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RESEARCH ARTICLE

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1-(Isoquinolin-1-yl)urea Library Generation via Three-Component Reaction of 2-Alkynylbenzaldoxime, Carbodiimide, with Electrophile

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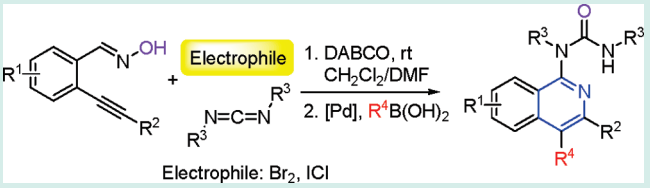
Supporting Information

ABSTRACT: A novel and highly efficient three-component reaction of 2-alkynylbenzaldoxime, carbodiimide, with electrophile (bromine or iodine monochloride) is disclosed, which generates 1-(4-haloisoquinolin-1-yl)ureas in good yields under mild conditions. Subsequent palladium-catalyzed Suzuki−Miyaura coupling reaction is introduced, leading to the diverse 1-(isoquinolin-1-yl)ureas.



KEYWORDS: three-component reaction, 2-alkynylbenzaldoxime, carbodiimide, Suzuki−Miyaura coupling, 1-(isoquinolin-1-yl)ureas, palladium-catalyzed

INTRODUCTION

Combinatorial chemistry has a great impact on the drug discovery process because it is well recognized as a powerful tool for providing large collection of small molecules.[1] In this field, intense interest has been directed toward the design and synthesis of natural-product-like compounds using combinatorial approaches since natural products play an important role in drug development and drug discovery. Among the scaffolds of natural products, isoquinoline has attracted growing interest since it is a core structure in many natural alkaloids and pharmaceuticals that display diverse biological and pharmacological activities.[2,3] Therefore, isoquinolines are regarded as a promising class of potentially useful pharmacologically active compounds, and their synthesis has found widespread application so far.[4] We have involved in the development of new and practical methods for the design and synthesis of natural-product-like compounds,[5] and we are interested in undertaking the construction of small-sized combinatorial libraries for biological screening applications in multiple assays. Recently, we reported the 1-(isoquinolin-1-yl)urea synthesis via a silver triflate-catalyzed tandem reaction of 2-alkynylbenzaldoxime with carbodiimide (Scheme 1, eq 1).[6] Although this reaction shows good generality for functional groups with a broad substrate scope, the diversity could not be introduced in the 4-position of isoquinoline scaffold. In addition, as we can see, the 1-(isoquinolin-1-yl)urea products possess hydrogen bond donor/acceptor capabilities that could confer interesting biological properties for applications in chemical biology and drug discovery. Consequently, it is of high demand for a small library construction of diverse 1-(isoquinolin-1-yl)ureas, with an expectation to find some hits from our specific biological assays. Thus, we initiated a program to develop efficient pathway for rapid access to functionalized isoquinolines. To our surprise, there are not many examples for combinatorial synthesis of functionalized isoquinolines.[7] Most of the isoquinoline generation centered on classical methods including the Pomeranz−Fritsch,[7a,7b] Bischler−Napieralski,[7c] and Pictet−Spengler reactions,[7d,7f] which generally suffered from either harsh conditions or tedious reaction procedures. Recently, transition metal-catalyzed isoquinoline formation was developed.[8] However, this method usually required high temperature and expensive metal catalysts. For example, Larock and co-workers[8] reported the solution-phase synthesis of a small library of isoquinoline through the palladium- and copper-catalyzed cyclization of iminoalkynes and the palladium-catalyzed iminoannulation of internal alkynes. The reaction proceeded at 100 °C to provide the isoquinoline compounds in low yields. To ensure the 1-(isoquinolin-1-yl)urea library construction, the strategy should be highly efficient with good substrate generality under mild conditions. Moreover, the starting materials should be easily available. Herein, we wish to report our recent efforts for diverse 1-(isoquinolin-1-yl)ureas generation via three-component reaction of 2-alkynylbenzaldoxime, carbodiimide, with electrophile under mild conditions. This metal-free process with high efficiency facilitates the rapid assembly of 1-(isoquinolin-1-yl)urea compounds.

Among the strategies used for natural-product-like compounds construction, multicomponent reactions are very attractive processes with high efficiency for the generation of combinatorial libraries based on privileged structures.[9] We conceived that an electrophile

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Scheme 1. Proposed Synthetic Route for Generation of Diverse 1-(Isoquinolin-1-yl)ureas via Three-Component Reaction of 2-Alkynylbenzaldoxime, Carbodiimide, with Electrophile

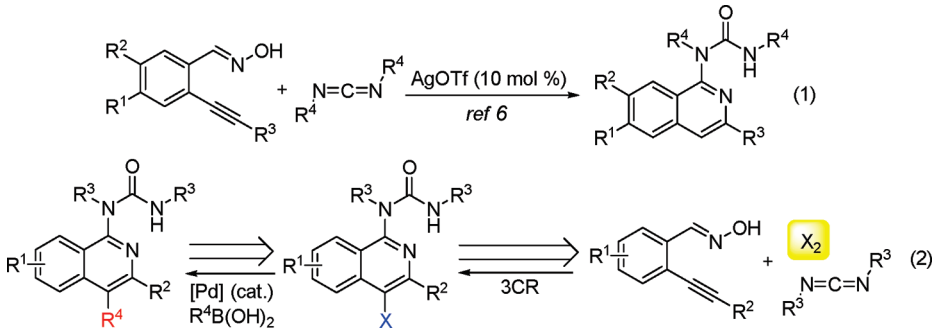
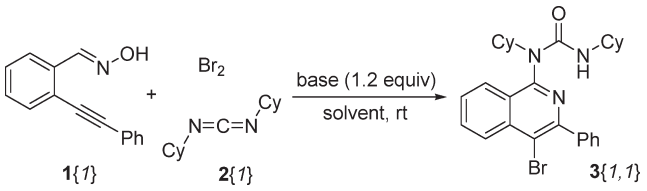


Table 1. Initial Studies for Three-Component Reaction of 2-Alkynylbenzaldoxime 1{*1*}, Carbodiimide 2{*1*}, with Bromine



entry	base	solvent	yield (%)[a]
1		CH_2Cl_2	trace
2		CH_2Cl_2/MeCN	28
3		CH_2Cl_2/DMF	51
4	KOH	CH_2Cl_2/DMF	73
5	LiOH	CH_2Cl_2/DMF	77
6	KOAc	CH_2Cl_2/DMF	71
7	Na_2CO_3	CH_2Cl_2/DMF	75
8	$NaHCO_3$	CH_2Cl_2/DMF	72
9	Cs_2CO_3	CH_2Cl_2/DMF	65
10	K_3PO_4	CH_2Cl_2/DMF	70
11	DABCO	CH_2Cl_2/DMF	92

[a] Isolated yield based on 2-alkynylbenzaldoxime **1**{*1*}.

could be involved in the reaction of 2-alkynylbenzaldoxime with carbodiimide (Scheme 1, eq 2). Thus, 1-(4-haloisoquinolin-1-yl)ureas would be formed under suitable conditions from the above three-component reaction. After subsequent palladium-catalyzed cross-coupling reactions, the functionalized 1-(isoquinolin-1-yl)ureas would be generated.

RESULT AND DISCUSSION

At the beginning of our investigations, we examined the three-component reaction of 2-alkynylbenzaldoxime **1**{*1*}, *N*-((cyclohexylimino)methylene)cyclohexanamine **2**{*1*}, with bromine under different conditions. Since 2-alkynylbenzaldoxime worked the most efficiently with bromine in dichloromethane,[10] the initial attempt was performed in CH_2Cl_2 at room temperature. However, only a trace amount of desired product **3**{*1,1*} was detected (Table 1, entry 1). In the reaction process, HBr would be generated as a byproduct. Thus, the basic solvents were used. To our delight, we observed the formation of compound **3**{*1,1*} with 28% isolated yield when the reaction was carried out in CH_2Cl_2/MeCN (Table 1, entry 2). The yield was increased to 51% when DMF was utilized as a replacement (Table 1, entry 3). Addition of base dramatically improved the reaction efficiency. Further screening of different bases revealed that DABCO was the best one, which furnished the corresponding product **3**{*1,1*} in 92% yield (Table 1, entry 11).

With the optimized conditions in hand [DABCO (1.2 equiv), CH_2Cl_2/DMF, room temperature], the scope of this three-component reaction was examined with a series of 2-alkynylbenzaldoximes **1** and carbodiimide **2** in the presence of bromine or iodine monochloride. The diversity reagents of 2-alkynylbenzaldoximes **1** and carbodiimide **2** are shown in Figures 1 and 2, and the results are displayed in Table 2. All reactions went to completion in 8−10 h, which afforded the expected 1-(4-haloisoquinolin-1-yl)ureas in good to excellent yields under mild conditions. All products were isolated by column chromatography on silica gel with >97% purity.

This three-component reaction shows a broad substrate scope. As shown in Table 2, the electron effect on the aromatic backbone of both the substrates was invisible. In some cases, the desired products were obtained in almost quantitative yields. Not only bromine but also iodine monochloride was workable under the standard conditions. For 2-alkynylbenzaldoximes **1**, the groups attached on the aromatic ring or the triple bond did not influence the final outcome. Additionally, no difference was observed in the reaction for alkyl or aryl substituted carbodiimides. The possible mechanism was proposed in Scheme 2. We reasoned that, in the presence of electrophile (bromine or iodine monochloride), 4-haloisoquinoline-*N*-oxide would be formed from 2-alkynylbenzaldoxime **1** via 6-endo-cyclization. Subsequently, 4-haloisoquinoline-*N*-oxide reacted with carbodiimide **2** via [3 + 2] cycloaddition leading to the key intermediate **A**. After base-promoted intramolecular rearrangement, the corresponding 4-halo-1-(isoquinolin-1-yl)urea would be generated. On the basis of this hypothesis, we conceived that the substituent (R^2 or R^3 group) attached on the substrates would affect the final outcome. Generally, the electrophility would be increased when R^3 was an electron-withdrawing group, while the reactivity was expected to be decreased for carbodiimide with an electron-donating group attached on the nitrogen. For instance, reaction of 2-alkynylbenzaldoxime **1**{*8*} with 4-methoxy-*N*-((4-methoxyphenylimino)-methylene)benzenamine **2**{*5*} gave rise to the desired product **3**{*8,5*} in 50% yield (Table 2, entry 49). A quantitative yield of

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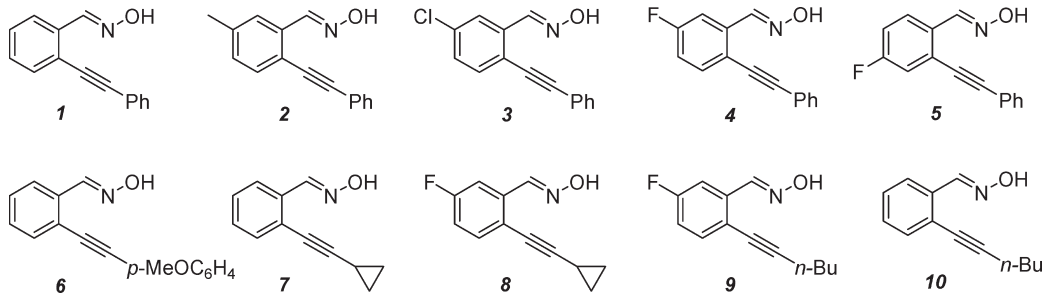


Figure 1. Diversity reagents **1**{*1*−*10*}.

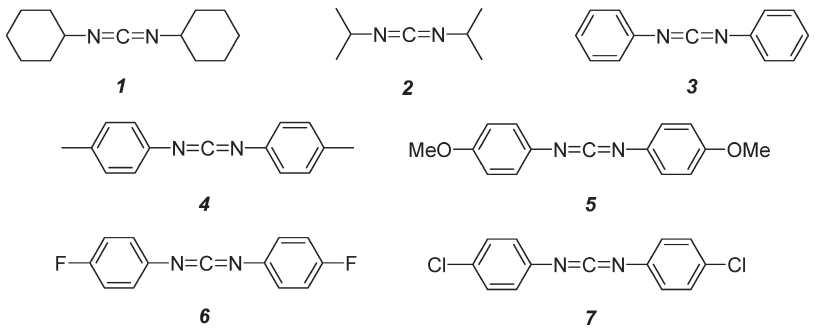


Figure 2. Carbodiimide reagents **2**{*1*−*7*}.

3{*8,7*} was isolated when 4-chloro-*N*-((4-chlorophenylimino)-methylene)benzenamine **2**{*7*} was used as a replacement in the reaction (Table 2, entry 51). For the effect of substituent (R^2 group) attached on the triple bond of 2-alkynylbenzaldoxime **1**, we reasoned that the group with π electron would facilitate the transformation, which would stabilize the 4-haloisoquinoline-*N*-oxide intermediate. As expected, reactions proceeded well for the 2-alkynylbenzaldoxime **1** with aryl or cyclopropyl group attached on the triple bond, while inferior results were generated when the R^2 group was changed to *n*-Bu group (Table 2, entries 53−61).

Some 1-(4-bromoisoquinolin-1-yl)ureas **3** were selected for further elaboration. Because of their easy availability, arylboronic acid derivatives would be the starting materials of choice. Thus, the palladium-catalyzed Suzuki−Miyaura coupling reaction[11] of 1-(4-bromoisoquinolin-1-yl)ureas **3** with arylboronic acid was tested. The selected representative of arylboronic acids was shown in Figure 3. As expected, the diversity on the 4-position could be easily introduced in the scaffold. The reactions proceeded efficiently in the presence of $Pd(OAc)_2$ (5 mol %), PPh_3 (10 mol %), and K_3PO_4 in toluene (Table 3). For most cases, the desired products **6** were generated in excellent yields.

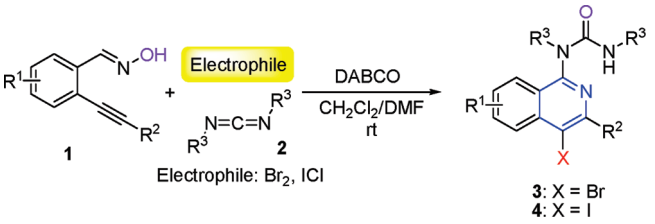
CONCLUSION

In summary, we have described a novel and highly efficient three-component reaction of 2-alkynylbenzaldoxime, carbodiimide, with electrophile, leading to 1-(4-haloisoquinolin-1-yl)-ureas in good yields under mild conditions. The scaffold could be further decorated to introduce more diversity through subsequent palladium-catalyzed Suzuki−Miyaura coupling reaction. The facile assembly of 1-(isoquinolin-1-yl)urea library could be expected becaue of the high efficiency, good substrate generality, mild conditions, and the easily availability of the starting materials.

EXPERIMENTAL PROCEDURES

General Procedure for Three-Component Reactions of 2-Alkynylbenzaldoxime 1, Carbodiimide 2, with Br_2 or ICl. 2-Alkynylbenzaldoxime **1** (0.2 mmol) was added to a solution of Br_2 or ICl in DCM (0.4 mmol/mL, 0.5 mL), and the solution was stirred at room temperature in air for 10 min. Then DABCO (1.2 equiv) was added, and the solution was stirred at room temperature in air for another 10 min. Subsequently, DMF (2.0 mL) and carbodiimide **2** (1.5 equiv) were added, and the mixture was stirred at room temperature in air for 12 h. After completion of reaction as indicated by TLC, the reaction was quenched by addition of saturated aqueous NH_4Cl (5.0 mL), and the mixture was extracted with EtOAc (4.0 mL × 3). The combined organic layer was dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography on silica gel to provide the desired product **3** or **4**. Data of selected examples: 1-(4-Bromo-3-phenylisoquinolin-1-yl)-1,3-dicyclohexylurea (**3**{*1,1*}): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.76 (q, J = 12.4 Hz, 2H), 0.84−1.00 (m, 2H), 1.20−1.60 (m, 10H), 1.70−1.76 (m, 4H), 1.98−1.99 (m, 2H), 3.59−3.66 (m, 1H), 3.72 (d, J = 7.7 Hz, 1H), 4.49−4.58 (m, 1H), 7.44−7.53 (m, 3H), 7.66 (t, J = 8.0 Hz, 1H), 7.79 (d, J = 7.0 Hz, 2H), 7.84 (t, J = 7.7 Hz, 1H), 8.12 (d, J = 8.8 Hz, 1H), 8.38 (d, J = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.8, 25.4, 25.5, 26.0, 31.9, 33.4, 49.4, 57.2, 117.8, 126.1, 127.2, 127.4, 127.8, 128.4, 128.5, 130.1, 132.1, 137.9, 139.8, 151.1, 151.4, 155.6; HRMS (ESI) calcd for $C_{28}H_{32}BrN_3O$ 528.1626 (M + Na^+), found 528.1606. 1-(4-Bromo-3-phenylisoquinolin-1-yl)-1,3-diisopropylurea (**3**{*1,2*}): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92 (d, J = 6.6 Hz, 6H), 1.25 (d, J = 6.6 Hz, 6H), 3.69 (d, J = 7.7 Hz, 1H), 3.95−4.01 (m, 1H), 4.92−4.98 (m, 1H), 7.44−7.53 (m, 3H), 7.67 (t, J = 8.1 Hz, 1H), 7.80 (d, J = 8.3 Hz, 2H), 7.85 (t, J = 7.7 Hz, 1H), 8.09 (d, J = 8.3 Hz, 1H), 8.40 (d, J = 8.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 23.0, 42.5, 49.4, 117.7, 126.0, 127.0, 127.5, 127.9, 128.4,

Table 2. Three-Component Reaction of 2-Alkynylbenzaldoxime 1, Carbodiimide 2, with Electrophile



entry	2-alkynylbenzaldoxime **1**	carbodiimide **2**	product	yield (%)[a]
1	**1**{*1*}	**2**{*1*}	**3**{*1,1*}	92
2	**1**{*1*}	**2**{*2*}	**3**{*1,2*}	85
3	**1**{*1*}	**2**{*3*}	**3**{*1,3*}	97
4	**1**{*1*}	**2**{*4*}	**3**{*1,4*}	91
5	**1**{*1*}	**2**{*5*}	**3**{*1,5*}	95
6	**1**{*1*}	**2**{*6*}	**3**{*1,6*}	97
7	**1**{*1*}	**2**{*7*}	**3**{*1,7*}	98
8	**1**{*1*}	**2**{*1*}	**4**{*1,1*}	83
9	**1**{*2*}	**2**{*1*}	**3**{*2,1*}	88
10	**1**{*2*}	**2**{*2*}	**3**{*2,2*}	78
11	**1**{*2*}	**2**{*3*}	**3**{*2,3*}	90
12	**1**{*2*}	**2**{*4*}	**3**{*2,4*}	88
13	**1**{*2*}	**2**{*5*}	**3**{*2,5*}	94
14	**1**{*2*}	**2**{*6*}	**3**{*2,6*}	93
15	**1**{*2*}	**2**{*7*}	**3**{*2,7*}	92
16	**1**{*2*}	**2**{*1*}	**4**{*2,1*}	93
17	**1**{*3*}	**2**{*1*}	**3**{*3,1*}	95
18	**1**{*3*}	**2**{*2*}	**3**{*3,2*}	84
19	**1**{*3*}	**2**{*3*}	**3**{*3,3*}	81
20	**1**{*3*}	**2**{*4*}	**3**{*3,4*}	75
21	**1**{*3*}	**2**{*5*}	**3**{*3,5*}	83
22	**1**{*3*}	**2**{*6*}	**3**{*3,6*}	60
23	**1**{*3*}	**2**{*7*}	**3**{*3,7*}	96
24	**1**{*3*}	**2**{*1*}	**4**{*3,1*}	80
25	**1**{*4*}	**2**{*1*}	**3**{*4,1*}	98
26	**1**{*4*}	**2**{*2*}	**3**{*4,2*}	86
27	**1**{*4*}	**2**{*3*}	**3**{*4,3*}	98
28	**1**{*4*}	**2**{*4*}	**3**{*4,4*}	92
29	**1**{*4*}	**2**{*5*}	**3**{*4,5*}	99
30	**1**{*4*}	**2**{*6*}	**3**{*4,6*}	97
31	**1**{*4*}	**2**{*7*}	**3**{*4,7*}	99
32	**1**{*4*}	**2**{*1*}	**4**{*4,1*}	83
33	**1**{*5*}	**2**{*1*}	**3**{*5,1*}	91
34	**1**{*5*}	**2**{*2*}	**3**{*5,2*}	87
35	**1**{*5*}	**2**{*3*}	**3**{*5,3*}	93
36	**1**{*5*}	**2**{*4*}	**3**{*5,4*}	91
37	**1**{*5*}	**2**{*5*}	**3**{*5,5*}	86
38	**1**{*5*}	**2**{*6*}	**3**{*5,6*}	98
39	**1**{*5*}	**2**{*7*}	**3**{*5,7*}	90
40	**1**{*5*}	**2**{*1*}	**4**{*5,1*}	82
41	**1**{*6*}	**2**{*2*}	**3**{*6,2*}	84
42	**1**{*6*}	**2**{*1*}	**4**{*6,1*}	78
43	**1**{*7*}	**2**{*1*}	**3**{*7,1*}	93
44	**1**{*7*}	**2**{*2*}	**3**{*7,2*}	92
45	**1**{*8*}	**2**{*1*}	**3**{*8,1*}	97
46	**1**{*8*}	**2**{*2*}	**3**{*8,2*}	96
47	**1**{*8*}	**2**{*3*}	**3**{*8,3*}	95
48	**1**{*8*}	**2**{*4*}	**3**{*8,4*}	88
49	**1**{*8*}	**2**{*5*}	**3**{*8,5*}	50
50	**1**{*8*}	**2**{*6*}	**3**{*8,6*}	96
51	**1**{*8*}	**2**{*7*}	**3**{*8,7*}	99
52	**1**{*8*}	**2**{*1*}	**4**{*8,1*}	97
53	**1**{*9*}	**2**{*1*}	**3**{*9,1*}	88
54	**1**{*9*}	**2**{*2*}	**3**{*9,2*}	80
55	**1**{*9*}	**2**{*3*}	**3**{*9,3*}	60
56	**1**{*9*}	**2**{*4*}	**3**{*9,4*}	53
57	**1**{*9*}	**2**{*5*}	**3**{*9,5*}	51
58	**1**{*9*}	**2**{*6*}	**3**{*9,6*}	53
59	**1**{*9*}	**2**{*7*}	**3**{*9,7*}	58
60	**1**{*9*}	**2**{*1*}	**4**{*9,1*}	77
61	**1**{*10*}	**2**{*2*}	**3**{*10,2*}	75

[a] Isolated yield based on 2-alkynylbenzaldoxime **1**.

128.5, 130.1, 132.1, 138.0, 139.8, 151.1, 151.3, 155.7; HRMS (ESI) calcd for $C_{22}H_{24}BrN_3O$ 448.1000 ($M + Na^+$), found 448.0992. 1,3-Dicyclohexyl-1-(4-iodo-3-phenylisoquinolin-1-yl)urea (**4**{*1,1*}): ^1H NMR (400 MHz, $CDCl_3$) δ 0.77 (q, J = 12.4 Hz, 2H), 0.86−1.98 (m, 2H), 1.18−1.58 (m, 10H), 1.69−1.76 (m, 4H), 1.98 (s, 2H), 3.61−3.65 (m, 1H), 3.74 (d, J = 7.7 Hz, 1H), 4.50−4.55 (m, 1H), 7.43−7.52 (m, 3H), 7.63−7.69 (m, 3H), 7.81 (t, J = 7.7 Hz, 1H), 8.08 (d, J = 8.4 Hz, 1H), 8.29 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.8, 25.3, 25.5, 26.0, 31.9, 33.4, 49.4, 57.2, 97.7, 126.2, 126.7, 127.8, 128.4, 128.6, 130.0, 132.5, 132.8, 140.5, 142.7, 152.4, 155.6, 155.8; HRMS (ESI) calcd for $C_{28}H_{32}IN_3O$ 576.1488 ($M + Na^+$), found 576.1460.

General Procedure for Palladium-Catalyzed Cross-Couplings of Compound 3 with Arylboronic Acids. Compound **3** (0.2 mmol) was added to a mixture of arylboronic acids (0.3 mmol, 1.5 equiv), $Pd(OAc)_2$ (0.01 mmol, 0.05 equiv), PPh_3 (0.02 mmol, 0.1 equiv), and K_3PO_4 (0.4 mmol, 2equiv) in toluene (2.0 mL). The mixture was then stirred at 80 °C. After completion of reaction as indicated by TLC, the solvent was evaporated and the residue was purified by column chromatography on silica gel to provide the product **6**. Data of selected examples: 1,3-Dicyclohexyl-1-(3,4-diphenylisoquinolin-1-yl)urea **6**{*1,1,1*}: ^1H NMR (400 MHz, $CDCl_3$) δ 0.81 (q, J = 11.7 Hz, 2H), 0.93−1.05 (m, 2H), 1.20−1.60 (m, 10H), 1.73−1.80 (m, 4H), 2.05−2.07 (m, 2H), 3.64−3.70 (m, 1H), 3.82 (d, J = 7.7 Hz, 1H), 4.54−4.61 (m, 1H), 7.20−7.24 (m, 3H), 7.29−7.31 (m, 2H), 7.37−7.43 (m, 5H), 7.55−7.63 (m, 2H), 7.69 (d, J = 7.7 Hz, 1H), 8.15 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.9, 25.5, 25.7, 26.2, 32.1, 33.5, 49.4, 57.4, 125.7, 125.9, 126.1, 127.3, 127.6, 127.7, 128.4, 130.3, 130.6, 130.8, 131.2, 136.9, 138.3, 139.9, 149.3, 151.6, 156.1; HRMS (ESI) calcd for $C_{34}H_{37}N_3O$ 526.2834 ($M + Na^+$), found 526.2812. 1,3-Dicyclohexyl-1-(7-methyl-3-phenyl-4-p-tolylisoquinolin-1-yl)urea **6**{*2,1,2*}: ^1H NMR (400 MHz, $CDCl_3$) δ 0.78−1.08 (m, 4H), 1.20−1.62 (m, 10H), 1.77−1.82 (m, 4H), 2.04−2.06 (m, 2H), 2.41 (s, 3H), 2.51 (s, 3H), 3.64−3.72 (m, 1H), 3.82 (d, J = 8.1 Hz, 1H), 4.56−4.62 (m, 1H), 7.15−7.24 (m, 7H), 7.38−7.43 (m, 3H), 7.60 (d, J = 8.0 Hz, 1H), 7.90 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3, 21.7, 24.9, 25.5, 25.7, 26.2, 32.0, 33.4, 49.3, 57.2, 124.3, 125.9, 126.0, 127.1, 127.6, 129.1, 130.3, 130.7, 131.0, 132.7, 133.9,

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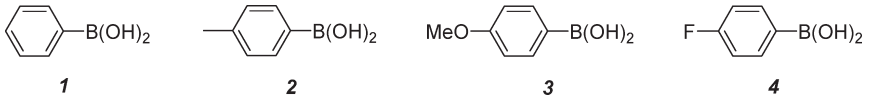


Figure 3. Boronic acid **5** {*1*−*4*}.

Scheme 2. Possible Mechanism for the Three-Component Reaction of 2-Alkynylbenzaldoxime 1, Carbodiimide 2, with Electrophile

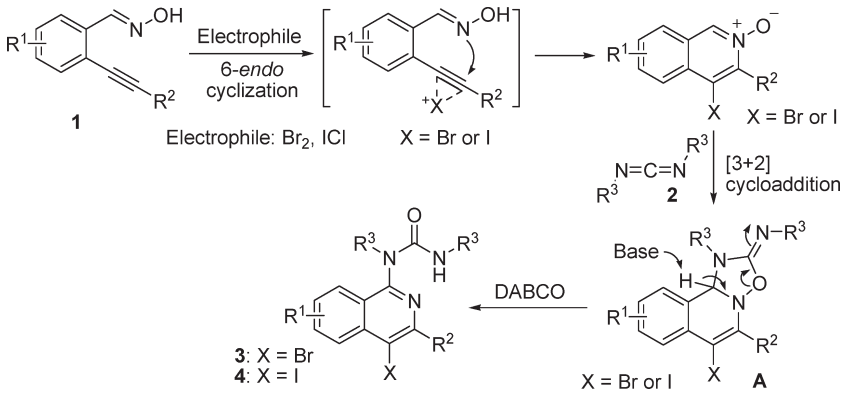
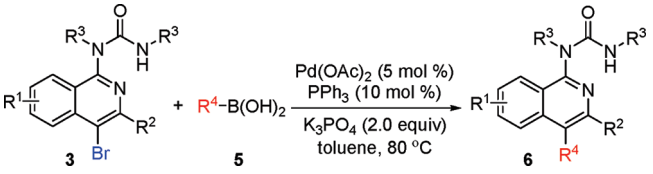


Table 3. Palladium-Catalyzed Suzuki−Miyaura Reaction of 1-(4-Bromoisoquinolin-1-yl)urea 3 with Arylboronic Acid 5



entry	compound **3**	boronic acid **4**	product	yield (%)[a]
1	**3**{*1,1*}	**5**{*1*}	**6**{*1,1,1*}	71
2	**3**{*1,1*}	**5**{*2*}	**6**{*1,1,2*}	93
3	**3**{*1,1*}	**5**{*3*}	**6**{*1,1,3*}	88
4	**3**{*1,1*}	**5**{*4*}	**6**{*1,1,4*}	55
5	**3**{*2,1*}	**5**{*2*}	**6**{*2,1,2*}	94
6	**3**{*3,1*}	**5**{*2*}	**6**{*3,1,2*}	82
7	**3**{*4,1*}	**5**{*2*}	**6**{*4,1,2*}	91
8	**3**{*7,1*}	**5**{*2*}	**6**{*7,1,2*}	97
9	**3**{*8,1*}	**5**{*2*}	**6**{*8,1,2*}	98
10	**3**{*8,2*}	**5**{*2*}	**6**{*8,2,2*}	96

[a] Isolated yield based on 1-(4-bromoisoquinolin-1-yl)urea **3**.

136.8, 137.2, 137.4, 140.1, 148.5, 150.6, 156.1; HRMS (ESI) calcd for $C_{36}H_{41}N_3O$ 554.3147 ($M + Na^+$), found 554.3131. For details, please see Supporting Information.

■ ASSOCIATED CONTENT

Supporting Information. Experimental procedures, characterization data, and ^1H and ^{13}C NMR spectra of all products. This material is available free of charge via the Internet at http://pubs.acs.org.

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Author Contributions

J.W. and S.Y. conceived and designed the experiments, S.Y. and H.W. performed the experiments, S.Y. and J.W. co-wrote the manuscript and Supporting Information.

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