[Bis-(trifluoroacetoxy)iodo]benzene-Mediated Oxidative Direct Amination C–N Bond Formation: Synthesis of 1*H*-Indazoles

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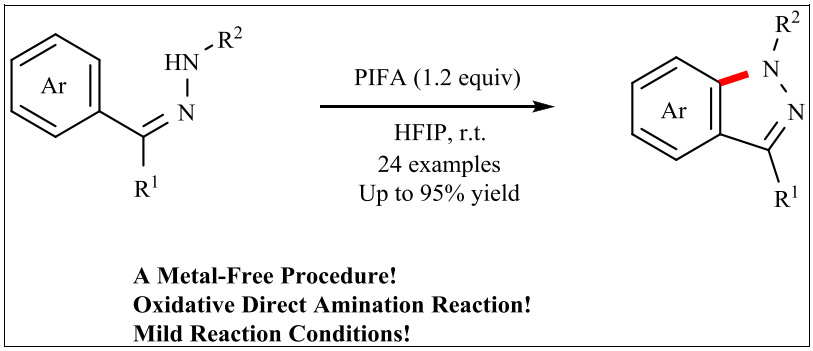
Additional Supporting Information may be found in the online version of this article.

Received April 20, 2016

DOI 10.1002/jhet.2839

Published online 00 Month 2017 in Wiley Online Library (wileyonlinelibrary.com).



An efficient [bis-(trifluoroacetoxy)iodo]benzene (PIFA)-mediated oxidative C-N bond formation is developed for the synthesis of 1*H*-indazoles from readily available arylhydrazones. The reaction tolerates a wide range of functional groups and has broad scope of substrates. Moreover, this method is a relative green and reliable method for rapid preparation of substituted 1*H*-indazoles under mild conditions.

1*H*-Indazoles-based molecules are important synthetic targets in biologically active molecules, synthetic drugs, and drug candidates [1]. In addition, they are used as ligands for generating metallic complexes [2]. To date, many methods have been established for the construction of the indazole skeleton (Fig. 1) [3]. Among them, Buchwald−Hartwig coupling, Ullmann-type aminations, and Goldberg-type *N*-arylations are the most reliable and widely used strategies, although prefunctionalized reactants are required in the conversion. (Fig. 1, type **a**) [4]. In addition, intramolecular direct C−H bond activation/oxidative C–N bond coupling method is also applied frequently for 1*H*-indazoles synthesis starting from arylhydrazones via an intramolecular cyclization, which realizes the direct C–N bond formation reaction (Fig. 1, type **b**) [5]. Besides, a highly active aryne intermediate is often introduced effectively in some cases via the strategy of [3 + 2] cycloaddition (Fig. 1, type **c**) [6]. In recent years, azides have emerged as powerful amino sources in the transition-metal-catalyzed direct amination/amidation of aromatic C−H bonds due to their readily availability, structural diversity, and environmental benignity of the reaction byproduct, gaseous N_2 (Fig. 1, type **d**) [7]. Other useful approaches, such as the application of ring transformation at a high temperature (Fig. 1, type **e**) [8], coupling of arylamino oximes, or their analogs via an intermolecular or intramolecular *N–N* bond formation reaction, are also included (Fig. 1, type **f**) [7,9]. Herein, we report an alternative approach for the preparation of 1*H*-indazoles by joining the *N*-moiety on the side-chain to the aryl ring via an intramolecular oxidative amination C–N bond formation mediated by [bis-(trifluoroacetoxy)iodo]benzene (PIFA).

Organoiodine (III) reagents [10] have been widely used for the synthesis of various five-membered, six-membered, and seven-membered *N*-containing spiro and fused heterocycles, including indoles [11], 1,4-diazepines [12], 1,2,4-triazolo[1,5-*a*]pyridines [13], pyrazole [9], oxazoles [14], indazoles [9], and pyrrolidinones [15], via an intramolecular nitrenium ion azaspirocyclization reaction [16]. Combining with our recent research on the synthesis of *N*-containing heterocycles from readily available acyclic amine precursors [17], we made efforts to realize an intramolecular cyclization of **1** to **2** by means of hypervalent iodine-mediated oxidative direct C–N bond formation (Table 1). As a model substrate [5], compound 1-(diphenylmethylene)-2-phenylhydrazine (**1a**) was first prepared and evaluated the feasibility to

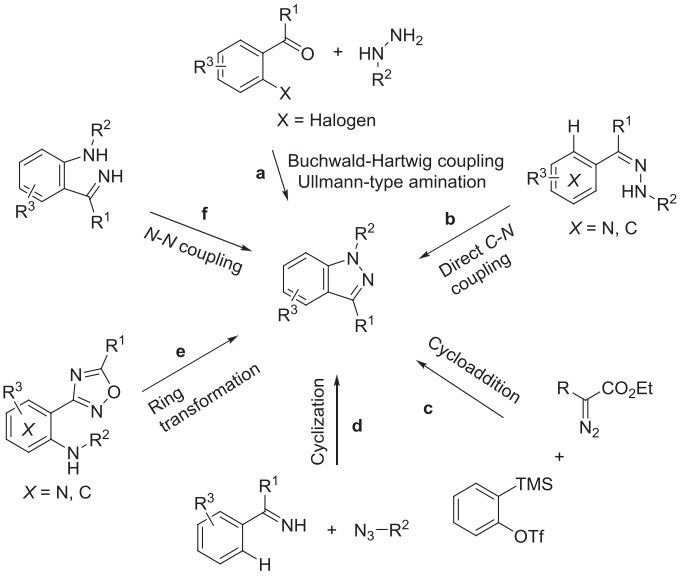
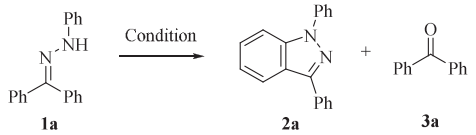


Figure 1. General synthetic routes to the indazole motif.

the desired 1,3-diphenyl-1*H*-indazole (**2a**) in the presence of a hypervalent iodine. After many attempts, compound **2a** was obtained in the yield of 84% as a white solid, along with a byproduct benzophenone (**3a**: 7% yield) when we treated **1a** with 120 mol% of PIFA in hexafluoroisopropanol (HFIP) [7] after 5 min at ambient temperature (Table 1, entry 1). It was found that decreasing or increasing the amount of PIFA was not useful to improve the yield of **2a** (Table 1, entries 2 and 3). Several other hypervalent iodine oxidants were also screened to the reaction, including 1,1,1-triacetoxy-1,1-dihydro-1,2-benziodoxol-3(1*H*)-one (DMP), 2-iodoxybenzoic acid, phenyliodonium diacetate, and PhIO (Table 1, entries). They showed a lower oxidative activity than PIFA (Table 1, entries 4–7). The screening of other fluorine-containing solvents including 2,2,2-trifluoroethanol, 2,2,3,3,4,4,5,5-octafluoro-1-pentanol, 2,2,3,3-tetrafluoro-1-propanol, and ethyl trifluoroacetate showed that they

Table 1

Survey of the reaction conditions.[a]



Entry	Oxidant (equiv)	Solvent	Time	Yield of **2a**/%	Recovered **1a**/% or yield of **3a**/%
1	PIFA (1.2)	HFIP	5 min	73	**3a**: 7
2	PIFA (1.0)	HFIP	3 h	66[b]	**1a**: 11
3	PIFA (1.5)	HFIP	5 min	72	0
4	DMP (1.2)	HFIP	4 h	8	**3a**: 70
5	IBX (1.2)	HFIP	3 h	5	**3a**: 73
6	PIDA (1.2)	HFIP	5 h	50	**3a**: 25
7	PhIO (1.2)	HFIP	24 h	35	**1a**: 20, **3a**: 13
8	PIFA (1.2)	TFE	10 min	20	0
9	PIFA (1.2)	OFP	1 h	60[b]	**1a**: 21
10	PIFA (1.2)	TFP	30 min	24[b]	**1a**: 18, **3a**: 37
11	PIFA (1.2)	ETFA	4 h	13[b]	**1a**: 36, **3a**: 22

[a]Unless otherwise indicated, all reactions were carried out with **1a** (0.5 mmol), and oxidant (1.2 equiv) in solvent (2.5 mL) at ambient temperature.
[b]The yield of **2a** could not be increased by prolonging the reaction time.
IBX, 2-iodoxybenzoic acid; PIDA, phenyliodonium diacetate; TFE, 2,2,2-trifluoroethanol; OFP, 2,2,3,3,4,4,5,5-octafluoro-1-pentanol; TFP, 2,2,3,3-tetrafluoro-1-propanol; ETFA, 2,2,3,3-tetrafluoro-1-propanol

were less effective than HFIP for this intramolecular coupling (Table 1, entries 8–11, and for more details, see the Supporting Information).

After screening various conditions, we have chosen 1.2 equiv. of PIFA in HFIP at ambient temperature to examine the further scope of this intramolecular oxidative C–N bond-forming reaction using various starting materials **1**. The results are summarized in Table 2. The starting materials with same of Ar and R^1 groups were extended first. It was found that the phenyl group (**1a**) and a variety of four-substituted phenyl groups with electron-withdrawing groups (e.g., −Cl and −F) (**1b–c**) and electron-donating groups (EDGs) (e.g., −Me and −OMe) (**1d–e**) could be easily tolerated to afford the corresponding products (**2a–e**) in 66–90% yields. In addition, the reaction led to some expected results as previous reports [5,18] when we used the starting materials which substituent R^1 was different from Ar. The reaction gave products **2f** and **2g** in the yields of 75% and 70%, respectively, when R^1 group was 4-Cl-phenyl or 4-F-phenyl, and no isomers were detected in the two reactions. However, the starting material **1h** with 4-Me-phenyl (R^1) substituent afforded a mixture of two products **2h** and **2h′** with same polar in the ratio of 5:1 judging from the ^{1}H NMR [5,18,19]. As expected, only sole product **2i** was obtained in 72% yield in the case of **1i** (R^1 = 4-MeO-phenyl), which indicated that a slightly strong EDG, like methoxy group, was favor for the electrophilic reaction. In addition, the effect of heterocyclic substituent (R^1) was also investigated. Starting materials **1j** and **1l** gave the phenyl ring bonded products **2j** [20] and **2k** in 91% and 94% yields, respectively. While compound **1k** afforded a thiophene ring bonded product **2l** in the yield of 95%. To our delight, the reaction still worked well when R^1 was methyl (**1m**), *n*-butyl (**1n**) and benzoyl (**1o**), and compounds **2m**, **2n**, and **2o** were obtained in the yields of 93%, 71%, and 65%, respectively.

The scope of R^2 group was also investigated carefully. The results showed that all of the tested starting materials bearing an electron-withdrawing group (e.g.,−CN, $-CO_2Et$, and −Cl) (**1p–t**) and EDG (e.g., −Me) (**1u–w**) at the *ortho*-, *meta*-, or *para*-position could be well tolerated and afforded the desired products **2p–w** in 65–88% yields. *N*-Benzyl substituted starting material **1x** afforded the desired **2x** in 53% yield. However, fewer experiments were conducted toward varying the aliphatic R^2 group because of the limited number of available substrates bearing *tert*-butyl and cyclohexyl groups at this position. In addition, the cyclization of starting materials **1y** bearing a tosyl group at the nitrogen atom [5,21] and **1z** did not react under the current optimal conditions. It is worth mentioning that byproduct **3** could not be inhibited, but the yield of **2** could not be further improved, and some of them were isolated even in a slightly lower yield when the reactions were performed under strict moistureless conditions in nitrogen atmosphere.

Based on the results of the information from the previous works, a plausible mechanism is proposed in Scheme 1. Initially, intermediate **A** is formed by the oxidation reaction of **1a** with PIFA by losing one molecule of CF_3COOH [12]. Then, followed by the liberation of iodobenzene, an *N*-nitrenium ion **B** is generated [9,11,16,22]. Next, the nitrenium ion leads to the target product **2a** [5] *via* a tandem procedure of nucleophilic arene attacks (**C**) and release of CF_3COOH. On the other hand, 2,2,6,6-tetramethylpiperidine-1-oxyl was added into the reaction of **1a** with the amount of 1 equiv (78 mg) and 10 equiv (780 mg), respectively, under the optimal conditions. Thus result, compound **2a** was isolated in the yield of 72% and 73%, respectively. This observation indicated that a radical pathway may not be involved in this transformation [5]. In addition, another possible mechanism involving the formation of π-complex could not be excluded at present [23].

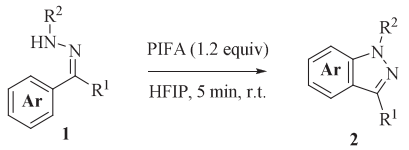
In summary, a metal-free, oxidative direct C–N coupling method has been developed for the synthesis of 1*H*-indazoles heterocycles from easily accessible starting materials. PIFA is employed as the oxidant in this transformation, and the method has been found to be generally useful for the preparation of a variety of multisubstituted 1*H*-indazoles derivatives. Compared with present metal-catalyzed and metal-free reactions, this reaction demonstrates better reactivity, functional group tolerance, and broader scope in the presence of sole catalyst PIFA. We believe this facile and efficient method will serve as a useful alternative to the existing methods for the synthesis of substituted 1*H*-indazoles.

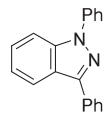
EXPERIMENTAL

General remarks. All reactions were carried out at ambient temperature, unless otherwise indicated. Other all reagents were purchased from commercial sources and used without further treatment, unless otherwise indicated. All of the hydrazones were obtained under literature conditions [5]. ^{1}H NMR and ^{13}C NMR spectra were recorded on a 400 MHz spectrometer (^{1}H: 400 MHz, ^{13}C: 100 MHz at 25°C) and TMS as internal standard. Data are represented as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = doublet, dd = double doublet, t = triplet, q = quartet, m = multiplet), coupling constants in Hertz (Hz). All high-resolution mass spectra (HRMS) were measured on a mass spectrometer (ESI-oa-TOF). Melting points were measured on an apparatus. All reactions were monitored by TLC with GF254 silica gel coated plates. Flash column chromatography was carried out using 200–300 mesh silica gel at increased pressure.

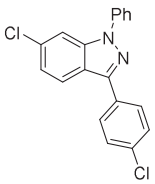
Table 2

Extension of the Reaction Scope.[a]

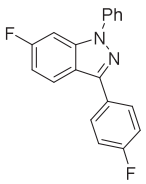




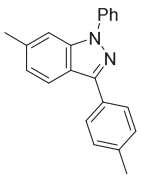
2a: 73%



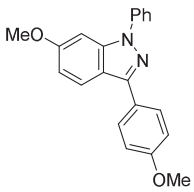
2b: 70%



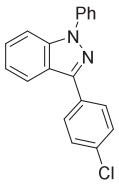
2c: 72%



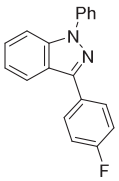
2d: 66%



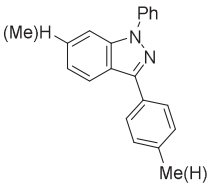
2e: 90%



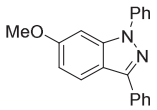
2f: 75%



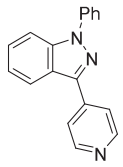
2g: 70%



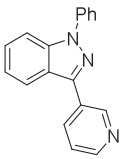
2h+2h': 71% (5:1)



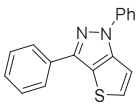
2i: 72%



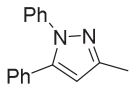
2j: 91%



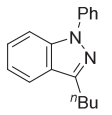
2k: 94%



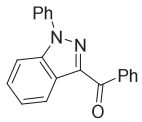
2l: 95%



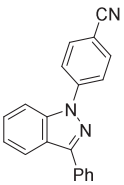
2m: 93%



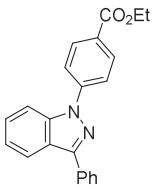
2n: 71%



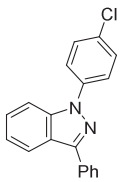
2o: 65%



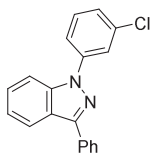
2p: 88%



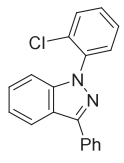
2q: 82%[d]



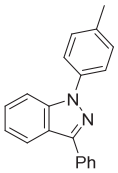
2r: 83%



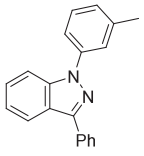
2s: 87%



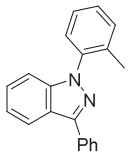
2t: 88%[e]



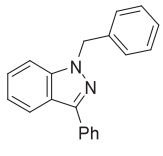
2u: 71%



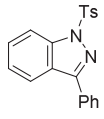
2v: 65% [f]



2w: 66%[g]



2x: 53%[h]

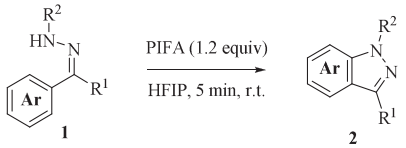


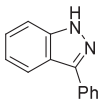
2y: 0%[i]

(*Continued*)

Table 2

(*Continued*)





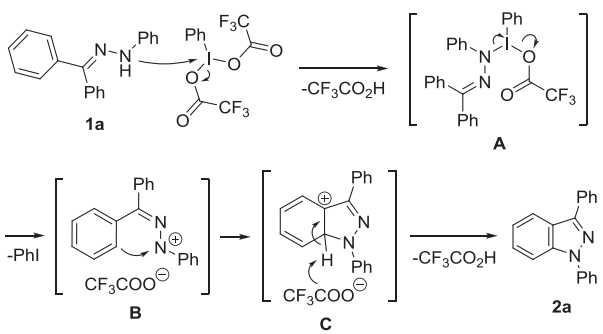
2z: 0%[j]

[a]Unless otherwise indicated, all reactions were carried out with **1a** (0.5 mmol), and PIFA (1.2 equiv) in HFIP (2.5 mL) under room temperature in 5 min.
[b]Isolated yield.
[c]10% of **3a** was obtained.
[d]13% of **3a** was obtained.
[e]8% of **3a** was obtained.
[f]14% of **3a** was obtained.
[g]11% of **3a** was obtained.
[h]Along with some unidentified complex mixture.
[i]70% of **3a** was obtained.
[j]52% of **3a** was obtained, along with some unidentified complex mixture.

General procedure for the synthesis of 2. To a solution of hydrazone (0.5 mmol, 1.0 equiv) in HFIP 2.5 mL was added PIFA (0.6 mmol, 1.2 equiv). The reaction mixture was then stirred at ambient temperature for 5–30 min, which was monitored by TLC. After the completion, the reaction was quenched by water (10 mL), and the mixture was extracted with dichloromethane (3 × 5 mL). The combined organic layers were dried over Na_2SO_4. After filtration and concentration, the crude product was purified by a short flash silica gel column chromatography (eluent: petroleum ether and EtOAc) to give product.

1,3-Diphenyl-1H-indazole (2a) [5]. The product was isolated by flash chromatography (eluent: ethyl acetate/petroleum ether = 1/100) as a white solid (99 mg, 73%): mp 95–97°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, J = 8.4 Hz, 1H), 8.07 (d, J = 7.6 Hz, 2H), 7.81 (t, J = 7.8 Hz, 3H), 7.56 (dd, J = 15.2, 7.6 Hz, 4H), 7.50–7.44 (m, 2H), 7.39 (t, J = 7.4 Hz, 1H), 7.31 (t, J = 7.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.1, 140.3, 140.1, 133.2, 129.5, 128.9, 128.3, 127.8, 127.2, 126.7, 123.1, 123.0, 122.0, 121.6, 110.7. HRMS (ESI), *m/z* Calcd for $C_{19}H_{15}N_2$ ([M + H]$^+$) 271.1230, found: 271.1232.

Scheme 1. Proposed mechanism.



6-Chloro-3-(4-chlorophenyl)-1-phenyl-1H-indazole (2b) [5]. The product was isolated by flash chromatography (eluent: ethyl acetate/petroleum ether = 1/80) as a white solid (119 mg, 70%): mp 148–150°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96–7.92 (m, 3H), 7.76–7.23 (m, 3H), 7.60–7.56 (m, 2H), 7.52–7.48 (m, 2H), 7.42 (t, J = 7.6 Hz, 1H), 7.28–7.25 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.0, 140.8, 139.4, 134.5, 133.8, 131.1, 129.6, 129.1, 128.8, 127.3, 123.12, 123.09, 122.2, 121.4, 110.6. HRMS (ESI), *m/z* Calcd for $C_{19}H_{13}Cl_2N_2$ ([M + H]$^+$) 339.0450, found: 339.0450.

6-Fluoro-3-(4-fluorophenyl)-1-phenyl-1H-indazole (2c) [5]. The product was isolated by flash chromatography (eluent: ethyl acetate/petroleum ether = 1/80) as a white solid (110 mg, 72%): mp 132–134°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99–7.93 (m, 3H), 7.76–7.73 (m, 2H), 7.57 (t, J = 7.8 Hz, 2H), 7.43–7.38 (m, 2H), 7.26–7.20 (m, 2H), 7.09–7.04 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0 (d, J = 246.5 Hz, C), 161.6 (d, J = 244.6 Hz, C), 145.4, 140.7 (d, J = 12.4 Hz, C), 139.6, 129.6, 129.4 (d, J = 8.2 Hz, CH), 128.9 (d, J = 3.1 Hz, C), 127.1, 122.8, 122.7, 119.8, 115.9 (d, J = 21.5 Hz, CH), 111.7 (d, J = 25.7 Hz, CH), 96.6 (d, J = 27.0 Hz, CH). HRMS (ESI), *m/z* Calcd for $C_{19}H_{13}F_2N_2$ ([M + H]$^+$) 307.1041, found: 307.1046.

6-Methyl-1-phenyl-3-(p-tolyl)-1H-indazole (2d) [5]. The product was isolated by flash chromatography (eluent: ethyl acetate/petroleum ether = 1/100) as a white solid (98 mg, 66%): mp 87–88°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (dd, J = 8.0, 1.6 Hz, 3H), 7.81 (dd, J = 8.8, 1.2 Hz, 2H), 7.59–7.55 (m, 3H), 7.37 (dd, J = 13.6, 7.2 Hz, 3H), 7.13 (d, J = 8.0 Hz, 1H), 2.54 (s, 3H), 2.46 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.9, 140.8, 140.2, 138.0, 137.4, 130.4, 129.5, 129.4, 127.5, 126.4, 123.9, 123.0, 121.24, 121.16, 22.0, 21.4. HRMS (ESI), *m/z* Calcd for $C_{21}H_{19}N_2$ ([M + H]$^+$) 299.1543, found: 299.1543.

6-Methoxy-3-(4-methoxyphenyl)-1-phenyl-1H-indazole (2e) [5]. The product was isolated by flash chromatography (eluent: ethyl acetate/petroleum ether = 1/100) as a white solid

(149 mg, 90%): mp 130–132°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96–7.89 (m, 3H), 7.77 (dd, J = 8.4, 0.8 Hz, 2H), 7.58–7.54 (m, 2H), 7.37 (t, J = 7.4 Hz, 1H), 7.11 (d, J = 2.0 Hz, 1H), 7.07–7.04 (m, 2H), 6.92 (dd, J = 8.8, 2.4 Hz, 1H), 3.89 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 159.7, 145.9, 141.5, 140.2, 129.4, 128.8, 126.5, 125.8, 122.9, 122.3, 117.6, 114.2, 113.3, 91.8, 55.5, 55.3. HRMS (ESI), *m/z* Calcd for $C_{21}H_{19}N_2O_2$ ([M + H]$^+$) 331.1441, found: 331.1440.

3-(4-Chlorophenyl)-1-phenyl-1H-indazole (2f) [5]. The product was isolated by flash chromatography (eluent: ethyl acetate/petroleum ether = 1/100) as a white solid (114 mg, 75%): mp 122–125°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 8.4 Hz, 1H), 8.01–7.98 (m, 2H), 7.79 (d, J = 8.0 Hz, 3H), 7.59–7.55 (m, 2H), 7.52–7.45 (m, 3H), 7.40 (t, J = 7.4 Hz, 1H), 7.33–7.29 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.9, 140.4, 139.9, 134.1, 131.7, 129.5, 129.0, 128.9, 127.2, 126.9, 123.0, 122.9, 122.1, 121.3, 110.8. HRMS (ESI), *m/z* Calcd for $C_{19}H_{14}ClN_2$ ([M + H]$^+$) 305.0840, found: 305.0840.

3-(4-Fluorophenyl)-1-phenyl-1H-indazole (2g) [5]. The product was isolated by flash chromatography (eluent: ethyl acetate/petroleum ether = 1/100) as a white solid (101 mg, 70%): mp 96–99°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84–7.79 (m, 3H), 7.60–7.53 (m, 3H), 7.36–7.31 (m, 2H), 7.25–7.21 (m, 1H), 7.18–7.14 (m, 1H), 7.08–6.99 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8 (d, J = 246.1 Hz, C), 145.1, 140.2, 140.0, 129.44, 129.41, 129.3, 127.2, 126.7, 122.9, 122.0, 121.3, 115.9, 115.7, 110.7. HRMS (ESI), *m/z* Calcd for $C_{19}H_{14}FN_2$ ([M + H]$^+$) 289.1136, found: 289.1122.

Mixture of compounds 6-methyl-1,3-diphenyl-1H-indazole (2h) and 1-phenyl-3-(p-tolyl)-1H-indazole (2h′) [19]. Compounds **2h** and **2h′** were isolated by flash chromatography (eluent: ethyl acetate/petroleum ether = 1/100) as a light yellow oil (101 mg, 71%), the regioisomer ratio was obtained from ^{1}H NMR spectrum about (5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12–8.08 (m, 1.8H), 7.99 (d, J = 8.4 Hz, 1.2H), 7.84–7.80 (m, 2.23H), 7.61–7.55 (m, 4.52H), 7.50–7.44 (m, 1.05H), 7.42–7.37 (m, 1.39H), 7.33–7.29 (m, 0.17H, **2h′**-isomer), 7.15 (dd, J = 8.4 Hz, 0.8 Hz, 0.87H, **2h**-isomer), 2.55 (s, 2.50H, **2h**-isomer), 2.48 (s, 0.50H, **2h′**-isomer). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.8, 140.8, 140.1, 137.4, 133.3, 129.4, 128.7, 128.1, 127.6, 127.6, 126.5, 124.0, 123.0, 121.1, 110.1, 22.0 (**2h**-isomer). HRMS (ESI), *m/z* Calcd for $C_{20}H_{17}N_2$ ([M + H]$^+$) 285.1386, found: 285.1384.

6-Methoxy-1,3-diphenyl-1H-indazole (2i) [19]. The product was isolated by flash chromatography (eluent: ethyl acetate/petroleum ether = 1/100) as a white solid (108 mg, 72%): mp 132–134°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05–8.03 (m, 2H), 7.94 (d, J = 8.8 Hz, 1H), 7.81–7.79 (m, 2H), 7.60–7.52 (m, 4H), 7.46–7.38 (m, 2H), 7.13 (d, J = 2.0 Hz, 1H), 6.95 (dd, J = 8.8, 2.0 Hz, 1H), 3.89 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 146.0, 141.6, 140.1, 133.1, 129.5, 128.8, 128.2, 127.6, 126.6, 123.0, 122.3, 117.7, 113.5, 91.8, 55.5. HRMS (ESI), *m/z* Calcd for $C_{20}H_{17}N_2O$ ([M + H]$^+$) 301.1335, found: 301.1327.

1-Phenyl-3-(pyridin-4-yl)-1H-indazole (2j) [5]. The product was isolated by flash chromatography (eluent: ethyl acetate/petroleum ether = 1/20) as a white solid (123 mg, 91%): mp 100–102°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (d, J = 5.6 Hz, 2H), 8.49 (d, J = 5.2 Hz, 2H), 8.16 (d, J = 8.0 Hz, 1H), 7.85 (d, J = 8.4 Hz, 1H), 7.79–7.77 (m, 2H), 7.64–7.55 (m, 3H), 7.52–7.46 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.1, 143.0, 141.0, 139.8, 139.0, 129.7, 128.2, 128.0, 124.2, 123.4, 122.8, 120.3, 111.7. HRMS (ESI), *m/z* Calcd for $C_{18}H_{14}N_3$ ([M + H]$^+$) 272.1182, found: 272.1195.

1-Phenyl-3-(pyridin-3-yl)-1H-indazole (2k) [24]. The product was isolated by flash chromatography (eluent: ethyl acetate/petroleum ether = 1/20) as a white solid (127 mg, 94%): mp 80–82°C; ^{1}H NMR (400 MHz, CDCl3) δ 9.51 (s, 1H), 8.84 (d, J = 8.0 Hz, 1H), 8.78 (d, J = 5.2 Hz, 1H), 8.10 (d, J = 8.0 Hz, 1H), 7.87–7.80 (m, 2H), 7.78 (d, J = 7.6 Hz, 2H), 7.60 (t, J = 8.0 Hz, 2H), 7.56–7.52 (m, 1H), 7.48–7.40 (m, 2H).^{13}C NMR (101 MHz, CDCl3) δ 149.3, 148.7, 143.0, 140.3, 139.8, 134.8, 129.5, 129.4, 127.4, 127.0, 123.7, 123.1, 122.9, 122.4, 121.1, 110.9. HRMS (ESI), *m/z* Calcd for $C_{18}H_{14}N_3$ ([M + H]$^+$) 272.1182, found: 272.1173.

1,3-Diphenyl-1H-thieno[3,2-c]pyrazole (2l) [18]. The product was isolated by flash chromatography (eluent: ethyl acetate/petroleum ether = 1/50) as a white solid (131 mg, 95%): mp 135–138°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08–8.05 (m, 2H), 7.87 (dd, J = 8.4, 0.8 Hz, 2H), 7.56–7.51 (m, 5H), 7.44–7.40 (m, 1H), 7.34–7.30 (m, 1H), 7.28 (d, J = 5.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.7, 143.2, 140.4, 132.8, 132.0, 129.4, 128.8, 128.2, 125.94, 125.87, 121.4, 119.6, 110.8. HRMS (ESI), *m/z* Calcd for $C_{17}H_{12}N_2SNa$ ([M + Na]$^+$) 299.0613, found: 299.0614.

3-Methyl-1,5-diphenyl-1H-pyrazole (2m) [19]. The product was isolated by flash chromatography (eluent: ethyl acetate/petroleum ether = 1/100) as a light yellow oil (109 mg, 93%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.26 (m, 8H), 7.24–7.21 (m, 2H), 6.32 (s, 1H), 2.39 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.4, 143.6, 140.1, 130.7, 128.8, 128.6, 128.4, 128.0, 127.0, 125.1, 107.7, 13.6. HRMS (ESI), *m/z* Calcd for $C_{16}H_{15}N_2$ ([M + H]$^+$) 235.1230, found: 235.1240.

3-Butyl-1-phenyl-1H-indazole (2n). The product was isolated by flash chromatography (eluent: ethyl acetate/petroleum ether = 1/100) as yellow oil (89 mg, 71%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 8.0 Hz, 1H), 7.73–7.71 (m, 3H), 7.54–7.50 (m, 2H), 7.43–7.39 (m, 1H), 7.32 (t, J = 7.4 Hz, 1H), 7.22–7.18 (m, 1H), 3.07–3.03 (m, 2H), 1.89–1.82 (m, 2H), 1.48 (dd, J = 15.2, 7.5 Hz, 2H), 0.98 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.3, 140.3, 139.5, 129.4, 127.0, 126.1, 124.4, 122.5, 120.72, 120.67, 110.4, 31.5, 26.8, 22.8, 13.9. HRMS (ESI), *m/z* Calcd for $C_{17}H_{19}N_2$ ([M + H]$^+$) 251.1543, found: 251.1555.

Phenyl(1-phenyl-1H-indazole-3-yl)methanone (2o) [18]. The product was isolated by flash chromatography (eluent: ethyl acetate/petroleum ether = 1/100) as a white solid (97 mg, 65%): mp 146–147°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, J = 8.4 Hz, 1H), 8.43–8.41 (m, 2H), 7.80 (d, J = 7.6 Hz, 3H), 7.63–7.56 (m, 3H), 7.55–7.51 (m, 3H), 7.48–7.43 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.6, 143.5, 139.9, 139.5, 137.8, 132.6, 130.7, 129.6, 128.2, 127.9, 127.8, 125.5, 124.2, 123.6, 123.5, 110.7. HRMS (ESI), *m/z* Calcd for $C_{20}H_{14}N_2ONa$ ([M + Na]$^+$) 321.0998, found: 321.0998.

4-(3-Phenyl-1H-indazole-1-yl)benzonitrile (2p) [5]. The product was isolated by flash chromatography (eluent: ethyl acetate/petroleum ether = 1/60) as a white solid (130 mg, 88%): mp 160–161°C; ^{1}H NMR (400 MHz, CDCl3) δ 8.11 (d, J = 8.4 Hz, 1H), 8.04–7.99 (m, 4H), 7.87–7.82 (m, 3H), 7.58–7.52 (m, 3H), 7.50–7.47 (m, 1H), 7.38–7.35 (m, 1H). ^{13}C NMR

(100 MHz, $CDCl_3$) δ 147.9, 143.7, 139.9, 133.5, 132.4, 128.94, 128.86, 128.0, 127.8, 124.1, 122.9, 122.1, 122.0, 118.6, 110.7, 109.1. HRMS (ESI), *m/z* Calcd for $C_{20}H_{14}N_3$ ($[M + H]^+$) 296.1182, found: 296.1183.

Ethyl 4-(3-phenyl-1H-indazole-1-yl)benzoate (2q) [5]. The product was isolated by flash chromatography (eluent: ethyl acetate/petroleum ether = 1/60) as colorless oil (140 mg, 82%); ^{1}H NMR (400 MHz, CDCl3) δ 8.25–8.23 (m, 2H), 8.09 (d, *J* = 8.4 Hz, 1H), 8.06–8.04 (m, 2H), 7.95–7.92 (m, 2H), 7.86 (d, *J* = 8.4 Hz, 1H), 7.57–7.45 (m, 4H), 7.32 (t, J = 7.6 Hz, 1H), 4.46–4.41 (m, 2H), 1.45 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 147.1, 143.7, 140.0, 132.7, 130.9, 128.8, 128.6, 127.82, 127.78, 127.6, 123.7, 122.4, 121.8, 121.5, 110.8, 61.1, 14.3. HRMS (ESI), *m/z* Calcd for $C_{22}H_{19}N_2O_2$ ($[M + H]^+$) 343.1441, found: 343.1438.

1-(4-Chlorophenyl)-3-phenyl-1H-indazole (2r) [5]. The product was isolated by flash chromatography (eluent: ethyl acetate/petroleum ether = 3/100) as white solid (126 mg, 83%): mp 120–121°C; ^{1}H NMR (400 MHz, CDCl3) δ 8.10 (d, *J* = 8.4 Hz, 1H), 8.07–8.05 (m, 2H), 7.78–7.73 (m, 3H), 7.58–7.52 (m, 4H), 7.50–7.45 (m, 2H), 7.31 (t, *J* = 7.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.4, 140.1, 138.6, 132.9, 131.9, 129.5, 128.8, 128.4, 127.7, 127.3, 123.8, 123.2, 122.1, 121.7, 110.4. HRMS (ESI), *m/z* Calcd for $C_{19}H_{14}ClN_2$ ($[M + H]^+$) 305.0840, found: 305.0844.

1-(3-Chlorophenyl)-3-phenyl-1H-indazole (2s) [5]. The product was isolated by flash chromatography (eluent: ethyl acetate/petroleum ether = 3/100) as colorless oil (132 mg, 87%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, *J* = 8.0 Hz, 1H), 8.07–8.05 (m, 2H), 7.87 (t, *J* = 2.0 Hz, 1H), 7.80 (d, *J* = 8.8 Hz, 1H), 7.74–7.72 (m, 1H), 7.56 (t, *J* = 7.6 Hz, 2H), 7.52–7.46 (m, 3H), 7.36–7.30 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.7, 141.1, 140.1, 135.1, 132.8, 130.4, 128.9, 128.5, 127.8, 127.5, 126.5, 123.3, 122.8, 122.2, 121.7, 120.5, 110.5. HRMS (ESI), *m/z* Calcd for $C_{19}H_{14}ClN_2$ ($[M + H]^+$) 305.0840, found: 305.0839.

1-(2-Chlorophenyl)-3-phenyl-1H-indazole (2t). The product was isolated by flash chromatography (eluent: ethyl acetate/petroleum ether = 3/100) as a colorless oil (134 mg, 88%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 8.0 Hz, 1H), 8.08–8.06 (m, 2H), 7.65–7.60 (m, 2H), 7.57–7.53 (m, 2H), 7.47–7.43 (m, 4H), 7.33–7.28 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.4, 141.8, 137.0, 133.1, 131.6, 130.7, 129.8, 129.7, 128.8, 128.3, 127.74, 127.71, 126.9, 122.1, 121.8, 121.4, 110.8. HRMS (ESI), *m/z* Calcd for $C_{19}H_{14}ClN_2$ ($[M + H]^+$) 305.0840, found: 305.0840.

3-Phenyl-1-(p-tolyl)-1H-indazole (2u) [19]. The product was isolated by flash chromatography (eluent: ethyl acetate/petroleum ether = 3/100) as a white solid (101 mg, 71%): mp 89–91°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (dd, *J* = 15.2, 8.4 Hz, 3H), 7.78 (d, *J* = 8.8 Hz, 1H), 7.72 (d, *J* = 8.0 Hz, 2H), 7.58 (t, *J* = 7.6 Hz, 2H), 7.49–7.45 (m, 2H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.33–7.29 (m, 1H), 2.48 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.7, 140.3, 137.5, 136.5, 133.3, 129.9, 128.8, 128.1, 127.7, 126.9, 122.91, 122.85, 121.7, 121.4, 110.6, 21.1. HRMS (ESI), *m/z* Calcd $C_{20}H_{17}N_2$ for ($[M + H]^+$) 285.1386, found: 285.1382.

3-Phenyl-1-(m-tolyl)-1H–indazole (2v) [5]. The product was isolated by flash chromatography (eluent: ethyl acetate/petroleum ether = 3/100) as colorless oil (92 mg, 65%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11–8.05 (m, 3H), 7.79 (d, *J* = 8.8 Hz, 1H), 7.64–7.60 (m, 2H), 7.55 (t, *J* = 7.6 Hz, 2H), 7.49–7.43 (m, 3H), 7.32–7.28 (m, 1H), 7.21 (d, *J* = 7.6 Hz, 1H), 2.49 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.0, 140.4, 140.0, 139.7, 133.3, 129.2, 128.9, 128.3, 127.8, 127.6, 127.1, 123.9, 123.1, 121.9, 121.6, 120.0, 110.8, 21.6. HRMS (ESI), *m/z* Calcd for $C_{20}H_{17}N_2$ ($[M + H]^+$) 285.1386, found: 285.1387.

3-Phenyl-1-(o-tolyl)-1H-indazole (2w) [6]. The product was isolated by flash chromatography (eluent: ethyl acetate/petroleum ether = 3/100) as a colorless oil (94 mg, 66%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18–8.12 (m, 3H), 7.58 (t, *J* = 7.6 Hz, 2H), 7.52–7.48 (m, 1H), 7.49–7.38 (m, 5H), 7.34–7.29 (m, 2H), 2.25 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.4, 142.0, 138.2, 135.9, 133.6, 131.6, 128.9, 128.2, 127.72, 127.65, 126.9, 126.8, 121.8, 121.6, 121.4, 110.5, 18.1. HRMS (ESI), *m/z* Calcd for $C_{20}H_{16}N_2Na$ ($[M + Na]^+$) 307.1206, found: 307.1208.

1-Benzyl-3-phenyl-1H-indazole (2x) [24]. The product was isolated by flash chromatography (eluent: ethyl acetate/petroleum ether = 1/50) as a white solid (75 mg, 53%): mp 79–82°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.0 Hz, 1H), 8.00 (d, *J* = 7.2 Hz, 2H), 7.52 (t, *J* = 7.6 Hz, 2H), 7.41 (t, *J* = 7.4 Hz, 1H), 7.36 (d, *J* = 4.0 Hz, 2H), 7.33–7.27 (m, 3H), 7.26–7.19 (m, 3H), 5.68 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.2, 139.1, 134.9, 131.6, 126.8, 126.7, 125.9, 125.7, 125.5, 125.1, 124.4, 120.1, 119.4, 119.1, 107.6, 51.1. HRMS (ESI), *m/z* Calcd for $C_{20}H_{17}N_2$ ($[M + H]^+$) 285.1386, found: 285.1389.

Acknowledgments. We thank the NSFC (21272057 and 21372065), Young Backbone Teachers Fund of Henan (2014GGJS-049), Key Project of Henan Educational Committee (15B610005, 14A150019, 14B150042, and 15A150015), Science and Technology Innovation Talents in Universities of Henan Province (17HASTIT002), the Program of Foundation and Frontier Technology Research of Henan Province (122300410296), Outstanding Young Talent Cultivation Project Funding of Henan Normal University (14YR002), and Open Project of Jilin Province Key Laboratory of Organic Functional Molecular Design and Synthesis (130028651).

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