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One-Pot, Multi-Step Reactions for Modular Synthesis of N,N'-Diarylindazol-3-ones

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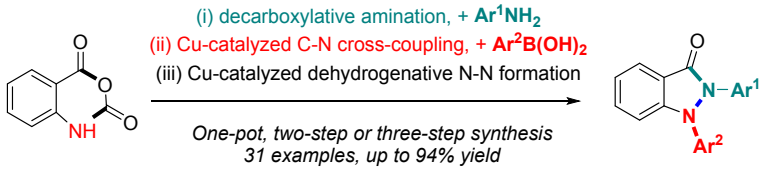


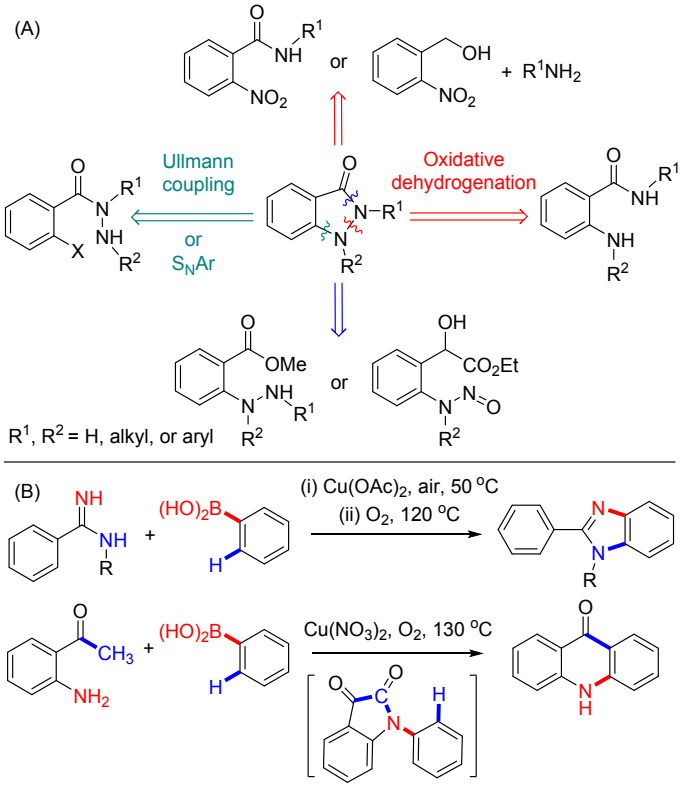
ABSTRACT: Pot-economic synthesis of N,N'-diarylindazol-3-ones has been developed using readily available isatoic anhydrides, aryl amines and aryl boronic acids. A Cu-catalyzed oxidative C–N cross-coupling and dehydrogenative N–N formation sequence under air atmosphere affords indazol-3-one derivatives in good to excellent yields. Such process merges well with the preceding decarboxylative amination reaction, resulting in a more modular and straightforward approach.

Indazol-3-one derivatives represent an important class of nitrogen heterocycles. They possess unique bioactivity and have potential medicinal application.[1] The main methods for the assembly of indazol-3-one skeleton include two types of intramolecular ring closure pathways. Conventionally, copper-catalyzed Ullmann[2] or metal-free[3] condensation was employed to assemble this skeleton through the use of hydrazine and its derivatives that may present considerable hazards, with the N–N bond already in place. Another approach constructed the N–N bond during cyclization process, including oxidative dehydrogenative coupling of N–H[4] and cyclization of nitro and nitroso groups.[5,6] As for the synthesis of N,N'-diarylindazol-3-ones, only the oxidative dehydrogenative coupling approach was workable from prefabricated N,N'-diaryl-2-aminobenzamides (**Scheme 1A**).[4c] Such strategy suffered from multiple synthetic steps and pre-functionalized starting materials. Thus, the development of a more straightforward and efficient approach is highly desirable.

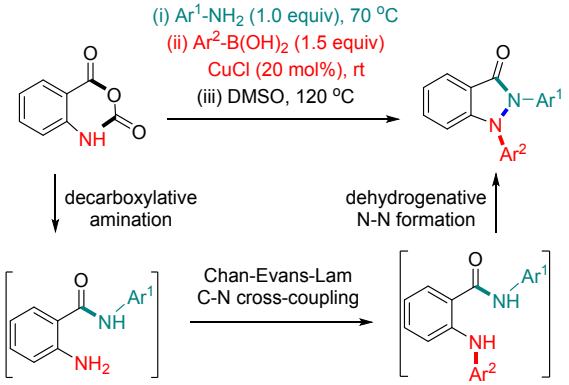
Combining traditional purification-dependent stepwise catalyzed reactions into one-pot strategies, which incorporate multiple synthetic transformations and bond-forming steps in a single vessel without isolation and purification of any intermediates represent a practical means to approach atom economy and green chemistry.[7] In this context, Cu-catalyzed oxidative C–N cross-coupling reactions, also known as Chan-Evans-Lam (CEL) reactions, natively have the potential to match up with aerobic Cu-catalyzed cross dehydrogenative cyclization reactions. Then, elegant integration of these two processes should benefit the quick construction of heterocycles. However, limited success has been achieved in this field, relative to the wide application of Cu-catalyzed one-pot sequential, cascade or tandem cyclization reactions.[8] In fact, most of Cu-catalyzed one-pot cyclization reactions were developed based on Ullmann reactions.[9] To our knowledge, only benzimidazole[10] and acridone[11] derivatives have been constructed via the oxidative CEL coupling/dehydrogenation

process. With these issues in mind, we became interested in applying this protocol into the synthesis of indazol-3-ones. Herein, we demonstrated the one-pot modular assembly of N,N'-diarylindazol-3-ones from readily available isatoic anhydrides, aryl amines and aryl boronic acids. (**Scheme 2**).

Scheme 1. (A) Representative approaches to form indazol-3-one derivatives; (B) One-pot Cu-catalyzed oxidative Chan-Evans-Lam coupling/dehydrogenation sequence.



Scheme 2. One-pot sequential synthesis of N,N'-diarylindazol-3-ones.

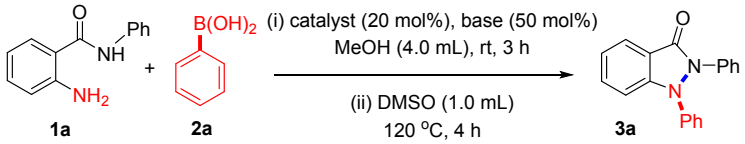


To examine the feasibility of the proposed strategy, N-phenyl-2-aminobenzamide **1a** and phenylboronic acid **2a** were used as model reaction components. The reactions were carried out in open flasks using air as oxidant. After screening of catalysts, additives, solvents and operation procedures, we discovered a Cu-catalyzed sequential C–N[12] and N–N formation[13] process afforded the target product **3a** in 94% yield (**Table 1, Entry 6**). Firstly, the reactants, 0.2 equivalent of CuCl and 0.5 equivalent of Et_3N were mixed in MeOH and stirred for 3 hours at room temperature. Then, simple addition of DMSO and adjustment of reaction temperature to 120 °C gave 94% of **3a** after stirring for 4 hours and purification by column chromatography. Although 1,4-benzodiazepine skeleton had been synthesized via oxidative C–N bond formation

from 2-(arylamino)benzamides,[14] such type of product was not observed with indazol-3-one structure formed preferentially.

Although the sequence worked more or less in the present of several common copper salts (54%-94%, **Entries 1-6**), cuprous halide generally afforded more product than their cupric analogs (**Entry 6** vs. **Entry 3** and **Entry 5** vs. **Entry 2**). In the meanwhile, $Cu(OAc)_2$ was found to be quite ineffective. When inorganic base K_2CO_3 was used in place of Et_3N, no target product can be observed after the reaction sequence (**Entry 7**). It was supposed that organic bases, such as TEA and pyridine, might act as not only bases but also ligands for copper catalysts. A slightly decreased yield was obtained when the solvent of the second step was changed to DMF (**Entry 10**). Notably, when only MeOH or DMSO was used as solvent for both steps, significant decreased yields were obtained (**Entry 11** and **12**), indicating the different demand of solvent for C–N and N–N formation steps.

Table 1. Optimization of reaction conditions[a]



1a 2a 3a

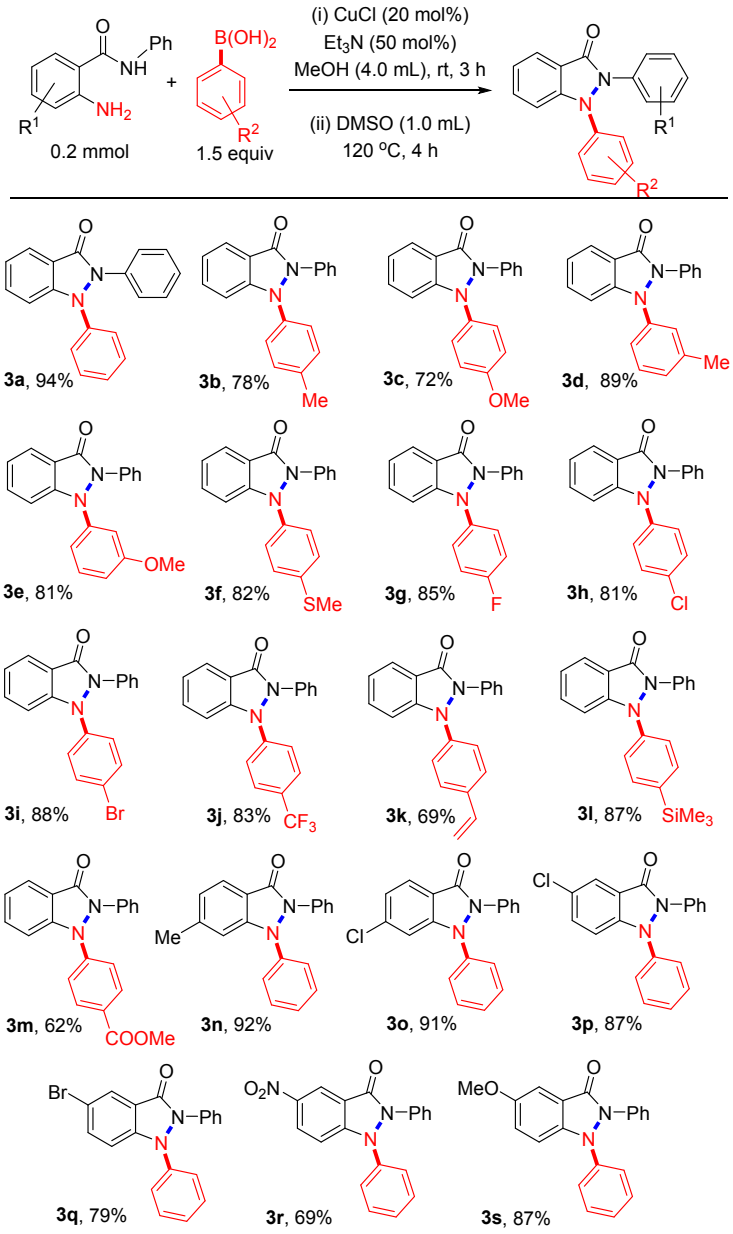
Entry	Catalyst	Base	Solvent	Yields (%)[b]
1	$Cu(OAc)_2$	Et_3N	MeOH/DMSO	10
2	$CuBr_2$	Et_3N	MeOH/DMSO	61
3	$CuCl_2$	Et_3N	MeOH/DMSO	55
4	CuI	Et_3N	MeOH/DMSO	54
5	CuBr	Et_3N	MeOH/DMSO	82
6	**CuCl**	**Et_3N**	**MeOH/DMSO**	**94**
7	CuCl	K_2CO_3	MeOH/DMSO	N.R.
8	CuCl	DBU	MeOH/DMSO	17
9	CuCl	pyridine	MeOH/DMSO	68
10	CuCl	Et_3N	MeOH/DMF	89
11	CuCl	Et_3N	MeOH[c]	17
12	CuCl	Et_3N	DMSO	28

[a] Reaction conditions: 0.2 mmol **1a** (1.0 equiv), 0.3 mmol **2a** (1.5 equiv), 0.04 mmol copper catalyst (20 mol%), 0.1 mmol base (0.5 equiv), MeOH (4.0 mL), rt, open flask, 3 h. Then DMSO (1.0 mL), 120 °C, 4h. [b] Isolated yields. [c] 70 °C.

The substrate scope of this protocol was subsequently investigated under the optimal conditions. The results were summarized in **Scheme 3**. A variety of *N*-phenyl-2-aminobenzamides were converted into the desired products in moderate to excellent yields. Aryl boronic acids containing electron-donating/withdrawing groups were all compatible with these reaction conditions, including methyl (**3b** and **3d**), methoxyl (**3c** and **3e**), methylthio (**3f**), trifluoromethyl (**3j**), alkenyl (**3k**), trimethylsilyl (**3l**) and carboxylic ester (**3m**). The electronic nature of the substituent had no obvious influence on the outcome of the reactions. The halogen atoms (such as Cl and Br) on the phenyl rings of the boronic acids, were also well tolerated and no competitive Cu-catalyzed Ullmann reactions were observed, which enabled further decoration of the obtained products. The variation of 2-aminobenzamide component with 4-Me, 3-OMe or 3-NO_2 led to 92%,87%, 69% yield of the corresponding products (**3n**, **3s**, **3r**) respectively. The halogen atoms on the 2-aminobenzamide moiety were also well tolerated (**3o**, **3p**, **3q**). The heteroaryl boronic acids and alkyl boronic acids were not suitable starting materials for this one-pot procedure, probably due to their incompatibility towards CuCl-catalyzed C—N coupling reactions under such conditions.

As illustrated in **Scheme 3**, the substituent on amide group remained as phenyl. When we tried to change the phenyl to other aryl groups. It occurred to us to combine the synthesis of *N*-aryl-2-aminobenzamides with the established Cu-catalyzed CEL coupling/dehydrogenation sequence. Such one-pot, three-step protocol might further enhance the operation convenience and enable modular assembly of disubstituted indazol-3-ones.

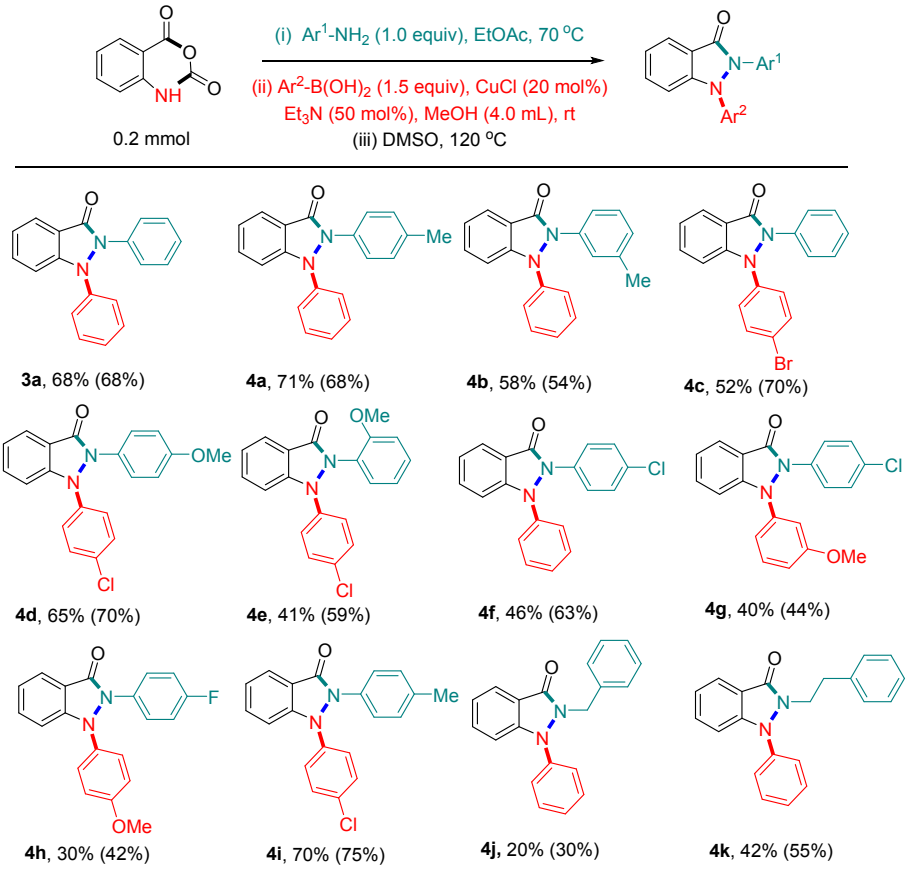
Scheme 3. Substrate scope of Cu-catalyzed one-pot construction of indazol-3-ones.



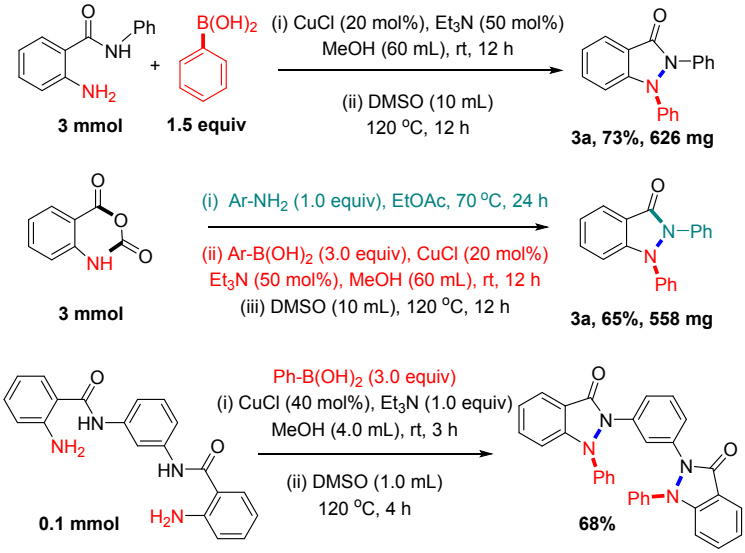
Previously, a Cu-catalyzed Ullmann protocol had been identified to enable the arylation of amide groups in 2-aminobenzamides, so a Cu-catalyzed sequential Ullmann/CEL/dehydrogenation reaction was firstly tested. However, no target product could be obtained after such sequence maybe due to the incompatibility between Ullmann and CEL conditions. The preparation of *N*-aryl-2-aminobenzamide could also be easily achieved by metal-free decarboxylative amination of isatoic anhydrides with aryl amines. The metal-free procedure, in combination with the elimination of by-product CO_2, should be helpful to relieve the complexity and incompatibility problem of the desired one-pot reactions. Fortunately, this decarboxylative amination reaction

could be combined well with the following two steps, affording the target product **3a** in 68% yield with two phenyl groups derived from phenylamine and phenylboronic acid separately.

Scheme 4. Substrate scope of one-pot, three-step construction of indazol-3-ones.



Scheme 5. Further exploration.



Substrate scope of such protocol was then explored (**Scheme 4**). Generally, aryl amines with electron-donating groups gave better yields than those ones bearing electron-withdrawing groups, when the use of aryl boronic acid remained unchanged (**4a**: 71%, **4b**: 58%, **4f**: 46%). In contrast, electron-rich boronic acid gave relative lower yield (**4f** vs. **4g**). Therefore, the combination of electron-deficient aryl amines and electron-rich boronic acid led to significant decreased yields, compared with the yield of **3a** (**4g**: 40%, **4h**: 30%). Additionally, alkyl amines were

also tested. While benzylamine led to a greatly decreased yield (**4j**: 20%), β-phenylethylamine could participate in this one-pot sequence and afforded **4k** in 42% yield. To improve the efficiency, additional CuBr catalyst could be added to the reaction mixture after the second step, along with the addition of solvent DMSO. Isolated yields could be increased by 5-18% yield (the yields in parenthesis in **Scheme 4**) based on different substrate combinations.

In addition, this one-pot protocol proved to be readily scalable. Simple amplification of the synthesis of **3a** without further optimization to a gram scale afforded 0.63 gram of product (73% yield, **Scheme 5**). Three-step synthesis was also easily amplified, in spite of the need of a larger amount of boronic acid. When a compound containing two *N*-aryl-2-aminobenzamide fragments was used as the starting material, two C–N bonds and two N–N bonds could be constructed simultaneously, affording final product in 68% yield.

In summary, this one-pot synthetical sequence enables fast modular assembly of indazol-3-one skeleton from readily available isatoic anhydrides, aryl amines and aryl boronic acids. Such pot-economical protocol circumvents isolation and purification processes and complements the existing synthetical methods of indazol-3-one derivatives. Furthermore, this disclosed methodology is expected to shed lights on developing other one-pot sequential, cascade or tandem transformations, which make best use of CEL C–N coupling reactions.

EXPERIMENTAL SECTION

General Information.

Unless otherwise noted, all reactions were carried out under an air atmosphere. Analytical thin-layer chromatography (TLC) was performed on glass plates coated with 0.25 mm 230–400 mesh silica gel containing a fluorescent indicator. Visualization was accomplished by exposure to a UV lamp. All the products in this article are compatible with standard silica gel chromatography. Column chromatography was performed on silica gel (200–300 mesh) using standard methods.

NMR spectra were measured on a Bruker Ascend 400 spectrometer and chemical shifts (δ) are reported in parts per million (ppm). ^{1}H NMR spectra were recorded at 400 MHz in NMR solvents and referenced internally to corresponding solvent resonance, and ^{13}C NMR spectra were recorded at 101 MHz and referenced to corresponding solvent resonance. Coupling constants are reported in Hz with multiplicities denoted as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet) and br (broad). Infrared spectra were collected on a Thermo Fisher Nicolet 6700 FT-IR spectrometer using ATR (Attenuated Total Reflectance) method. Absorption maxima (ν max) are reported in wavenumbers (cm-1). High resolution mass spectra (HRMS) were acquired on Thermo Scientific LTQ Orbitrap XL with an ESI source.

Commercial reagents including N-phenyl-2-aminobenzamide **1a** and solvent were purchased from Adamas, J&K, Energy, Sigma-Aldrich, Alfa Aesar, Acros Organics, TCI and used as received unless otherwise stated.

Preparation of 1n, 1o, 1p, 1q, 1r, and 1s.

According to a literature procedure,[15] **1n**, **1o** and **1p** were prepared via Cu-catalyzed C–N cross coupling reactions. A Schlenk tube was charged with CuI (9.7 mg, 0.050 mmol, 5.0 mol%), 2-aminobenzamide (1.2 mmol), K_2CO_3 (276 mg, 2.0 equiv), evacuated and backfilled with nitrogen. N,N'-dimethylethylenediamine (11 μL, 0.10 mmol, 10 mol%), bromobenzenes (1.0 mmol) and toluene (1.0 mL) were then added under nitrogen. The Schlenk tube was sealed and the reaction mixture was stirred in an oil bath at 110 °C for 22 hours.

*2-amino-4-methyl-N-phenylbenzamide(**1n**).* Follow above-mentioned procedure, purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 8:1. **1n** was obtained as yellow solid (160.5 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (br, 1H), 7.55 (dd, *J* = 8.6, 1.0 Hz, 2H), 7.36 (m, 3H), 7.16 – 7.10 (m, 1H), 6.53 (m, 2H), 5.50 (br, 2H), 2.28 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 167.6, 149.2, 143.4, 138.0, 129.1, 127.1, 124.4, 120.5, 118.1, 117.9, 113.5, 21.5. Melting point(°C): 107.1-108.8. HRMS (ESI) m/z calcd for $C_{14}H_{15}N_2O^+$ $(M+H)^+$ 227.1179, found 227.1177. IR (cm^{-1}): 3462, 3278, 2914, 1525, 1440, 1258, 746, 690.

*2-amino-4-chloro-N-phenylbenzamide **(10)**.* Follow above-mentioned procedure, purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 8:1. **10** was obtained as yellow solid (161.1 mg, 66%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (br, 1H), 7.54 (dd, *J* = 8.6, 1.0 Hz, 2H), 7.41 – 7.33 (m, 3H), 7.18 – 7.13 (m, 1H), 6.70 (d, *J* = 2.0 Hz, 1H), 6.66 (dd, *J* = 8.4, 2.0 Hz, 1H), 5.681 (br, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 166.9, 150.1, 138.6, 137.6, 129.1, 128.5, 124.7, 120.7, 116.9, 116.8, 114.5. Melting point(°C): 138.2-140.9. HRMS (ESI) m/z calcd for $C_{13}H_{12}ClN_2O^+$ $(M+H)^+$ 247.0633, found 247.0633. IR (cm^{-1}): 3490, 3380, 3282, 1933, 1443, 1255, 1102, 846, 690.

*2-amino-5-chloro-N-phenylbenzamide **(1p)**.* Follow above-mentioned procedure, purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 8:1. **1p** was obtained as yellow solid (148.7 mg, 60%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (br, 1H), 7.56 (dd, *J* = 8.5, 1.0 Hz, 2H), 7.43 (d, *J* = 2.4 Hz, 1H), 7.37 (t, *J* = 8.0 Hz, 2H), 7.22 – 7.14 (m, 2H), 6.66 (d, *J* = 8.8 Hz, 1H), 5.48 (br, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 166.4, 147.5, 137.5, 132.6, 129.1, 126.8, 124.8, 121.2, 120.7, 118.8, 117.2. Melting point(°C): 154.4-160.1. HRMS (ESI) m/z calcd for $C_{13}H_{11}ClN_2O^+$ $(M+H)^+$ 247.0633, found 247.0634. IR (cm^{-1}): 3409, 3282, 1882, 1517, 1331, 821, 691.

According to a literature procedure,[4c] **1q**, **1r** and **1s** were prepared via decarboxylative amination of corresponding isatoic anhydrides. A flame-dried 50 mL pear shaped flask were placed with a stirring bar. Isatoic anhydride (214.5 mg, 1 mmol, 1.0 equiv), aromatic amine (1 mmol, 1.0 equiv), and EtOAc (2.0 mL) were added. The resulting mixture was stirred vigorously at 70 °C temperature for 12 hours.

*2-amino-5-bromo-N-phenylbenzamide **(1q)**.* Follow above-mentioned procedure, purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 5:1. **1q** was obtained as yellow solid (185.6 mg, 64%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (s, 1H), 7.56 (dd, *J* = 8.6, 1.4 Hz, 3H), 7.41 – 7.35 (m, 2H), 7.32 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.20 – 7.13 (m, 1H), 6.61 (d, *J* = 8.4 Hz, 1H), 5.50 (s, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 166.3, 147.9, 137.5, 135.4, 129.6, 129.1, 124.8, 120.7, 119.1, 117.8, 107.9. Melting point(°C): 159.7-163.2. HRMS (ESI) m/z calcd for $C_{13}H_{12}BrN_2O^+$ $(M+H)^+$ 291.0128, found 291.0130. IR (cm^{-1}): 3467, 3372, 3288, 1637, 1537, 1442, 1252, 818, 752,690.

*2-amino-5-nitro-N-phenylbenzamide **(1r)**.* Follow above-mentioned procedure, purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 3:1. **1r** was obtained as yellow solid (138.8 mg, 54%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (s, 1H), 8.15 (d, *J* = 8.4 Hz, 1H), 7.84 (s, 1H), 7.59 (d, *J* = 8.0 Hz, 2H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.21 (t, *J* = 7.6 Hz, 1H), 6.71 (d, *J* = 8.8 Hz, 1H), 6.49 (s, 2H). ^{13}C{^{1}H} NMR (101 MHz, DMSO) δ 166.5, 155.7, 139.2, 135.4, 129.1, 128.1, 126.9, 124.4, 121.3, 116.4, 114.0. Melting point(°C): 207.8-209.8. HRMS (ESI) m/z calcd for $C_{13}H_{12}N_3O_3^+$ $(M+H)^+$ 258.0873, found 258.0875. IR (cm^{-1}): 3478, 3368, 3341, 2923, 1638, 1321, 1131, 749.

*2-amino-5-methoxy-N-phenylbenzamide **(1s)**.* Follow above-mentioned procedure, purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 4:1. **1s** was obtained as yellow solid (121 mg, 50%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.58 (d, *J* = 7.6 Hz, 2H), 7.36 (t, *J* = 7.8 Hz, 2H), 7.14 (t, *J* = 7.4 Hz, 1H), 7.06 (d, *J* = 2.8 Hz, 1H), 6.91 (dd, *J* = 8.8, 2.8 Hz, 1H), 6.72 (d, *J* = 8.8 Hz, 1H), 4.91 (s, 2H), 3.78 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 167.0, 151.7, 142.0, 137.9, 129.1, 124.5, 120.5, 119.7, 119.4, 118.2, 112.2, 56.1. Melting point(°C):

127.1-128.3. HRMS (ESI) m/z calcd for $C_{14}H_{15}N_2O_2^+$ $(M+H)^+$ 243.1128, found 243.1125. IR (cm^{-1}): 3422, 3295, 1647, 1502, 1248, 1044, 824, 693.

Preparation of N,N'-(1,3-phenylene)bis(2-aminobenzamide)

A flame-dried 50 mL pear shaped flask were placed with a stirring bar. Isatoic anhydride (800 mg, 4.4 mmol, 2.2 equiv), benzene-1,3-diamine (216.4 mg, 2 mmol, 1.0 equiv), and EtOAc (2.0 mL) were added. The resulting mixture was stirred in an oil bath at 70 °C for 24 hours.[4c] Purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 3:1. The product was obtained as white solid (415.2 mg, 60%). ^1H NMR (400 MHz, CD_3CN) δ 8.65 (s, 2H), 8.15 (s, 1H), 7.61 (d, *J* = 7.6 Hz, 2H), 7.44 – 7.31 (m, 3H), 7.26 (t, *J* = 7.4 Hz, 2H), 6.78 (d, *J* = 8.2 Hz, 2H), 6.68 (t, *J* = 7.5 Hz, 2H), 5.78 (s, 4H). $^{13}C\{^1H\}$ NMR (101 MHz, CD_3CN) δ 168.9, 150.6, 140.2, 133.5, 129.8, 129.3, 118.3, 117.7, 117.3, 116.7, 114.1. Melting point(°C): 184.8-186.8. HRMS (ESI) m/z calcd for $C_{20}H_{19}N_4O_2^+$ $(M+H)^+$ 347.1503, found 347.1504. IR (cm^{-1}): 3495, 3367, 3266, 1931, 1435, 1248, 1158, 752, 690.

Typical experimental procedures.

General Procedures A:

A flame-dried 50 mL pear shaped flask were placed with a stirring bar. Then, N-Phenyl-2-aminobenzamide (42.4 mg, 0.2 mmol, 1.0 equiv), CuCl (4.0 mg, 0.04 mmol, 20 mol%), Et_3N (14.0 μL, 0.1 mmol, 0.5 equiv), arylboronic acid (0.3 mmol, 1.5 equiv), and MeOH (4.0 mL) were added. The resulting mixture was stirred vigorously at ambient temperature for 3 hours. Then DMSO (1.0 mL) was added and the temperature was raised to 120 °C in an oil bath. The mixture was stirred for 4 hours. MeOH (4.0 mL) was distilled into a beaker. After cooling, the reaction mixture was treated with EtOAc (5.0 mL) and water (5.0 mL). The organic layer was separated, and the aqueous layer was extracted with EtOAc (3 × 5.0 mL). The combined organic layer was dried over sodium sulfate, and concentrated to afford residue, which was purified by column chromatography on silica gel to give the target product.

General Procedures B:

A flame-dried 50 mL pear shaped flask were placed with a stirring bar. Isatoic anhydride (32.0 mg, 0.2 mmol, 1.0 equiv), Amine (0.2 mmol, 1.0 equiv), and EtOAc (0.5 mL) were added. The resulting mixture was stirred vigorously at 70 °C temperature for 12 hours. Cooling to room temperature, CuCl (4.0 mg, 0.04 mmol, 20 mol%), Et_3N (14.0 μL, 0.1 mmol, 0.5 equiv), arylboronic acid (0.3 mmol, 1.5 equiv), and MeOH (4.0 mL) were added. Then DMSO (1.0 mL) was added and the temperature was raised to 120 °C in an oil bath. The mixture was stirred for 4 hours. MeOH (4.0 mL) was distilled into a beaker. After cooling, the reaction mixture was treated with EtOAc (5.0 mL) and water (5.0 mL). The organic layer was separated, and the aqueous layer was extracted with EtOAc (3 × 5.0 mL). The combined organic layer was dried over sodium sulfate, and concentrated to afford residue, which was purified by column chromatography on silica gel to give the target product.

Experimental procedures for large-scale synthesis of N,N'-Diaryl Indazole-3-ones:

A flame-dried 250 mL pear shaped flask were placed with a stirring bar. Then, N-Phenyl-2-aminobenzamide (636 mg, 3 mmol, 1.0 equiv), CuCl (60 mg, 0.6 mmol, 20 mol%), Et_3N (210 μL, 1.5 mmol, 0.5 equiv), phenylboronic acid (548 mg, 4.5 mmol, 1.5 equiv), and MeOH (60.0 mL) were added. The resulting mixture was stirred vigorously at ambient temperature for 12 hours. Then DMSO (10.0 mL) was added and the temperature was raised to 120 °C in an oil bath. The mixture was stirred for 12 hours. MeOH (60.0 mL) was distilled into a beaker. After cooling, the reaction mixture was treated with EtOAc (30 mL) and water (30 mL). The organic layer was separated, and the aqueous layer was extracted with EtOAc (3 ×

30 mL). The combined organic layer was dried over sodium sulfate, and concentrated to afford residue, which was purified by column chromatography on silica gel to give the target product as yellow solid (626 mg, 73%).

A flame-dried 250 mL pear shaped flask were placed with a stirring bar. Isatoic anhydride (489.4 mg, 3 mmol, 1.0 equiv), aniline (3 mmol, 1.0 equiv), and EtOAc (5.0 mL) were added. The resulting mixture was stirred vigorously at 70 °C temperature for 12 hours. Cooling to room temperature， then CuCl (60 mg, 0.6 mmol, 20 mol%), Et_3N (210 μL, 1.5 mmol, 0.5 equiv), phenylboronic acid (1097 mg, 9 mmol, 3 equiv), and MeOH (60.0 mL) were added. The mixture was stirred vigorously at ambient temperature for 12 hours. Then DMSO (10.0 mL) was added and the temperature was raised to 120 °C in an oil bath. The mixture was stirred for 12 hours. MeOH (60.0 mL) was distilled into a beaker. The mixture was stirred for 12 hours. After cooling,the reaction mixture was treated with EtOAc (30 mL) and water (30 mL). The organic layer was separated, and the aqueous layer was extracted with EtOAc (3 × 30 mL). The combined organic layer was dried over sodium sulfate, and concentrated to afford residue, which was purified by column chromatography on silica gel to give the target product as yellow solid (558 mg, 65%).

Preparation and characterization data for isolated products.

Compounds **3a**,[4c] **3b**,[4c] **3c**,[4c] **3d**,[4c] **3e**,[4c] **3g**,[4c] **3h**,[4c] **3n**,[4c] **3o**,[4c] **3p**,[4c] **3q**,[4c] **3r**,[4c] **4a**,[4c] **4b**,[4c] **4f**,[4c] are known compounds and the characterization data were in accordance with the literature. ^1H / ^{13}C NMR data for these compounds are provided here for completion sake.

*1,2-diphenyl-1H-indazol-3(2H)-one (**3a**).* Follow general procedures A, purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 5:1. **3a** was obtained as yellow solid (53.7 mg, 94%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.6 Hz, 1H), 7.60 (dd, *J* = 8.8, 1.2 Hz, 2H), 7.50 (ddd, *J* = 8.4, 7.3, 1.2 Hz, 1H), 7.37 – 7.27 (m, 6H), 7.20 (m, 3H), 7.15 – 7.10 (m, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 162.7, 150.2, 142.3, 135.9, 133.1, 129.7, 128.9, 127.5, 125.9, 124.5, 124.2, 123.5, 123.3, 118.3, 112.4.

*2-phenyl-1-(p-tolyl)-1H-indazol-3(2H)-one (**3b**).* Follow general procedures A, purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 5:1. **3b** was obtained as yellow solid (46.9 mg, 78%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 7.6 Hz, 1H), 7.59 (dd, J = 8.8, 1.2 Hz, 2H), 7.51 (ddd, J = 8.4, 7.2, 1.2 Hz, 1H), 7.38 – 7.31 (m, 2H), 7.25 – 7.23 (m, 1H), 7.19 – 7.12 (m, 6H), 2.29 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 162.7, 150.5, 139.8, 137.5, 135.9, 133.0, 130.2, 128.8, 125.9, 124.5, 124.3, 123.4, 123.3, 118.3, 112.5, 21.0.

*1-(4-methoxyphenyl)-2-phenyl-1H-indazol-3(2H)-one **(3c)*** Follow general procedures A, purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 3:1. **3c** was obtained as yellow solid (45.5 mg, 72%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.0 Hz, 1H), 7.58 (dd, *J* = 8.8, 1.2 Hz, 2H), 7.50 (m, 1H), 7.34 (t, *J* = 8.0 Hz, 2H), 7.25 (d, *J* = 6.0 Hz, 1H), 7.23 – 7.17 (m, 2H), 7.15 (t, *J* = 7.4 Hz, 1H), 7.08 (d, *J* = 8.4 Hz, 1H), 6.84 (d, *J* = 8.8 Hz, 2H), 3.74 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 162.5, 158.9, 150.9, 135.7, 135.0, 133.0, 128.8, 126.2, 126.0, 124.4, 123.7, 123.2, 118.3, 114.8, 112.6, 55.4.

*2-phenyl-1-(m-tolyl)-1,2-dihydro-3H-indazol-3-one **(3d)*** Follow general procedures A, purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 5:1. **3d** was obtained as yellow solid (53.2 mg, 89%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.0 Hz, 1H), 7.61 (dd, *J* = 8.4, 1.2 Hz, 2H), 7.52 (m, 1H), 7.35 (t, *J* = 8.0 Hz, 2H), 7.25 – 7.13 (m, 4H), 7.12 – 7.07 (m, 2H), 7.04 (d, *J* = 7.4 Hz, 1H), 2.31 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 162.8, 150.4, 142.4, 139.8, 136.0, 133.0, 129.4, 128.9, 128.4, 125.9, 124.7, 124.5, 123.4, 123.3, 121.4, 118.3, 112.5, 21.4.

*1-(3-methoxyphenyl)-2-phenyl-1H-indazol-3(2H)-one **(3e)*** Follow general procedures A, purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 3:1. **3e** was obtained as yellow solid (51.2 mg, 81%) ^1H

NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 7.6 Hz, 1H), 7.61 (dd, *J* = 8.4, 1.2 Hz, 2H), 7.54 – 7.48 (m, 1H), 7.38 – 7.31 (m, 2H), 7.24 (d, *J* = 7.2 Hz, 3H), 7.17 – 7.12 (m, 1H), 6.91 (ddd, *J* = 8.0, 2.0, 0.8 Hz, 1H), 6.80 (t, *J* = 2.2 Hz, 1H), 6.75 (ddd, *J* = 8.4, 2.4, 0.4 Hz, 1H), 3.70 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 162.8, 160.5, 150.1, 143.5, 136.0, 133.1, 130.3, 128.9, 125.9, 124.5, 123.5, 123.2, 118.3, 116.4, 112.9, 112.4, 109.9, 55.4.

1-(4-(methylthio)phenyl)-2-phenyl-1H-indazol-3(2H)-one ***(3f)*** Follow general procedures A, purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 3:1. **3f** was obtained as yellow solid (54.5 mg, 82%) ^1H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.6 Hz, 1H), 7.58 (dd, *J* = 8.8, 1.2 Hz, 2H), 7.55 – 7.50 (m, 1H), 7.35 (t, *J* = 8.0 Hz, 2H), 7.28 (d, *J* = 7.2 Hz, 1H), 7.21 (s, 4H), 7.16 (t, *J* = 8.0 Hz, 2H), 2.44 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 162.7, 150.4, 139.4, 138.3, 135.8, 133.1, 128.9, 127.2, 126.0, 124.9, 124.5, 123.5, 123.4, 118.3, 112.4, 15.6. Melting point(°C): 53.9-60.3. HRMS (ESI) m/z calcd for $C_{20}H_{17}N_2OS^+$ $(M+H)^+$ 333.1056, found 333.1060. IR (cm^{-1}): 2919, 2366, 1676, 1457, 1272, 715, 694.

1-(4-fluorophenyl)-2-phenyl-1H-indazol-3(2H)-one ***(3g)*** Follow general procedures A, purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 5:1. **3g** was obtained as yellow solid (51.9 mg, 85%) ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.0 Hz, 1H), 7.60 – 7.51 (m, 3H), 7.39 – 7.32 (m, 2H), 7.29 (m, 3H), 7.20 – 7.15 (m, 1H), 7.12 (d, *J* = 8.4 Hz, 1H), 7.08 – 7.01 (m, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 162.6, 161.5 (d, *J* = 247), 160.3, 150.5, 138.4 (d, *J* = 3 Hz), 135.6, 133.2, 129.0, 126.4 (d, *J* = 9 Hz), 126.2, 124.6, 123.6, 123.5, 118.4, 116.7 (d, *J* = 23 Hz), 112.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ -113.18.

1-(4-chlorophenyl)-2-phenyl-1,2-dihydro-3H-indazol-3-one ***(3h)*** Follow general procedures A, purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 5:1. **3h** was obtained as yellow solid (51.6 mg, 81%) ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.0 Hz, 1H), 7.60 – 7.51 (m, 3H), 7.39 – 7.28 (m, 5H), 7.26 – 7.22 (m, 2H), 7.18 (t, *J* = 7.9 Hz, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 162.7, 150.1, 141.0, 135.7, 133.3, 133.2, 129.9, 129.0, 126.2, 125.6, 124.7, 123.8, 123.3, 118.4, 112.3.

1-(4-bromophenyl)-2-phenyl-1,2-dihydro-3H-indazol-3-one ***(3i)*** Follow general procedures A, purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 5:1. **3i** was obtained as yellow solid (64.2 mg, 88%) ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.0 Hz, 1H), 7.56 (m, 3H), 7.48 (d, *J* = 8.8 Hz, 2H), 7.36 (t, *J* = 8.0 Hz, 2H), 7.29 (t, *J* = 7.6 Hz, 1H), 7.21 – 7.15 (m, 4H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 162.7, 159.0, 141.6, 135.7, 133.3, 132.9, 129.0, 126.2, 125.8, 124.7, 123.8, 123.3, 121.0, 118.4, 112.3. Melting point(°C): 130.3-132.1. HRMS (ESI) m/z calcd for $C_{19}H_{14}BrN_2O^+$ $(M+H)^+$ 365.0284, found 365.0288. IR (cm^{-1}): 3051, 2343, 1686, 1476, 1272, 927, 749.

2-phenyl-1-(4-(trifluoromethyl)phenyl)-1,2-dihydro-3H-indazol-3-one ***(3j)*** Follow general procedures A, purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 5:1. **3j** was obtained as yellow solid (58.9 mg, 83%) ^1H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 7.6 Hz, 1H), 7.64 (d, *J* = 8.4 Hz, 2H), 7.60 – 7.55 (m, 3H), 7.43 (d, *J* = 8.4 Hz, 2H), 7.37 (d, *J* = 8.0 Hz, 2H), 7.32 (t, *J* = 7.4 Hz, 1H), 7.28 (s, 1H), 7.19 (t, *J* = 7.6 Hz, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 162.9, 149.4, 145.6, 135.8 133.5, 129.1, 129.1 (q, *J* = 33 Hz), 127.0 (q, *J* = 3 Hz), 126.2, 125.6 (d, *J* = 371 Hz), 124.8, 124.1, 123.9, 123.0, 118.4, 112.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.49. Melting point(°C): 52.9-54.9. HRMS (ESI) m/z calcd for $C_{20}H_{14}F_3N_2O^+$ $(M+H)^+$ 355.1053, found 355.1054. IR (cm^{-1}): 3066, 2360, 1694, 1607, 1324, 1065, 929, 782, 609.

2-phenyl-1-(4-vinylphenyl)-1,2-dihydro-3H-indazol-3-one ***(3k)*** Follow general procedures A, purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 4:1. **3k** was obtained as yellow solid (43.0 mg, 69%) ^1H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.6 Hz, 1H), 7.59 (d, *J* = 7.6 Hz, 2H), 7.56 – 7.49 (m, 1H), 7.41 – 7.31 (m, 4H), 7.27 (d, *J* = 7.3 Hz, 1H), 7.26 – 7.23 (m, 2H), 7.20 (d, *J* = 8.4 Hz, 1H), 7.15 (m, 1H), 6.64 (dd, *J* = 17.6, 10.8 Hz, 1H), 5.69 (d, *J* = 17.6 Hz, 1H), 5.25 (d, *J* = 11.2 Hz, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 162.7, 150.1, 141.7, 136.8, 135.9, 135.6, 133.1, 128.9, 127.4, 126.0, 124.6, 124.3, 123.5, 123.3, 118.3, 114.9, 112.3. Melting point(°C): 53.8-55.5. HRMS (ESI) m/z calcd for $C_{21}H_{17}N_2O^+$ $(M+H)^+$ 313.1335, found 313.1333. IR (cm^{-1}): 3440, 2970, 1693, 1463, 1309, 754.

2-phenyl-1-(4-(trimethylsilyl)phenyl)-1,2-dihydro-3H-indazol-3-one ***(3l)*** Follow general procedures A, purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 4:1. **3l** was obtained as yellow solid (55.4 mg, 87%) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.6 Hz, 1H), 7.62 (dd, *J* = 8.4, 1.2 Hz, 2H), 7.55 – 7.47 (m, 3H), 7.36 (t, *J* = 8.0 Hz, 2H), 7.28 (s, 2H), 7.24 (m, 2H), 7.16 (t, *J* = 7.4 Hz, 1H), 0.22 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 164.1, 151.3, 144.0, 141.1, 137.2, 135.8, 134.3, 130.1, 127.1, 125.7, 124.6, 124.4, 124.3, 119.4, 113.6. Melting point(°C): 213.6-215.4. HRMS (ESI) m/z calcd for $C_{22}H_{23}N_2OSi^+$ $(M+H)^+$ 359.1574, found 359.1578. IR (cm^{-1}): 2952, 2343, 1698, 1458, 1105, 836, 749.

Methyl 4-(3-oxo-2-phenyl-2,3-dihydro-1H-indazol-1-yl)benzoate ***(3m)*** Follow general procedures A, purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 3:1. **3m** was obtained as yellow solid (42.4 mg, 62%) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.4 Hz, 2H), 7.99 (d, *J* = 7.2 Hz, 1H), 7.56 (m, 3H), 7.34 (m, 6H), 7.16 (t, *J* = 7.4 Hz, 1H), 3.88 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 166.1, 162.8, 149.2, 146.3, 135.8, 133.4, 131.2, 129.1, 128.8, 126.1, 124.8, 123.9, 123.4, 123.0, 118.4, 111.9, 52.3. Melting point(°C): 178.9-182.1. HRMS (ESI) m/z calcd for $C_{21}H_{17}N_2O_3^+$ $(M+H)^+$ 345.1234, found 345.1231. IR (cm^{-1}): 3044, 2949, 2342, 1686, 1475, 1262, 1105, 926, 746.

6-methyl-1,2-diphenyl-1H-indazol-3(2H)-one ***(3n)*** Follow general procedures A, purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 5:1. **3n** was obtained as yellow solid (55.1 mg, 92%) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.0 Hz, 1H), 7.58 (m, 2H), 7.40 – 7.27 (m, 6H), 7.23 (m, 1H), 7.16 – 7.11 (m, 1H), 7.08 (dd, *J* = 8.0, 0.4 Hz, 1H), 6.98 (s, 1H), 2.41 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 162.9, 150.7, 144.3, 142.5, 136.1, 129.6, 128.8, 127.4, 125.8, 125.1, 124.3, 124.2, 123.2, 115.9, 112.2, 22.3.

6-chloro-1,2-diphenyl-1H-indazol-3(2H)-one ***(3o)*** Follow general procedures A, purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 5:1. **3o** was obtained as yellow solid (58.3 mg, 91%) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.4 Hz, 1H), 7.55 (dd, *J* = 8.4, 1.2 Hz, 2H), 7.36 (m, 4H), 7.30 – 7.26 (m, 3H), 7.23 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.17 (m, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 161.9, 150.5, 141.5, 139.5, 135.6, 129.9, 120.0, 127.9, 126.2, 125.7, 124.3, 124.3, 123.4, 116.7, 112.5.

5-chloro-1,2-diphenyl-1H-indazol-3(2H)-one ***(3p)*** Follow general procedures A, purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 5:1. **3p** was obtained as yellow solid (55.7 mg, 87%) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 2.0 Hz, 1H), 7.57 (dd, *J* = 8.6, 1.0 Hz, 2H), 7.46 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.39 – 7.32 (m, 4H), 7.28 (d, *J* = 2.4 Hz, 2H), 7.25 – 7.22 (m, 1H), 7.16 (t, *J* = 7.6 Hz, 1H), 7.12 (d, *J* = 8.8 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 161.4, 148.5, 141.8, 135.5, 133.4, 129.8, 129.1, 129.0, 127.9, 126.3, 124.3, 124.0, 123.4, 119.6, 113.8.

5-bromo-1,2-diphenyl-1H-indazol-3(2H)-one ***(3q)*** Follow general procedures A, purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 5:1. **3q** was obtained as yellow solid (57.7 mg, 79%) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, *J* = 1.7 Hz, 1H), 7.58 (ddd, *J* = 9.7, 8.6, 1.5 Hz, 3H), 7.35 (dt, *J* = 10.7, 7.7 Hz, 4H), 7.27 (d, *J* = 2.0 Hz, 1H), 7.16 (t, *J* = 7.4 Hz, 1H), 7.07 (d, *J* = 8.7 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 161.2, 148.8, 141.7, 136.0, 135.5, 129.8, 129.0, 127.9, 127.1, 126.3, 124.3, 123.4, 120.0, 116.3, 114.1.

5-nitro-1,2-diphenyl-1H-indazol-3(2H)-one ***(3r)*** Follow general procedures A, purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 3:1. **3r** was obtained as yellow solid (45.4 mg, 69%) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (d, *J* = 2.0 Hz, 1H), 8.38 (dd, *J* = 9.1, 2.3 Hz, 1H), 7.50 (dd, *J* = 8.6, 1.1 Hz, 2H), 7.45 – 7.40 (m, 2H), 7.34 (dt, *J* = 14.2, 8.0 Hz, 5H), 7.26 (d, *J* = 9.0 Hz, 1H), 7.24 – 7.19 (m, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 161.0, 151.3, 143.7, 134.7, 130.10, 129.2, 128.6, 128.2, 127.1, 124.8, 124.0, 121.9, 117.8, 112.3.

5-methoxy-1,2-diphenyl-1H-indazol-3(2H)-one ***(3s)*** Follow general procedures A, purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 4:1. **3s** was obtained as yellow solid (54.9 mg, 87%) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 7.6 Hz, 2H), 7.38 – 7.35 (m, 2H), 7.33 (d, *J* = 8.0 Hz, 3H), 7.27 (d, *J* = 6.8 Hz, 2H), 7.21 (t, *J* = 7.2 Hz, 1H), 7.17 – 7.08 (m, 3H), 3.86 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 162.8, 156.6, 145.4, 143.0, 136.0, 129.6, 128.9, 127.4, 125.9,

124.0, 123.5, 123.2, 118.9, 113.9, 104.6, 55.9. Melting point(°C): 91.6-94.2. HRMS (ESI) m/z calcd for $C_{20}H_{17}N_2O_2^+$ $(M+H)^+$ 317.1285, found 317.1288. IR (cm^{-1}): 3442, 2833, 1684, 1489, 1250, 1025, 824, 739.

1,2-diphenyl-1H-indazol-3(2H)-one ***(3a)*** Follow general procedures B, purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 5:1. **3a** was obtained as white solid (38.8 mg, 68%) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.6 Hz, 1H), 7.60 (dd, *J* = 8.8, 1.2 Hz, 2H), 7.50 (ddd, *J* = 8.4, 7.2, 1.2 Hz, 1H), 7.37 – 7.27 (m, 6H), 7.20 (m, 3H), 7.15 – 7.10 (m, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 162.7, 150.2, 142.3, 135.9, 133.1, 129.7, 128.9, 127.5, 125.9, 124.5, 124.2, 123.5, 123.3, 118.3, 112.4.

1-phenyl-2-(p-tolyl)-1H-indazol-3(2H)-one ***(4a)*** Follow general procedures B, purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 5:1. **4a** was obtained as white solid (38.8 mg, 68%) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.0 Hz, 1H), 7.55 – 7.42 (m, 3H), 7.35 (t, *J* = 7.6 Hz, 2H), 7.26 (m, 4H), 7.18 (d, *J* = 8.4 Hz, 1H), 7.13 (d, *J* = 8.0 Hz, 2H), 2.27 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 162.7, 150.1, 142.3, 135.9, 133.3, 132.9, 129.6, 129.5, 127.5, 124.5, 124.4, 123.4, 123.3, 118.3, 112.3, 21.0.

1-phenyl-2-(m-tolyl)-1H-indazol-3(2H)-one ***(4b)*** Follow general procedures B, purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 5:1. **4b** was obtained as white solid (34.6 mg, 58%) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.6 Hz, 1H), 7.51 (m, 1H), 7.47 (s, 1H), 7.39 – 7.27 (m, 6H), 7.24 – 7.17 (m, 3H), 6.96 (d, *J* = 7.6 Hz, 1H), 2.33 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 162.8, 150.2, 142.4, 138.8, 135.8, 133.0, 129.6, 128.6, 127.5, 126.9, 124.5, 124.3, 124.2, 123.4, 120.5, 118.3, 112.4, 21.5.

1-(4-bromophenyl)-2-phenyl-1H-indazol-3(2H)-one ***(4c)*** Follow general procedures B, purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 4:1. **4c** was obtained as yellow solid (38.0 mg, 52%) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.0 Hz, 1H), 7.56 (m, 3H), 7.48 (d, *J* = 8.8 Hz, 2H), 7.36 (t, *J* = 7.9 Hz, 2H), 7.29 (t, *J* = 7.6 Hz, 1H), 7.21 – 7.15 (m, 4H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 162.7, 150.0, 141.6, 135.7, 133.3, 132.9, 129.0, 126.2, 125.8, 124.7, 123.8, 123.3, 121.0, 118.4, 112.3. Melting point(°C): 130.3-132.1. HRMS (ESI) m/z calcd for $C_{19}H_{14}BrN_2O^+$ $(M+H)^+$ 365.0284, found 365.0288. IR (cm^{-1}): 3051, 2343, 1686, 1476, 1272, 927, 749.

1-(4-chlorophenyl)-2-(4-methoxyphenyl)-1H-indazol-3(2H)-one ***(4d)*** Follow general procedures B, purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 3:1. **4d** was obtained as yellow solid (45.4 mg, 65%) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.6 Hz, 1H), 7.53 (m, 1H), 7.46 – 7.41 (m, 2H), 7.35 – 7.31 (m, 2H), 7.30 – 7.27 (m, 1H), 7.23 – 7.19 (m, 2H), 7.13 (d, *J* = 8.0 Hz, 1H), 6.90 – 6.86 (m, 2H), 3.77 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 162.7, 158.0, 149.8, 140.8, 133.2, 133.0, 129.9, 128.5, 125.9, 125.4, 124.6, 123.6, 118.4, 114.4, 112.2, 55.4. Melting point(°C): 152.5-157.3. HRMS (ESI) m/z calcd for $C_{20}H_{16}ClN_2O_2^+$ $(M+H)^+$ 351.0895, found 351.0893 IR (cm^{-1}): 3365, 3271, 1680, 1506, 1464, 1245, 1089, 1020, 817.

1-(4-chlorophenyl)-2-(2-methoxyphenyl)-1H-indazol-3(2H)-one ***(4e)*** Follow general procedures B, purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 3:1. **4e** was obtained as yellow solid (28.8 mg, 41%) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 7.6 Hz, 1H), 7.51 (m, 1H), 7.32 – 7.27 (m, 3H), 7.25 (s, 1H), 7.21 (m, 3H), 7.06 (d, *J* = 8.4 Hz, 1H), 6.98 (dd, *J* = 8.4, 0.8 Hz, 1H), 6.91 (td, *J* = 7.7, 1.2 Hz, 1H), 3.85 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 162.9, 155.8, 149.6, 140.0, 133.4, 132.7, 130.3, 129.6, 129.5, 126.8, 124.5, 124.1, 122.9, 120.8, 118.0, 112.7, 111.8, 56.1. Melting point(°C): 73.1-78.5. HRMS (ESI) m/z calcd for $C_{20}H_{16}ClN_2O_2^+$ $(M+H)^+$ 351.0895, found 351.0899. IR (cm^{-1}): 3435, 3065, 2838, 2360, 1694, 1461, 1285, 751.

2-(4-chlorophenyl)-1-phenyl-1H-indazol-3(2H)-one ***(4f)*** Follow general procedures B, purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 5:1. **4f** was obtained as yellow solid (29.2 mg, 46%) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.6 Hz, 1H), 7.58 – 7.51 (m, 3H), 7.38 (m, 2H), 7.29 (ddd, *J* = 6.9, 5.0, 3.8 Hz, 6H), 7.19

(d, *J* = 8.4 Hz, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 162.8, 150.4, 142.2, 134.5, 133.4, 131.4, 129.8, 129.1, 127.7, 124.6, 124.2, 124.2, 123.7, 118.1, 112.5.

2-(4-chlorophenyl)-1-(3-methoxyphenyl)-1H-indazol-3(2H)-one ***(4g)*** Follow general procedures B, purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 3:1. **4g** was obtained as yellow solid (28.3 mg, 40%) ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.0 Hz, 1H), 7.60 – 7.51 (m, 3H), 7.34 – 7.27 (m, 4H), 7.24 (d, *J* = 8.3 Hz, 1H), 6.93 – 6.87 (m, 1H), 6.81 – 6.75 (m, 2H), 3.74 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 162.8, 160.6, 150.3, 143.4, 134.6, 133.4, 131.3, 130.5, 129.1, 124.6, 124.1, 123.7, 118.1, 116.3, 113.0, 112.5, 110.0, 55.4. Melting point(°C): 63.3-71.5. HRMS (ESI) m/z calcd for $C_{20}H_{16}ClN_2O_2^+$ $(M+H)^+$ 351.0895, found 351.0891. IR (cm^{-1}): 3435, 2934, 1694, 1489, 1090, 754.

2-(4-fluorophenyl)-1-(4-methoxyphenyl)-1H-indazol-3(2H)-one ***(4h)*** Follow general procedures B, purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 3:1. **4h** was obtained as yellow solid (20.0 mg, 30%) ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.0 Hz, 1H), 7.57 – 7.49 (m, 3H), 7.28 (s, 1H), 7.18 (d, *J* = 8.8 Hz, 2H), 7.05 (m, 3H), 6.86 (m, 2H), 3.77 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 162.6, 160.6 (d *J* = 245), 159.1, 150.9, 134.7, 133.1, 131.7 (d, *J* = 3 Hz), 126.4, 125.6 (d, *J* = 9 Hz), 124.4, 123.3, 118.1, 115.8 (d, *J* = 22 Hz), 114.8, 112.6, 55.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ -115.51. Melting point(°C): 97.5-99.4. HRMS (ESI) m/z calcd for $C_{20}H_{16}FN_2O_2^+$ $(M+H)^+$ 335.1190, found 335.1197. IR (cm^{-1}): 3435, 3070, 1686, 1503, 1219, 835.

1-(4-chlorophenyl)-2-(p-tolyl)-1H-indazol-3(2H)-one ***(4i)*** Follow general procedures B, purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 5:1. **4i** was obtained as yellow solid (46.6 mg, 70%) ^1H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.0 Hz, 1H), 7.53 (m, 1H), 7.42 (d, *J* = 8.4 Hz, 2H), 7.31 (m, 3H), 7.25 – 7.21 (dt, *J* = 8.8 Hz, 2.8H), 7.15 (dd, *J* = 8.3, 2.4 Hz, 3H), 2.30 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 162.6, 149.9, 141.0, 136.2, 133.1, 133.1, 133.1, 129.9, 129.6, 125.7, 124.6, 123.7, 123.5, 118.4, 112.2, 21.0. Melting point(°C): 156.3-157.8. HRMS (ESI) m/z calcd for $C_{20}H_{16}ClN_2O^+$ $(M+H)^+$ 335.0946, found 335.0950. IR (cm^{-1}): 3043, 2344, 1689, 1506, 1307, 1151, 1087, 802.

2-benzyl-1-phenyl-1,2-dihydro-3H-indazol-3-one ***(4j)*** Follow general procedures B, purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 3:1. **4j** was obtained as yellow solid (12.1 mg, 20%) ^1H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.6 Hz, 1H), 7.49 – 7.36 (m, 4H), 7.23 – 7.15 (m, 6H), 7.09 (m, 2H), 6.94 (d, *J* = 8.4 Hz, 1H), 4.95 (s, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 163.9, 149.8, 140.5, 136.3, 132.4, 129.8, 128.4, 128.4, 128.2, 127.7, 125.9, 124.1, 122.6, 118.0, 111.9, 46.2. Melting point(°C): 58.4-60.1. HRMS (ESI) m/z calcd for $C_{20}H_{17}N_2O^+$ $(M+H)^+$ 301.1335, found 301.1336. IR (cm^{-1}): 3431, 2924, 1682, 1445, 1305, 753, 700.

2-phenethyl-1-phenyl-1,2-dihydro-3H-indazol-3-one ***(4k)*** Follow general procedures B, purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 2:1. **4k** was obtained as yellow solid (26.2 mg, 42%) ^1H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 7.6 Hz, 1H), 7.51 – 7.36 (m, 4H), 7.24 – 7.15 (m, 6H), 7.05 (dd, *J* = 7.8, 1.4 Hz, 2H), 6.99 (d, *J* = 8.4 Hz, 1H), 4.04 – 3.94 (m, 2H), 2.96 – 2.85 (m, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 163.8, 149.8, 140.6, 138.2, 132.4, 129.9, 128.8, 128.5, 128.3, 126.5, 125.5, 123.9, 122.7, 118.3, 111.8, 44.2, 34.3. Melting point(°C): 94.1-98.7. HRMS (ESI) m/z calcd for $C_{21}H_{19}N_2O^+$ $(M+H)^+$ 315.1492, found 315.1494. IR (cm^{-1}): 3432, 2936, 1678, 1454, 1307, 929, 748, 703.

2,2'-(1,3-phenylene)bis(1-phenyl-1,2-dihydro-3H-indazol-3-one) Follow general procedures A, and arylboronic acid (3.0 equiv), CuCl (40 mol%), Et_3N (1.0 equiv). purification by flash chromatography on silica gel using petroleum ether : ethyl acetate = 1.5:1. target product was obtained as yellow solid (33.6 mg, 68%) ^1H NMR (400 MHz, $CDCl_3$) δ 7.94 (m, 3H), 7.52 (m, 2H), 7.41 (dd, *J* = 2.0, 1.0 Hz, 1H), 7.39 (d, *J* = 2.0 Hz, 1H), 7.35 – 7.27 (m, 6H), 7.26 – 7.21 (m, 7H), 7.18 (d, *J* = 8.3 Hz, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 162.7, 150.4, 142.3, 136.3, 133.2, 129.7, 129.2, 127.5, 124.5, 124.3, 123.5, 120.6, 118.3, 118.2, 112.6. Melting point(°C): 217.7-222.8. HRMS (ESI) m/z calcd for $C_{32}H_{23}N_4O_2^+$ $(M+H)^+$ 495.1816, found 495.1817. IR (cm^{-1}): 3448, 3054, 1679, 1490, 1285, 769, 697.

ASSOCIATED CONTENT

Supporting Information

Additional ^{1}H and ^{13}C spectra and spectral data for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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