.4, 6.4, 6.4$ Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 201.4, 171.1, 153.1, 135.8, 134.3, 127.9, 126.5, 125.0, 72.9, 70.7, 58.6, 52.9, 41.6, 37.0, 30.5; IR: (ATR) 2951, 2926, 2870, 1743, 1713, 1196, 1113, 750 cm^{-1} ; HRMS (CI) m/z : $[\text{M}+\text{H}]^+$ Calculated for $\text{C}_{15}\text{H}_{20}\text{NO}_4$ 278.1387; Found 278.1394

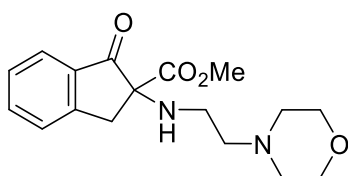
methyl 2-((3-hydroxypropyl)amino)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (18)



According to the general procedure **I**, the reaction using methyl 1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**2a**, 57.1 mg, 0.30 mmol, 1.0 equiv), K₂CO₃ (45.4 mg, 0.33 mmol, 1.1 equiv), DMF (3 mL), and hypervalent iodine reagent **1g** (158.1 mg, 0.60 mmol, 2.0 equiv) was conducted at 80 °C for 30 min. Purification by flash column chromatography on silica gel (hexane/EtOAc = 20:80) gave the product as an orange viscous liquid (30.6 mg, 50% yield).

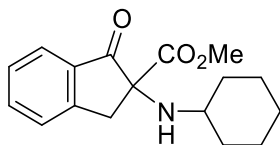
¹H NMR: (400 MHz, CDCl₃) δ 7.78 (d, *J* = 7.6 Hz, 1H), 7.66 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.51 (d, *J* = 7.6 Hz, 1H), 7.42 (dd, *J* = 7.6, 7.6 Hz, 1H), 3.85–3.74 (m, 3H), 3.70 (s, 3H), 3.22 (d, *J* = 17.2 Hz, 1H), 2.85 (dt, *J* = 12.0, 6.0 Hz, 1H), 2.74 (dt, *J* = 12.0, 6.0 Hz, 1H), 1.75 (ddt, *J* = 6.0, 6.0, 6.0 Hz, 2H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 200.7, 170.8, 152.8, 136.0, 134.1, 128.1, 126.5, 125.1, 72.6, 62.9, 53.0, 43.3, 37.2, 31.9; IR: (ATR) 3308, 2951, 2932, 2868, 1742, 1709, 1198, 1038, 750, 712 cm⁻¹; HRMS (CI) *m/z*: [M+H]⁺ Calculated for C₁₄H₁₈NO₄ 264.1230; Found 264.1233

methyl 2-((2-morpholinoethyl)amino)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (19**)**



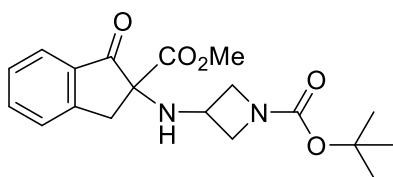
According to the general procedure **I**, the reaction using methyl 1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**2a**, 38.2 mg, 0.20 mmol, 1.0 equiv), K₂CO₃ (27.9 mg, 0.20 mmol, 1.0 equiv), DMF (2 mL), and hypervalent iodine reagent **1h** (112.9 mg, 0.30 mmol, 1.5 equiv) was conducted at 80 °C for 30 min. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 80:20) gave the product as an orange viscous liquid (28.2 mg, 44% yield).

¹H NMR: (400 MHz, CDCl₃) δ 7.78 (d, *J* = 7.6 Hz, 1H), 7.65 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.50 (d, *J* = 7.6 Hz, 1H), 7.41 (dd, *J* = 7.6, 7.6 Hz, 1H), 3.80–3.70 (m, 5H), 3.69 (s, 3H), 3.22 (d, *J* = 16.8 Hz, 1H), 2.74 (dt, *J* = 11.2, 5.6 Hz, 1H), 2.63 (dt, *J* = 11.2, 5.6 Hz, 1H), 2.56–2.40 (m, 6H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 201.4, 171.2, 152.8, 135.8, 134.3, 127.9, 126.4, 125.0, 72.2, 67.0, 58.1, 53.4, 52.8, 40.2, 37.3; IR: (ATR) 2953, 2855, 2810, 1742, 1713, 1202, 1115, 748 cm⁻¹; HRMS (EI) *m/z*: [M]⁺ Calculated for C₁₇H₂₂N₂O₄ 318.1574; Found 318.1587

methyl 2-(cyclohexylamino)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (20)

According to the general procedure **I**: the reaction using methyl 1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**2a**, 37.4 mg, 0.20 mmol, 1.0 equiv), K₂CO₃ (30.5 mg, 0.22 mmol, 1.1 equiv), DMF (2 mL), and hypervalent iodine reagent **1i** (138.8 mg, 0.40 mmol, 2.0 equiv) was conducted at 80 °C for 30 min. Purification by flash column chromatography on silica gel (hexane/EtOAc = 80:20) gave the product as an orange viscous liquid (19.1 mg, 34% yield).

¹H NMR: (400 MHz, CDCl₃) δ 7.77 (d, *J* = 7.6 Hz, 1H), 7.64 (ddd, *J* = 7.6, 7.6, 1.2 Hz, 1H), 7.49 (d, *J* = 7.6 Hz, 1H), 7.39 (dd, *J* = 7.6, 7.6 Hz, 1H), 3.85 (d, *J* = 17.2 Hz, 1H), 3.68 (s, 3H), 3.22 (d, *J* = 17.2 Hz, 1H), 2.57–2.45 (m, 1H), 1.88–1.76 (m, 2H), 1.76–1.63 (m, 2H), 1.60–1.52 (m, 1H), 1.29–1.05 (m, 5H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 201.3, 171.6, 152.9, 135.8, 134.0, 127.8, 126.4, 125.0, 73.0, 53.9, 52.9, 38.4, 35.3, 35.1, 25.6, 25.3, 25.2; IR: (ATR) 2926, 2853, 1744, 1715, 1211, 1196 cm⁻¹; HRMS (EI) *m/z*: [M]⁺ Calculated for C₁₇H₂₁NO₃ 287.1516; Found 287.1514

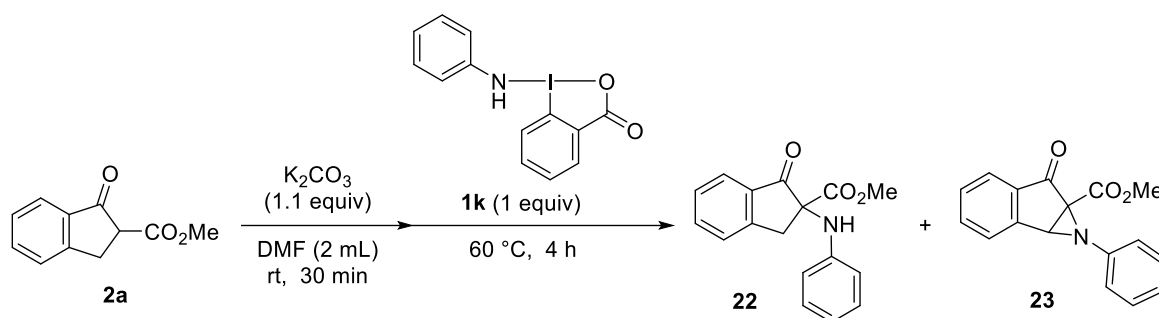
***tert*-butyl 3-((2-(methoxycarbonyl)-1-oxo-2,3-dihydro-1*H*-inden-2-yl)amino)azetidine-1-carboxylate (21)**

According to the general procedure **I**, the reaction using methyl 1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**2a**, 37.9 mg, 0.20 mmol, 1.0 equiv), K₂CO₃ (30.8 mg, 0.22 mmol, 1.1 equiv), DMF (2 mL), and hypervalent iodine reagent **1j** (101.6 mg, 0.24 mmol, 1.2 equiv) was conducted at 50 °C for 4 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 70:30) gave the product as a pale yellow solid (52.7 mg, 73% yield).

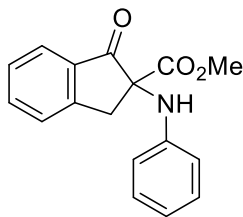
mp: 111.7–115.0 °C; ¹H NMR: (400 MHz, CDCl₃) δ 7.78 (d, *J* = 7.6 Hz, 1H), 7.67 (dd, *J* = 7.6, 7.6 Hz,

1H), 7.50 (d, $J = 7.6$ Hz, 1H), 7.43 (dd, $J = 7.6, 7.6$ Hz, 1H), 4.09 (dd, $J = 7.6, 7.6$ Hz, 1H), 4.00 (dd, $J = 7.6, 7.6$ Hz, 1H), 3.77–3.61 (m, 4H), 3.69 (s, 3H), 3.08 (d, $J = 17.2$ Hz, 1H), 1.41 (s, 9H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 201.0, 171.3, 156.2, 152.3, 136.0, 134.0, 128.1, 126.4, 125.1, 79.4, 71.5, 58.2, 53.0, 44.4, 38.1, 28.3; IR: (ATR) 2974, 2955, 2932, 2880, 1746, 1690, 1402, 1393, 1155, 1126, 752 cm^{-1} ; HRMS (CI) m/z : $[\text{M}]^-$ Calculated for $\text{C}_{19}\text{H}_{24}\text{N}_2\text{O}_5$ 360.1691; Found 360.1673

Aziridination of β -ketoesters: experimental procedure and product data



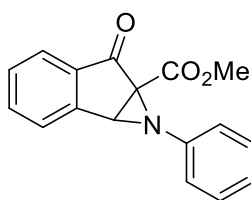
A reaction flask charged with a magnetic stirring bar was flame-dried under vacuum. After cooling down to room temperature, methyl 1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**2a**, 37.6 mg, 0.20 mmol, 1.0 equiv), K_2CO_3 (31.2 mg, 0.23 mmol, 1.1 equiv), and DMF (2 mL) were added. The mixture was stirred at room temperature for 30 min, and $\text{PhI}(\text{OAc})_2$ (66.1 mg, 0.21 mmol, 1.0 equiv) and hypervalent iodine reagent **1k** (68.3 mg, 0.20 mmol, 1.0 equiv) were added. Then, the flask was placed in an aluminum block, which was preheated at 60 °C. After the mixture was stirred at 60 °C for 4 h, sat. NaHCO_3 aq. was added, and the mixture was extracted with AcOEt (2×15 mL). The organic solution was washed three times with brine. The combined organic layers were dried over Na_2SO_4 , filtrated, and concentrated under reduced pressure to give the crude product, which was analyzed by ^1H NMR spectroscopy using 1,1,2,2-tetrachloroethane as an internal standard (**22**: 3%, **23**: 64%). Purification by flash column chromatography on silica gel (hexane/ $\text{EtOAc} = 80:20$) gave the product **23** as an orange solid (35.3 mg, 64% yield). Recrystallization of **23** from hexane/ CHCl_3 gave single crystals suitable for X-ray analysis.

methyl 1-oxo-2-(phenylamino)-2,3-dihydro-1*H*-indene-2-carboxylate (22)

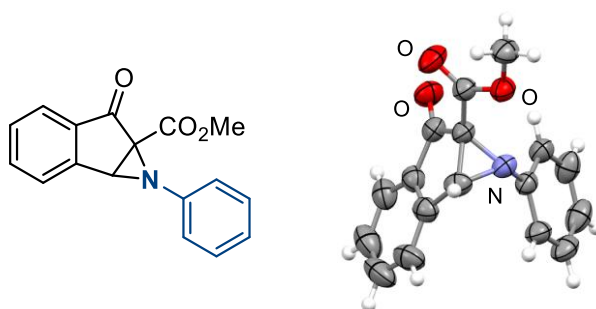
The title compound was synthesized and isolated as described below.

A reaction flask charged with a magnetic stirring bar was flame-dried under vacuum. After cooling down to room temperature, methyl 1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**2a**, 95.0 mg, 0.5 mmol, 1.0 equiv), K₂CO₃ (75.6 mg, 0.55 mmol, 1.1 equiv), and MeCN (5 mL) were added. The mixture was stirred at room temperature for 30 min, and hypervalent iodine reagent **1k** (190.0 mg, 0.56 mmol, 1.1 equiv) was added. Then, the flask was placed in an aluminum block, which was preheated at 60 °C. After the mixture was stirred at 60 °C for 4 h, sat. NaHCO₃ aq. was added, and the mixture was extracted with CHCl₃ (3 × 20 mL). The combined organic layers were dried over Na₂SO₄, filtrated, and concentrated under reduced pressure to give the crude product. Purification by flash column chromatography on silica gel (hexane/EtOAc = 90:10) gave the product as a yellow viscous oil (5.6 mg, 4% yield).

¹H NMR: (400 MHz, CDCl₃) δ 7.85 (d, *J* = 7.6 Hz, 1H), 7.71 (ddd, *J* = 7.6, 7.6, 1.2 Hz, 1H), 7.55 (d, *J* = 7.6 Hz, 1H), 7.46 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.20–7.13 (m, 2H), 6.82–6.75 (m, 1H), 6.59–6.53 (m, 2H), 5.14 (brs, 1H), 4.12 (d, *J* = 16.8 Hz, 1H), 3.63 (s, 3H), 3.43 (d, *J* = 16.8 Hz, 1H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 199.4, 170.3, 152.8, 144.8, 136.4, 133.4, 129.3, 128.2, 126.6, 125.4, 118.9, 114.2, 70.8, 53.5, 38.6; HRMS (CI) *m/z*: [M+H]⁺ Calculated for C₁₇H₁₆NO₃ 282.1125; Found 282.1140

methyl 6-oxo-1-phenyl-1a,6-dihydroindeno[1,2-*b*]azirine-6a(1*H*)-carboxylate (23)

mp: 101.6–105.3 °C; ^1H NMR: (400 MHz, CDCl_3) δ 7.63 (d, $J = 7.6$ Hz, 1H), 7.53 (dd, $J = 7.6$, 7.6 Hz, 1H), 7.44 (d, $J = 7.6$ Hz, 1H), 7.29–7.21 (m, 1H), 7.01 (dd, $J = 7.6$, 7.6 Hz, 2H), 6.81 (t, $J = 7.6$ Hz, 1H), 6.69 (d, $J = 7.6$ Hz, 2H), 4.58 (s, 1H), 3.95 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 191.8, 166.5, 143.8, 143.2, 134.8, 134.7, 129.4, 128.7, 127.1, 124.9, 123.2, 120.5, 53.1, 53.0, 50.3; IR: (ATR) 3393, 2961, 2922, 2853, 1740, 1709, 1593, 1491, 1439, 1364, 1302, 1283, 1254, 1196, 1134, 962, 928, 783, 758 cm^{-1} ; HRMS (CI) m/z : $[\text{M}+\text{H}]^+$ Calculated for $\text{C}_{17}\text{H}_{14}\text{NO}_3$ 280.0968; Found 280.0969



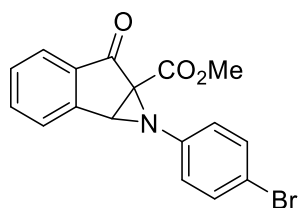
The structure of **23** was determined by X-ray structural analysis. CCDC 2498274 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

CCDC number	2498274
Empirical formula	$\text{C}_{17}\text{H}_{13}\text{NO}_3$
Formula weight	279.28
Temperature/K	293
Crystal system	monoclinic
Space group	$\text{P2}_1/\text{n}$
$a/\text{\AA}$	9.0663(2)
$b/\text{\AA}$	5.95630(10)
$c/\text{\AA}$	26.0085(7)
$\alpha/^\circ$	90
$\beta/^\circ$	90.642(2)
$\gamma/^\circ$	90
Volume/ $\text{\AA}^3$	1404.41(5)
Z	4
$\rho_{\text{calc}}/\text{g cm}^{-3}$	1.321

μ/mm^{-1}	0.747
F(000)	584.0
Crystal size/ mm^3	$0.2 \times 0.2 \times 0.1$
Radiation	Cu K α ($\lambda = 1.54184$)
2Θ range for data collection/ $^\circ$	6.798 to 150.278
Index ranges	$-11 \leq h \leq 11, -6 \leq k \leq 7, -32 \leq l \leq 31$
Reflections collected	14657
Independent reflections	2857 [$R_{\text{int}} = 0.0345, R_{\text{sigma}} = 0.0311$]
Data/restraints/parameters	2857/0/191
Goodness-of-fit on F^2	1.094
Final R indexes [$I \geq 2\sigma(I)$]	$R_1 = 0.0407, wR_2 = 0.1154$
Final R indexes [all data]	$R_1 = 0.0457, wR_2 = 0.1192$
Largest diff. peak/hole / $e \text{ \AA}^{-3}$	0.18/-0.15

General procedure III: A reaction flask charged with a magnetic stirring bar was flame-dried under vacuum. After cooling down to room temperature, β -ketoester **2** (0.20–0.40 mmol, 1.0 equiv), K_2CO_3 (0.22–0.44 mmol, 1.1 equiv), and DMF (2–4 mL) were added. The mixture was stirred at room temperature for 30 min, and $\text{PhI}(\text{OAc})_2$ (0.2–0.4 mmol, 1.0 equiv) and hypervalent iodine reagent **1** (0.20–0.40 mmol, 1.0 equiv) were added. Then, the flask was placed in an aluminum block, which was preheated at 60 $^\circ\text{C}$. After the mixture was stirred at 60 $^\circ\text{C}$ for 4 h, sat. NaHCO_3 aq. was added, and the mixture was extracted with AcOEt (2×15 mL). The organic solution was washed three times with brine. The combined organic layers were dried over Na_2SO_4 , filtrated, and concentrated under reduced pressure to give the crude product. Purification by flash column chromatography on silica gel (hexane/ EtOAc) gave the product.

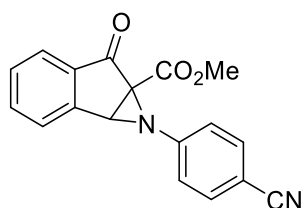
methyl 1-(4-bromophenyl)-6-oxo-1a,6-dihydroindeno[1,2-*b*]azirine-6a(1*H*)-carboxylate (24**)**



According to the general procedure **III**, the reaction using methyl 1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**2a**, 76.1 mg, 0.40 mmol, 1.0 equiv), K₂CO₃ (63.1 mg, 0.46 mmol, 1.1 equiv), DMF (4 mL), PhI(OAc)₂ (129.0 mg, 0.40 mmol, 1.0 equiv), and hypervalent iodine reagent **II** (169.0 mg, 0.40 mmol, 1.0 equiv) was conducted. Purification by flash column chromatography on silica gel (hexane/EtOAc = 90:10) gave the product as an orange viscous liquid (88.7 mg, 61% yield).

¹H NMR: (400 MHz, CDCl₃) δ 7.62 (d, *J* = 7.6 Hz, 1H), 7.54 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.47 (d, *J* = 7.6 Hz, 1H), 7.29 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.12 (d, *J* = 8.0 Hz, 2H), 6.57 (d, *J* = 8.0 Hz, 2H), 4.56 (s, 1H), 3.94 (s, 3H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 191.4, 166.2, 143.1, 142.9, 135.0, 134.7, 131.7, 129.8, 127.1, 125.2, 122.1, 116.1, 53.2, 53.1, 50.1; IR: (ATR) 3030, 2953, 2158, 1744, 1721, 1483, 1287, 1240, 1134, 1007, 826, 766, 710 cm⁻¹; HRMS (CI) *m/z*: [M+H]⁺ Calculated for C₁₇H₁₃BrNO₃ 358.0073; Found 358.0089

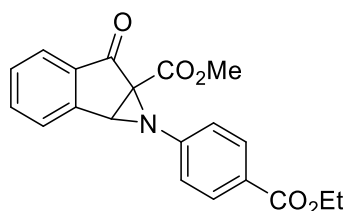
methyl 1-(4-cyanophenyl)-6-oxo-1a,6-dihydroindeno[1,2-*b*]azirine-6a(1*H*)-carboxylate (25**)**



According to the general procedure **III**, the reaction using methyl 1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**2a**, 37.5 mg, 0.20 mmol, 1.0 equiv), K₂CO₃ (30.6 mg, 0.22 mmol, 1.1 equiv), DMF (2 mL), PhI(OAc)₂ (65.3 mg, 0.20 mmol, 1.0 equiv), and hypervalent iodine reagent **1m** (73.7 mg, 0.20 mmol, 1.0 equiv) was conducted. Purification by flash column chromatography on silica gel (hexane/EtOAc = 80:20) gave the product as an orange viscous liquid (48.7 mg, 81% yield).

¹H NMR: (400 MHz, CDCl₃) δ 7.66 (d, *J* = 7.6 Hz, 1H), 7.57 (ddd, *J* = 7.6, 7.6, 1.2 Hz, 1H), 7.49 (d, *J* = 7.6 Hz, 1H), 7.37–7.28 (m, 3H), 6.76 (d, *J* = 8.4 Hz, 2H), 4.62 (s, 1H), 3.96 (s, 3H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 190.8, 165.7, 148.4, 142.7, 135.2, 134.0, 132.9, 130.0, 127.2, 125.5, 121.0, 118.6, 106.7, 53.3, 53.0, 49.9; IR: (ATR) 3019, 2955, 2224, 1746, 1724, 1601, 1501, 1294, 1281, 1242, 1134, 750, 731 cm⁻¹; HRMS (CI) *m/z*: [M+H]⁺ Calculated for C₁₈H₁₃N₂O₃ 305.0921; Found 305.0920

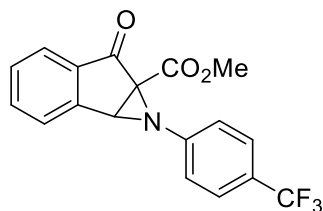
methyl 1-(4-(ethoxycarbonyl)phenyl)-6-oxo-1a,6-dihydroindeno[1,2-*b*]azirine-6a(1*H*)-carboxylate (26)



According to the general procedure **III**, the reaction using methyl 1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**2a**, 38.0 mg, 0.20 mmol, 1.0 equiv), K₂CO₃ (32.4 mg, 0.23 mmol, 1.1 equiv), DMF (2 mL), PhI(OAc)₂ (67.0 mg, 0.21 mmol, 1.0 equiv), and hypervalent iodine reagent **1n** (83.5 mg, 0.20 mmol, 1.0 equiv) was conducted. Purification by flash column chromatography on silica gel (hexane/EtOAc = 80:20) gave the product as a pale yellow solid (56.4 mg, 80% yield).

mp: 145.1–146.4 °C; ¹H NMR: (400 MHz, CDCl₃) δ 7.71 (d, *J* = 8.8 Hz, 2H), 7.65 (d, *J* = 7.6 Hz, 1H), 7.54 (ddd, *J* = 7.6, 7.6, 1.2 Hz, 1H), 7.45 (d, *J* = 7.6 Hz, 1H), 7.30–7.23 (m, 1H), 6.73 (d, *J* = 8.8 Hz, 2H), 4.61 (s, 1H), 4.32–4.20 (m, 2H), 3.96 (s, 3H), 1.31 (t, *J* = 7.2 Hz, 3H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 191.1, 165.99, 165.97, 148.2, 142.9, 134.9, 134.3, 130.4, 129.7, 127.2, 125.4, 125.2, 120.1, 60.7, 53.2, 52.9, 50.0, 14.2; IR: (ATR) 2968, 1749, 1697, 1599, 1368, 1308, 1269, 1250, 1161, 1138, 1105, 1092, 970, 862, 789, 775, 762, 708 cm⁻¹; HRMS (CI) *m/z*: [M+H]⁺ Calculated for C₂₀H₁₈NO₅ 352.1179; Found 352.1186

methyl 6-oxo-1-(4-(trifluoromethyl)phenyl)-1a,6-dihydroindeno[1,2-*b*]azirine-6a(1*H*)-carboxylate (27)

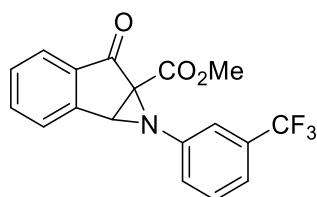


According to the general procedure **III**, the reaction using methyl 1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**2a**, 37.1 mg, 0.20 mmol, 1.0 equiv), K₂CO₃ (31.3 mg, 0.23 mmol, 1.1 equiv), DMF (2 mL),

PhI(OAc)₂ (65.9 mg, 0.20 mmol, 1.0 equiv), and hypervalent iodine reagent **1o** (83.5 mg, 0.21 mmol, 1.0 equiv) was conducted. Purification by flash column chromatography on silica gel (hexane/EtOAc = 80:20) gave the product as a pale yellow solid (43.4 mg, 64% yield).

mp: 150.6–154.6 °C; ¹H NMR: (400 MHz, CDCl₃) δ 7.66 (d, *J* = 7.6 Hz, 1H), 7.59 (ddd, *J* = 7.6, 7.6, 1.2 Hz, 1H), 7.47 (d, *J* = 7.6 Hz, 1H), 7.32–7.25 (m, 3H), 6.77 (d, *J* = 8.0 Hz, 2H), 4.61 (s, 1H), 3.96 (s, 3H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 191.2, 166.0, 147.2, 142.9, 135.1, 134.4, 129.9, 127.2, 126.0 (q, *J*_{CF} = 3.8 Hz), 125.4, 125.3 (q, *J*_{CF} = 32.5 Hz), 124.0 (q, *J*_{CF} = 270.3 Hz), 120.5, 53.3, 53.0, 50.0; ¹⁹F{¹H} NMR: (377 MHz, CDCl₃) δ –62.0; IR: (ATR) 3019, 2965, 2928, 2160, 1742, 1726, 1323, 1287, 1248, 1107, 1067, 860, 847 cm^{–1}; HRMS (CI) *m/z*: [M][–] Calculated for C₁₈H₁₂F₃NO₃ 347.0775; Found 347.0760

methyl 6-oxo-1-(3-(trifluoromethyl)phenyl)-1a,6-dihydroindeno[1,2-*b*]azirine-6a(1*H*)-carboxylate (28)

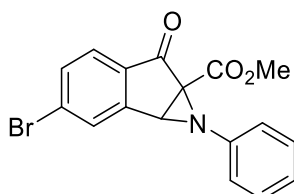


According to the general procedure **III**, the reaction using methyl 1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**2a**, 37.0 mg, 0.20 mmol, 1.0 equiv), K₂CO₃ (31.4 mg, 0.23 mmol, 1.1 equiv), DMF (2 mL), PhI(OAc)₂ (65.8 mg, 0.20 mmol, 1.0 equiv) and hypervalent iodine reagent **1p** (84.5 mg, 0.21 mmol, 1.0 equiv) was conducted. Purification by flash column chromatography on silica gel (hexane/EtOAc = 80:20) gave the product as a pale yellow solid (45.8 mg, 68% yield).

mp: 110.0–112.4 °C; ¹H NMR: (400 MHz, CDCl₃) δ 7.67 (d, *J* = 7.6 Hz, 1H), 7.56 (ddd, *J* = 7.6, 7.6, 1.2 Hz, 1H), 7.46 (d, *J* = 7.6 Hz, 1H), 7.31–7.24 (m, 1H), 7.15 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.07 (d, *J* = 8.0 Hz, 1H), 6.91 (d, *J* = 8.0 Hz, 1H), 6.87 (s, 1H), 4.61 (s, 1H), 3.96 (s, 3H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 191.1, 166.0, 144.6, 142.8, 135.0, 134.5, 131.1 (q, *J*_{CF} = 32.4 Hz), 129.8, 129.4, 127.2, 125.3, 123.9, 123.5 (q, *J*_{CF} = 271.1 Hz), 119.9 (q, *J*_{CF} = 3.8 Hz), 117.2 (q, *J*_{CF} = 3.8 Hz), 53.3, 53.1, 50.1;

$^{19}\text{F}\{^1\text{H}\}$ NMR: (377 MHz, CDCl_3) δ -66.1; IR: (ATR) 3067, 3044, 1722, 1321, 1256, 1182, 1146, 1117, 1098, 905, 754, 702 cm^{-1} ; HRMS (CI) m/z : $[\text{M}]^-$ Calculated for $\text{C}_{18}\text{H}_{12}\text{F}_3\text{NO}_3$ 347.0775; Found 347.0773

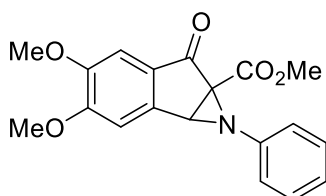
methyl 3-bromo-6-oxo-1-phenyl-1a,6-dihydroindeno[1,2-*b*]azirine-6a(1*H*)-carboxylate (29)



According to the general procedure **III**, the reaction using methyl 5-bromo-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**2k**, 53.6 mg, 0.20 mmol, 1.0 equiv), K_2CO_3 (30.4 mg, 0.22 mmol, 1.1 equiv), DMF (2 mL), $\text{PhI}(\text{OAc})_2$ (64.5 mg, 0.20 mmol, 1.0 equiv), and hypervalent iodine reagent **1k** (68.1 mg, 0.20 mmol, 1.0 equiv) was conducted. Purification by flash column chromatography on silica gel (hexane/EtOAc = 80:20) gave the product as a pale yellow solid (33.5 mg, 47% yield).

mp: 141.0–143.6 $^\circ\text{C}$; ^1H NMR: (400 MHz, CDCl_3) δ 7.79 (d, J = 1.6 Hz, 1H), 7.39 (dd, J = 8.0, 1.6 Hz, 1H), 7.29 (d, J = 8.0 Hz, 1H), 7.05 (dd, J = 7.6, 7.6 Hz, 2H), 6.85 (t, J = 7.6 Hz, 1H), 6.69 (d, J = 7.6 Hz, 2H), 4.54 (s, 1H), 3.94 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 190.6, 166.0, 144.8, 143.4, 133.6, 132.9, 130.4, 130.0, 128.9, 126.1, 123.5, 120.4, 53.2, 53.1, 49.5; IR: (ATR) 3040, 3003, 2951, 1742, 1717, 1593, 1491, 1275, 1238, 1144, 754, 731 cm^{-1} ; HRMS (CI) m/z : $[\text{M}]^-$ Calculated for $\text{C}_{17}\text{H}_{12}\text{BrNO}_3$ 357.0006; Found 356.9991

methyl 3,4-dimethoxy-6-oxo-1-phenyl-1a,6-dihydroindeno[1,2-*b*]azirine-6a(1*H*)-carboxylate (30)



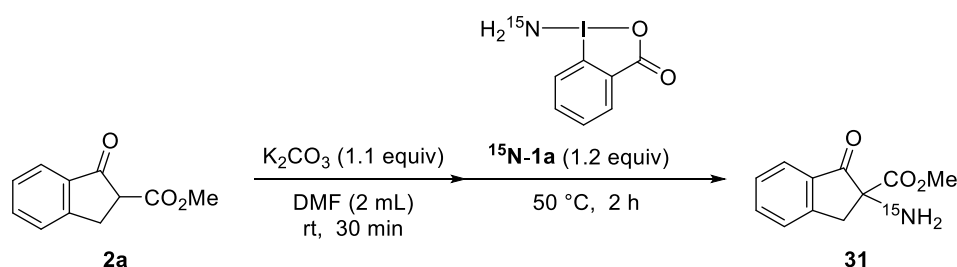
According to the general procedure **III**, the reaction using methyl 5,6-dimethoxy-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**2d**, 50.2 mg, 0.20 mmol, 1.0 equiv), K_2CO_3 (31.0 mg, 0.22 mmol, 1.1 equiv),

DMF (2 mL), $\text{PhI}(\text{OAc})_2$ (64.5 mg, 0.20 mmol, 1.0 equiv), and hypervalent iodine reagent **1k** (68.3 mg, 0.20 mmol, 1.0 equiv) was conducted. Purification by flash column chromatography on silica gel (hexane/EtOAc = 80:20) gave the product as a pale yellow solid (37.3 mg, 55% yield).

mp: 184.7 °C (decomposed); ^1H NMR: (400 MHz, CDCl_3) δ 7.08 (s, 1H), 7.03 (dd, $J = 7.2, 7.2$ Hz, 2H), 6.88 (s, 1H), 6.84 (t, $J = 7.2$ Hz, 1H), 6.71 (d, $J = 7.2$ Hz, 2H), 4.45 (s, 1H), 4.00 (s, 3H), 3.93 (s, 3H), 3.75 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 190.9, 166.7, 154.9, 150.1, 144.0, 138.7, 128.8, 127.7, 123.1, 120.5, 108.9, 105.9, 56.5, 56.0, 53.14, 53.09, 49.7; IR: (ATR) 3049, 3013, 2970, 2951, 2843, 1736, 1705, 1587, 1242, 1225, 1099, 764, 735, 700 cm^{-1} ; HRMS (CI) m/z : $[\text{M}]^-$ Calculated for $\text{C}_{19}\text{H}_{17}\text{NO}_5$ 339.1112; Found 339.1097

Synthesis of ^{15}N -labelled compounds

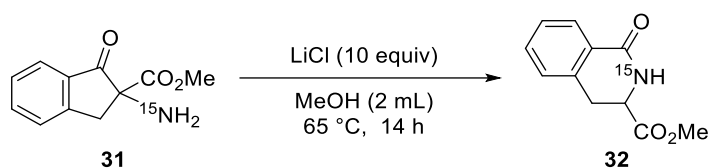
methyl 2-(amino- ^{15}N)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**31**)



A reaction flask charged with a magnetic stirring bar was flame-dried under vacuum. After cooling down to room temperature, methyl 1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**2a**, 57.6 mg, 0.30 mmol, 1.0 equiv), K_2CO_3 (46.0 mg, 0.33 mmol, 1.1 equiv), and DMF (3 mL) were added. The mixture was stirred at room temperature for 30 min, and hypervalent iodine reagent ^{15}N -**1a** (96.0 mg, 0.36 mmol, 1.2 equiv) was added. Then, the flask was placed in an aluminum block, which was preheated at 50 °C. After the mixture was stirred at 50 °C for 2 h, sat. NaHCO_3 aq. was added, and the mixture was extracted with AcOEt (3×15 mL). The organic solution was washed three times with brine. The combined organic layers were dried over Na_2SO_4 , filtrated, and concentrated under reduced pressure to give the crude product. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 70:30) gave the product as a colorless oil (47.9 mg, 77% yield).

^1H NMR: (400 MHz, CDCl_3) δ 7.84–7.78 (m, 1H), 7.66 (ddd, $J = 7.6, 7.6, 1.2$ Hz, 1H), 7.52–7.47 (m, 1H), 7.47–7.39 (m, 1H), 3.76–3.66 (m, 1H), 3.69 (s, 3H), 3.09 (dd, $J = 17.2, 3.2$ Hz, 1H), 2.13 (br, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 202.1, 172.9, 152.4, 135.8, 133.9, 128.0, 126.5, 125.3, 67.0 (d, $J_{\text{CN}} = 4.3$ Hz), 53.0, 41.2 (d, $J_{\text{CN}} = 4.3$ Hz); $^{15}\text{N}\{^1\text{H}\}$ NMR: (41 MHz, CDCl_3) δ 36.9; IR: (ATR) 3364, 2953, 1740, 1709, 1607, 1587, 1464, 1433, 1242, 1198, 1180, 1051, 934, 897, 851 cm^{-1} ; HRMS (CI) m/z : $[\text{M}+\text{H}]^+$ Calculated for $\text{C}_{11}\text{H}_{12}^{15}\text{NO}_3$ 207.0782; Found 207.0786

methyl 1-oxo-1,2,3,4-tetrahydroisoquinoline-3-carboxylate- ^{15}N (32)

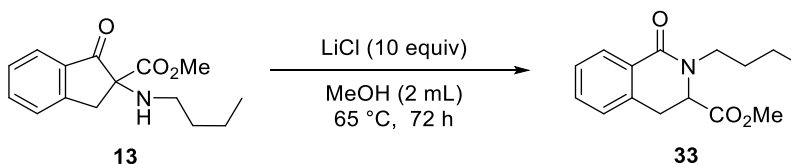


An oven-dried reaction vial containing a magnetic stir bar was charged with methyl 2-(amino- ^{15}N)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**31**, 41.2 mg, 0.20 mmol, 1.0 equiv), LiCl (86.0 mg, 2.0 mmol, 10 equiv), and MeOH (2 mL). Then, the vial was sealed and placed in an aluminum block, which was preheated at 65 °C. After the mixture was stirred at 65 °C for 14 h, water was added, and the mixture was extracted with CHCl_3 (3×15 mL). The combined organic layers were dried over Na_2SO_4 , filtrated, and concentrated under reduced pressure to give the crude product. Purification by flash column chromatography on NH silica gel (hexane/EtOAc = 50:50) gave the product as a white solid (36.7 mg, 89% yield).

mp: 112.5–113.2 °C; ^1H NMR: (400 MHz, CDCl_3) δ 8.08 (d, $J = 7.6$ Hz, 1H), 7.47 (ddd, $J = 7.6, 7.6, 1.6$ Hz, 1H), 7.38 (dd, $J = 7.6, 7.6$ Hz, 1H), 7.25 (d, $J = 7.6$ Hz, 1H), 6.63 (d, $J_{\text{NH}} = 90.8$ Hz, 1H), 4.42 (ddd, $J = 9.6, 5.2, 2.0$ Hz, 1H), 3.80 (s, 3H), 3.38–3.29 (m, 1H), 3.22 (ddd, $J = 15.6, 9.6, 2.0$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR: (100 MHz, CDCl_3) δ 170.8, 165.1 (d, $J_{\text{CN}} = 14.8$ Hz), 136.1, 132.5, 128.3 (d, $J_{\text{CN}} = 6.7$ Hz), 128.1, 127.6, 127.4, 53.0 (d, $J_{\text{CN}} = 10.4$ Hz), 52.9, 31.1; $^{15}\text{N}\{^1\text{H}\}$ NMR: (41 MHz, CDCl_3) δ 108.8; IR: (ATR) 3194, 3061, 2914, 1746, 1661, 1601, 1578, 1460, 1439, 1406, 1346, 1227, 1206, 1173, 1018, 837, 793 cm^{-1} ; HRMS (EI) m/z : $[\text{M}]^+$ Calculated for $\text{C}_{11}\text{H}_{11}^{15}\text{NO}_3$ 206.0704; Found 206.0716

Transformations of the α -aminated products

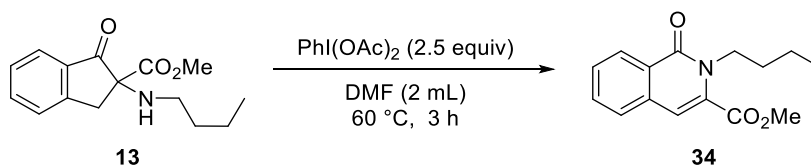
methyl 2-butyl-1-oxo-1,2,3,4-tetrahydroisoquinoline-3-carboxylate (**33**)



An oven-dried reaction vial containing a magnetic stir bar was charged with methyl 2-(butylamino)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**13**, 52.0 mg, 0.20 mmol, 1.0 equiv), LiCl (86.0 mg, 2.0 mmol, 10 equiv), and MeOH (2 mL). Then, the vial was sealed and placed in an aluminum block, which was preheated at 65 °C. After the mixture was stirred at 65 °C for 72 h, water was added, and the mixture was extracted with CHCl₃ (3 × 15 mL). The combined organic layers were dried over Na₂SO₄, filtrated, and concentrated under reduced pressure to give the crude product. Purification by flash column chromatography on silica gel (hexane/EtOAc = 80:20) gave the product as a white solid (45.9 mg, 88% yield).

mp: 77.3–79.0 °C; ¹H NMR: (400 MHz, CDCl₃) δ 8.08 (dd, J = 7.6, 1.2 Hz, 1H), 7.39 (ddd, J = 7.6, 7.6, 1.2 Hz, 1H), 7.37–7.30 (m, 1H), 7.14 (d, J = 7.6 Hz, 1H), 4.29 (dd, J = 6.8, 2.0 Hz, 1H), 4.20 (ddd, J = 15.2, 7.2, 7.2 Hz, 1H), 3.61 (s, 3H), 3.43 (dd, J = 16.0, 6.8 Hz, 1H), 3.27 (dd, J = 16.0, 2.0 Hz, 1H), 3.00–2.91 (m, 1H), 1.67–1.57 (m, 2H), 1.40 (ddq, J = 7.2, 7.2, 7.2 Hz, 2H), 0.96 (t, J = 7.2 Hz, 3H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) 171.6, 164.2, 134.6, 131.7, 129.1, 128.1, 127.4, 127.0, 58.4, 52.6, 47.1, 31.2, 30.1, 20.1, 13.8; IR: (ATR) 2953, 2893, 1740, 1643, 1609, 1468, 1449, 1422, 1225, 1192, 1173, 1117, 1016, 1101, 835, 733 cm⁻¹; HRMS (CI) m/z : [M+H]⁺ Calculated for C₁₅H₂₀NO₃ 262.1438; Found 262.1437

methyl 2-butyl-1-oxo-1,2-dihydroisoquinoline-3-carboxylate (**34**)



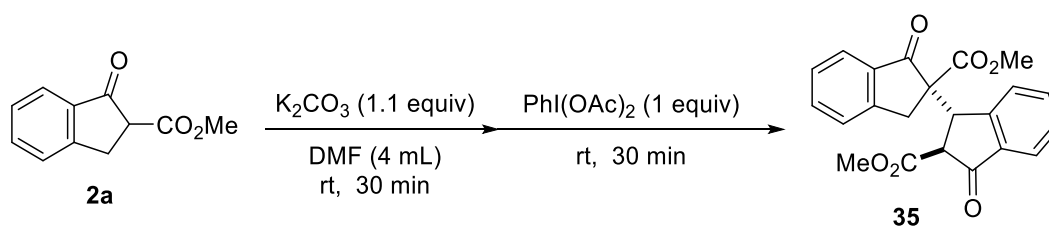
An oven-dried reaction flask containing a magnetic stir bar was charged with methyl 2-(butylamino)-1-

oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**13**, 44.2 mg, 0.17 mmol, 1.0 equiv), PhI(OAc)₂ (136.3 mg, 0.42 mmol, 2.5 equiv), and DMF (2 mL). Then, the vial was sealed and placed in an aluminum block, which was preheated at 60 °C. After the mixture was stirred at 60 °C for 3 h, sat. NaHCO₃ aq. was added, and the mixture was extracted with AcOEt (3 × 15 mL). The organic solution was washed three times with brine. The combined organic layers were dried over Na₂SO₄, filtrated, and concentrated under reduced pressure to give the crude product. Purification by flash column chromatography on silica gel (hexane/EtOAc = 90:10) gave the product as a colorless oil (30.5 mg, 70% yield).

¹H NMR: (400 MHz, CDCl₃) δ 8.48–8.41 (m, 1H), 7.71–7.63 (m, 1H), 7.62–7.55 (m, 2H), 7.20 (s, 1H), 4.39–4.31 (m, 2H), 3.95 (s, 3H), 1.78–1.68 (m, 2H), 1.39 (qt, *J* = 7.6, 7.6 Hz, 2H), 0.96 (t, *J* = 7.6 Hz, 3H); ¹³C{¹H} NMR: (100 MHz, CDCl₃) δ 163.5, 162.4, 134.4, 132.8, 132.5, 128.9, 128.2, 127.2, 127.0, 112.5, 52.9, 45.3, 31.5, 20.1, 13.8; IR: (ATR) 2957, 2932, 1763, 1726, 1647, 1618, 1595, 1435, 1414, 1337, 1300, 1240, 1209, 1173, 1113, 1094, 1036, 773, 754 cm⁻¹; HRMS (EI) *m/z*: [M]⁺ Calculated for C₁₅H₁₇NO₃ 259.1203; Found 259.1205

Mechanistic investigations for aziridination

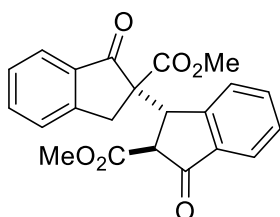
a) The reaction of β-ketoester **2a** with PhI(OAc)₂



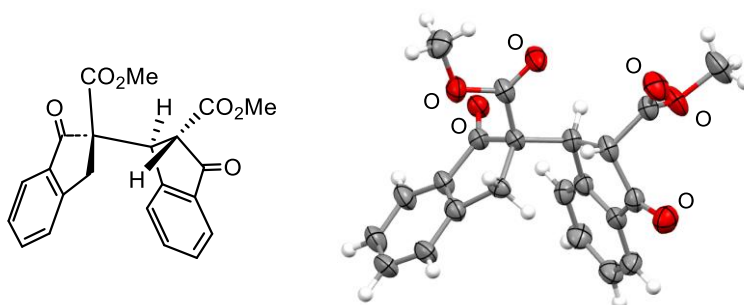
A reaction flask charged with a magnetic stirring bar was flame-dried under vacuum. After cooling down to room temperature, methyl 1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (77.2 mg, 0.41 mmol, 1.0 equiv), K₂CO₃ (61.7 mg, 0.45 mmol, 1.1 equiv), and DMF (4 mL) were added. The mixture was stirred at room temperature for 30 min, and PhI(OAc)₂ (131.3 mg, 0.41 mmol, 1.0 equiv) was added. After the mixture was stirred at room temperature for 30 min, 1M Na₂S₂O₃ aq. was added, and the mixture was extracted with AcOEt (2 × 15 mL). The organic solution was washed three times with brine. The combined organic layers were dried over Na₂SO₄, filtrated, and concentrated under reduced

pressure to give the crude product. Purification by flash column chromatography on silica gel (hexane/EtOAc = 80:20) gave the product **35** as a white solid (58.7 mg, 76% combined yield of two diastereomers, *dr* = 2.2:1). Recrystallization from Et₂O gave single crystals suitable for X-ray analysis.

dimethyl 1',3-dioxo-1',2,3,3'-tetrahydro-1*H*,2'*H*-[1,2'-biindene]-2,2'-dicarboxylate (35**)**



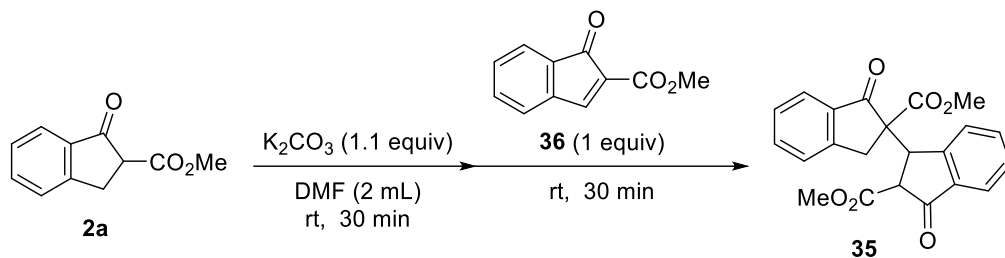
mp (mixture of two diastereomers): 135.5–137.0 °C; ¹H NMR of a mixture of two diastereomers: (400 MHz, CDCl₃) δ 7.86 (d, *J* = 8.0 Hz, 0.7H), 7.82–7.74 (m, 1.3H), 7.63 (dd, *J* = 7.6, 7.6 Hz, 0.7H), 7.57 (ddd, *J* = 7.6, 7.6, 1.2 Hz, 0.7H), 7.50–7.38 (m, 1.9H), 7.38–7.28 (m, 2H), 7.18–7.12 (m, 0.7H), 5.14 (d, *J* = 3.6 Hz, 0.3H), 5.01 (d, *J* = 3.6 Hz, 0.7H), 3.85 (s, 0.9H), 3.82 (s, 2.1H), 3.77 (s, 0.9H), 3.69 (s, 2.1H), 3.65–3.56 (m, 1.7H), 3.05 (d, *J* = 4.0 Hz, 0.3H), 2.56 (m, 1H); ¹³C{¹H} NMR of a mixture of two diastereomers: (100 MHz, CDCl₃) 201.0, 199.5, 198.0, 197.8, 170.1, 169.9, 168.5, 168.3, 153.4, 153.2, 151.9, 136.3, 136.1, 136.0, 135.9, 135.8, 135.6, 135.5, 134.6, 128.90, 128.86, 128.3, 128.1, 126.4, 126.1, 125.9, 125.3, 124.9, 124.85, 124.83, 64.3, 63.9, 58.4, 56.4, 53.4, 53.2, 53.0, 52.9, 46.3, 45.8, 33.5, 33.1 (two sp² signals were not observed because of overlapping); IR of a mixture of two diastereomers: (ATR) 3015, 2955, 2843, 1738, 1705, 1211, 1198, 1179, 1153, 752 cm⁻¹; HRMS (DART) *m/z*: [M+H]⁺ Calculated for C₂₂H₁₉O₆ 379.1176; Found 379.1183



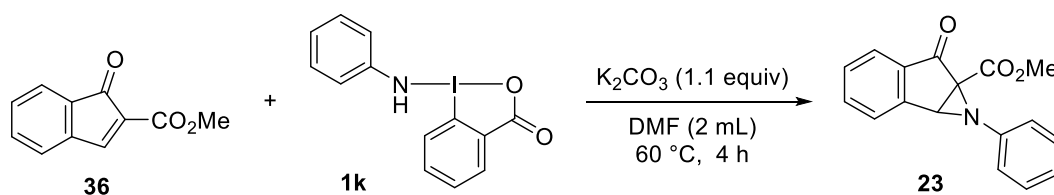
The structure of **35** (one of the diastereomers) was determined by X-ray structural analysis. CCDC 2498275 contains the supplementary crystallographic data for this paper. These data can be obtained

free of charge from The Cambridge Crystallographic Data Centre via
www.ccdc.cam.ac.uk/data_request/cif.

CCDC number	2498275
Empirical formula	C ₂₂ H ₁₈ O ₆
Formula weight	378.36
Temperature/K	123
Crystal system	monoclinic
Space group	Pc
a/Å	9.1578(6)
b/Å	12.3777(7)
c/Å	8.3823(5)
$\alpha/^\circ$	90
$\beta/^\circ$	106.935(6)
$\gamma/^\circ$	90
Volume/Å ³	908.95(10)
Z	2
$\rho_{\text{calc}}/\text{g cm}^{-3}$	1.382
μ/mm^{-1}	0.839
F(000)	396.0
Crystal size/mm ³	0.103 × 0.078 × 0.058
Radiation	Cu K α (λ = 1.54184)
2 Θ range for data collection/ $^\circ$	7.142 to 155.544
Index ranges	-11 ≤ h ≤ 11, -14 ≤ k ≤ 15, -10 ≤ l ≤ 10
Reflections collected	10744
Independent reflections	3318 [R_{int} = 0.1916, R_{sigma} = 0.1023]
Data/restraints/parameters	3318/2/256
Goodness-of-fit on F ²	1.339
Final R indexes [$I \geq 2\sigma(I)$]	R_1 = 0.1006, wR_2 = 0.2809
Final R indexes [all data]	R_1 = 0.1159, wR_2 = 0.3317
Largest diff. peak/hole / e Å ⁻³	0.56/-0.45

b) The reaction of α,β -unsaturated ketoester **36** with β -ketoester **2a**

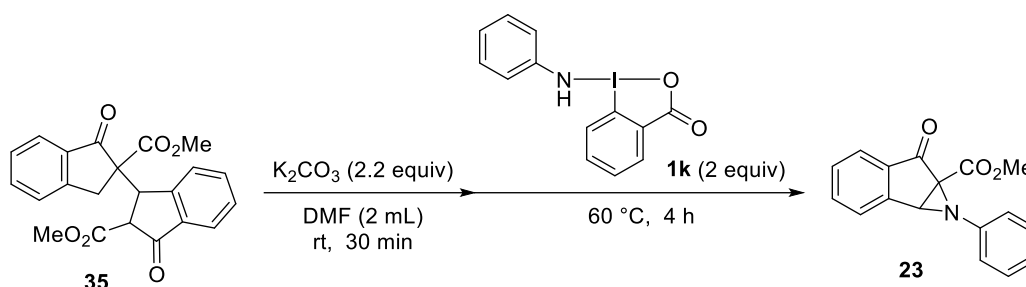
A reaction flask charged with a magnetic stirring bar was flame-dried under vacuum. After cooling down to room temperature, methyl 1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**2a**, 38.0 mg, 0.20 mmol, 1.0 equiv), K_2CO_3 (30.8 mg, 0.22 mmol, 1.1 equiv), and DMF (2 mL) were added. The mixture was stirred at room temperature for 30 min, and methyl 1-oxo-1H-indene-2-carboxylate (**36**, 38.6 mg, 0.20 mmol, 1.0 equiv) was added. After the mixture was stirred at room temperature for 30 min, sat. $NaHCO_3$ aq. was added, and the mixture was extracted with AcOEt (2×15 mL). The organic solution was washed three times with brine. The combined organic layers were dried over Na_2SO_4 , filtrated, and concentrated under reduced pressure to give the crude product, which was analyzed by 1H NMR spectroscopy using 1,1,2,2-tetrachloroethane as an internal standard (**35**: 78% combined yield of two diastereomers, $dr = 2.5:1$).

c) Aziridination of α,β -unsaturated ketoester **36** with hypervalent iodine reagent **1k**

A reaction flask charged with a magnetic stirring bar was flame-dried under vacuum. After cooling down to room temperature, methyl 1-oxo-1H-indene-2-carboxylate (**36**, 38.8 mg, 0.20 mmol, 1.0 equiv), K_2CO_3 (31.0 mg, 0.22 mmol, 1.1 equiv), hypervalent iodine reagent **1k** (68.6 mg, 0.20 mmol, 1.0 equiv), and DMF (2 mL) were added. Then, the flask was placed in an aluminum block, which was preheated at 60 °C. After the mixture was stirred at 60 °C for 4 h, sat. $NaHCO_3$ aq. was added, and the mixture was extracted with AcOEt (2×15 mL). The organic solution was washed three times with brine. The

combined organic layers were dried over Na₂SO₄, filtrated, and concentrated under reduced pressure to give the crude product, which was analyzed by ¹H NMR spectroscopy using 1,1,2,2-tetrachloroethane as an internal standard (**23**: 77% yield).

d) Aziridination using **35**



A reaction flask charged with a magnetic stirring bar was flame-dried under vacuum. After cooling down to room temperature, dimethyl 1',3-dioxo-1',2,3,3'-tetrahydro-1H,2'H-[1,2'-biindene]-2,2'-dicarboxylate (**35**, 30.6 mg, 0.081 mmol, 1.0 equiv), K₂CO₃ (28.6 mg, 0.21 mmol, 2.2 equiv), and DMF (2 mL) were added. The mixture was stirred at room temperature for 30 min, and hypervalent iodine reagent **1k** (63.2 mg, 0.19 mmol, 2.0 equiv) was added. Then, the flask was placed in an aluminum block, which was preheated at 60 °C. After the mixture was stirred at 60 °C for 4 h, sat. NaHCO₃ aq. was added, and the mixture was extracted with AcOEt (2 × 15 mL). The organic solution was washed three times with brine. The combined organic layers were dried over Na₂SO₄, filtrated, and concentrated under reduced pressure to give the crude product, which was analyzed by ¹H NMR spectroscopy using 1,1,2,2-tetrachloroethane as an internal standard (**23**: 77% yield).

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Conclusion

This thesis addresses the development of the synthesis of the novel hypervalent iodine reagents containing various amino groups and their applications to oxidative amination reactions. The results obtained in this thesis are summarized as follows:

In Chapter 1, the synthesis of aminobenziodoxolones as a new class of hypervalent iodine-based aminating reagents was accomplished using disilazanes. They could be used in the transition-metal-free electrophilic amination of arylboronic acid derivatives. This method was successfully applied to a wide range of substrates including challenging ones in the existing reagents. Furthermore, investigations of the reaction mechanism suggested that the reaction proceeded via the 1,2-aryl migration from borate complex containing B–N bond.

In Chapter 2, the scope of amino groups accessible for the synthesis of aminobenziodoxolones was significantly expanded by utilizing ammonia and primary amines. With the diverse range of aminobenziodoxolones, various arylamines could be synthesized including valuable secondary arylamines and ^{15}N -labelled arylamines by the reaction of arylboronic acids.

In Chapter 3, aminobenziodoxolones were applied to the oxidative amination of β -ketoesters. Using NH_2 - and alkylamine-substituted benziodoxolones, α -amination proceeded, various α -amino- β -ketoesters were obtained. In contrast, arylamine-derived benziodoxolones promoted aziridination, providing fused aziridines. Moreover, mechanistic experiments revealed that the aziridination proceeded through the formation of unsaturated ketoester intermediates.

A wide variety of amines can be synthesized by using the developed methods. As amines are useful building blocks, the methods find wide application in the synthesis of biologically active molecules and functional compounds. Aminobenziodoxolones developed in this study provide valuable platforms for amine synthesis and are expected to stimulate further advances in oxidative amination chemistry.

List of Publications

The content of this thesis has been published in the following papers.

- 1) Amino- λ^3 -iodane-Enabled Electrophilic Amination of Arylboronic Acid Derivatives
Kensuke Kiyokawa, Kazuki Kawanaka, Satoshi Minakata
Angew. Chem. Int. Ed. **2024**, 63, e202319048.
- 2) Versatile method for the synthesis of aminobenziodoxolones and its application to one-pot coupling of arylboronic acids with simple amines
Kazuki Kawanaka, Shusuke Narita, Kensuke Kiyokawa, Satoshi Minakata
Chem. Sci. **2025**, 16, 19389–19396.
- 3) Oxidative α -Amination and Aziridination of Cyclic β -Ketoesters Using Aminobenziodoxolones
Kazuki Kawanaka, Kotaro Muraoka, Kensuke Kiyokawa, Satoshi Minakata
Org. Lett. **2025**, 27, 13607–13613.

List of Supplementary Publication

- 1) α -Amination of Carbonyl Compounds by Using Hypervalent Iodine-Based Aminating Reagents Containing a Transferable (Diarylmethylene)amino Group
Daichi Okumatsu, Kazuki Kawanaka, Shunpei Kainuma, Kensuke Kiyokawa, Satoshi Minakata
Chem. Eur. J. **2023**, 29, e202203722.
- 2) Streamlining the Synthesis of Pyridones through Oxidative Amination of Cyclopentenones
Bence B. Botlik, Micha Weber, Florian Ruepp, Kazuki Kawanaka, Patrick Finkelstein, Bill Morandi
Angew. Chem. Int. Ed. **2024**, 63, e202408230.

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