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# Microwave-assisted Transition Metal-catalyzed Coupling Approach to Indazole Diversity

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Diverse mono or biaryl substituents were introduced to indazole moieties under microwave-assisted palladium-catalyzed coupling reactions with isomeric bromoindazoles and aryl boronic acids. 1,3-Disubstituted indazoles were also obtained by C═C or C—N coupling of monosubstituted indazoles with functionalized terminal alkenes and arylhalides. Facile introduction of diverse substituents to indazoles showed useful synthetic approach for creating indazole compound library to discover biologically active small molecules.

**Keywords:** Indazole, Diversity microwave, Transition metal, Coupling reaction

## Introduction

Microwave heating has been applied to various chemistry fields, such as nanotechnology, solid state, and organic synthesis.[1] In particular, microwave-assisted organic synthesis (MAOS) has demonstrated potential for speeding up small molecule organic synthesis.[2–4] The high-speed organic synthetic method could be utilized to synthesize new small heterocyclic compounds for drug discovery.[5–8]

Many natural and synthetic indazole derivatives exhibit various biological activities, including anticancer, antibacterial, antiprotozoal, anti-inflammatory, inhibition of protein kinase, HIV protease, nitric oxide synthase, and monoamine oxidase.[9,10] The molecular shape and electrostatic distribution of indazole moieties contribute extensively to binding affinity, making indazoles especially active in enzyme and receptor recognition mechanisms.

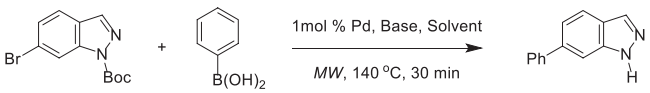
Many synthetic methods involving indazoles utilize thermal or transition metal-catalyzed indazole formation to create useful organic compounds.[11–19]

Recently, palladium–catalyzed coupling methods have shown essential synthetic tools for functionalization and formation of variety heterocycles.[20–22] Our reported microwave-assisted copper or palladium-catalyzed diversification of heterocycles boasts significant advantages over conventional heating.[23–27] In drug discovery research, establishment of functionally diversified small molecule compound library is very efficient way to find biologically active substances with biomolecular targets.[28,29] Indazole moieties contain two aromatic rings with different electronic configurations, which could be functionalized at multiple positions. Thus, diversification using an isomeric haloindazole moiety may be a promising synthetic approach for discovering new biologically active compounds. In this study, we examined palladium or copper-catalyzed cross coupling with an isomeric haloindazole moiety under microwave heating. This synthetic approach affords functionally diversified indazoles for creating potentially bioactive compound library.

## Results and Discussion

Many aryl-substituted indazole derivatives are potential pharmaceuticals.[9,10] Initially, we optimized microwave-assisted, palladium-catalyzed coupling reaction conditions using *N*-Boc-6-bromo-*1H*-indazole and phenylboronic acid with a variety of Pd catalysts, bases, and solvents. The reaction conditions are shown in Table 1. The coupling product 6-phenyl-*1H*-indazole was obtained with a deprotected Boc group. The reaction was performed with different palladium-based catalysts, with $Pd(PPh_3)_2Cl_2$ yielding the best results (Table 1, entries 1–3). The use of $Na_2CO_3$ as a base afforded greater yields than reactions employing

**Table 1.** Optimization of aryl-coupling with *N*-Boc −6-bromoindazole with phenylboronic acid.




| Entry | Pd source | Base | Solvent | Yield (%) |
|---|---|---|---|---|
| 1 | $Pd(OAc)_2$ | $Na_2CO_3$ | 1,4-Dioxane | 34 |
| 2 | $Pd(PPh_3)_4$ | $Na_2CO_3$ | 1,4-Dioxane | 73 |
| 3 | $Pd(PPh_3)_2Cl_2$ | $Na_2CO_3$ | 1,4-Dioxane | 93 |
| 4 | $Pd(PPh_3)_2Cl_2$ | $K_2CO_3$ | 1,4-Dioxane | 85 |
| 5 | $Pd(PPh_3)_2Cl_2$ | $Cs_2CO_3$ | 1,4-Dioxane | 83 |
| 6 | $Pd(PPh_3)_2Cl_2$ | $Na_2CO_3$ | EtOH | NR |
| 7 | $Pd(PPh_3)_2Cl_2$ | $Na_2CO_3$ | Dioxane: EtOH (4:1) | 94 |

$K_2CO_3$ or $Cs_2CO_3$ (entries 3–5). Furthermore, although reactions performed in dioxane or a mixed solvent (Dioxane:EtOH = 4:1) gave similarly high yields, the mixed solvent was selected for further use due to the greater solubility of arylboronic acid and base.

The ary–aryl coupling with *N*-Boc protected isomeric bromoindazoles and arylboronic acids were examined under established optimization conditions. The synthesized monoaryl indazoles and yields are shown in Table 2.

The positional isomeric aryl substituted indazole products were obtained with free NH indazoles. The reactions using *N*-Boc 3-bromoindazole with carbo, thio, and aza, arylboronic acid provided excellent yields of 3-arylindazoles (compound **1a–1d**). From aryl-aryl coupling results, the variation of heteroatom in heteroarylboronic acids did not change yields of aryl coupled products. The reactions using 4–6 positional isomeric bromoindazoles with various arylboronic acid gave very high yields of 4–6 aryl substituted indazoles (compound **1e–1p**). The coupling reaction proceeded very well with many different aromatic boronic acids, such as phenyl, thiophenyl, benzothiophenyl, and pyridinyl boronic acids.

Furthermore, we explored palladium-catalyzed coupling reaction conditions using *N*-Boc 3,6-dibromoindazole and arylboronic acid for double arylated indazoles. The optimization of double arylation conditions are 10 mol % $Pd(PPh_3)_2Cl_2$, 4 equiv arylborornic acids, 4 equiv $Na_2CO_3$ with mixed solvents (Dioxane: EtOH: $H_2O$ = 6:2:1). The 3,6-diaryl coupled indazole and yields were shown in Table 3.

The reactions using methoxy pyridinylboronic acids provided high yields of 3,6-diaryl coupled indazoles without any significant reactivity different with positional methoxy group of pyridine (**2a** and **2b**). The reaction using 3-thiophenylboronic acid also gave good yields of diarylated product (**2c**). The reactions using different functional group substituted phenylboronic acids provided good yields of diaryl coupled products (**2d–2i**) without any significant different electronic substitution effects of phenylboronic acids.

We investigated 1,3-diarylated indazoles formation using 3-arylsubstituted indazole and substituted arylhalides with copper catalyzed *N*-arylation based on our previously established reaction conditions.[24] The optimal conditions for *N*-arylation of indazole were 1.5 equiv $Cs_2CO_3$ and 10 mol % $Cu_2O$ in DMA at 200°C. Diverse *N*-arylated indazole products and yields are shown in Table 4.

The *N*-arylation of 3-thiophenylindazole was performed with different substituted phenyl bromides. The reaction using methyl or methoxy substituted phenyl bromides provided moderate yield of 1,3-diaryl indazoles with slightly decrease with electron donation groups of phenyl halides. The reaction using 3-phenylindazole and 2-bromopyridine or 3-bromobenzothiophene also gave reasonable yield of 1,3-diaryl coupled desired product. Additionally, the reactions using 3-benzothiophenyl or 3-pyridyl indazole with

**Table 2.** Synthesis of diverse monoarylated indazoles under palladium-catalyzed aryl-coupling with 3–6 isomeric N-Boc-bromoindazoles.

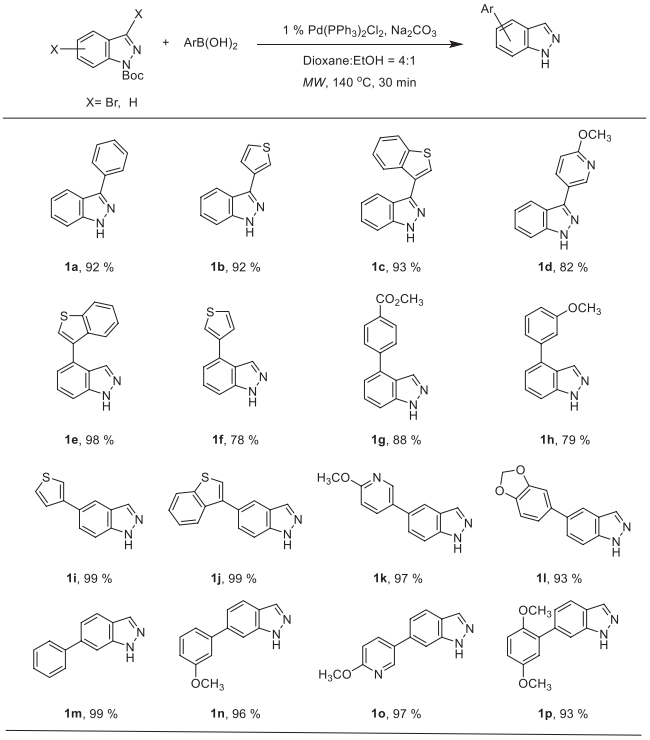



**Table 3.** Synthesis of 3,6-diarylated indazoles under palladium-catalyzed diaryl-coupling reaction.

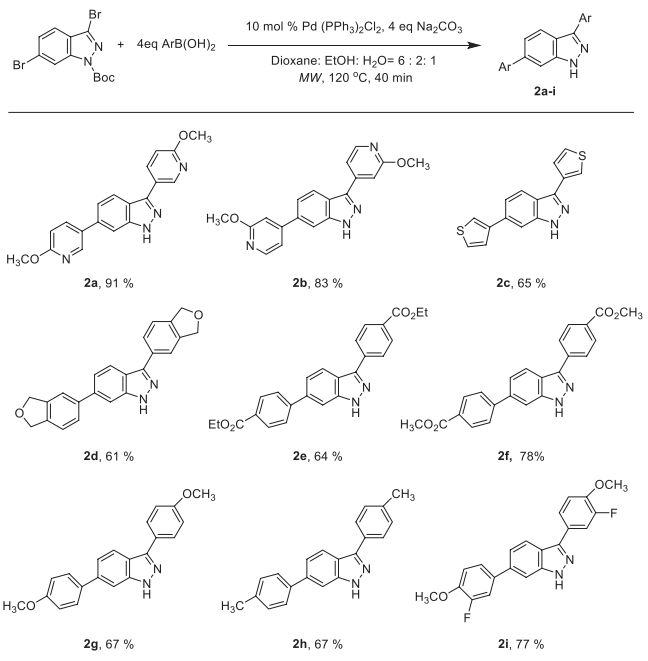
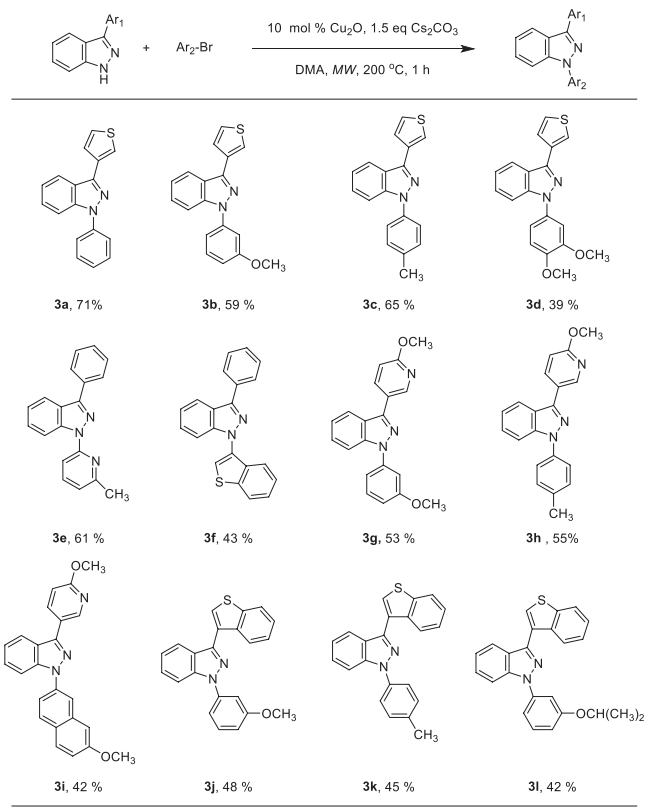


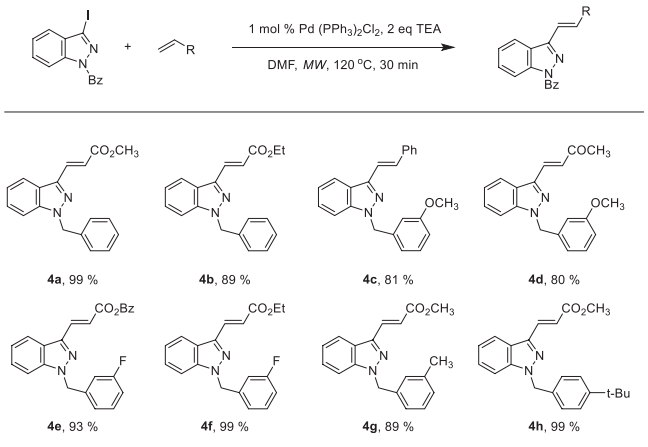

  

**Table 4.** Synthesis of 1,3-diarylated indazoles by copper-catalyzed *N*-arylation with 3- arylindazoles with arylbromides.




substituted aryl bromide also provided 1,3-diaryl substituted indazoles. The results showed that reactions using nitrogen contain heterocycles had similar reactivity with benzene ring, but the reaction using the 3-benzothiophenyl substituted indazole provided low yield of products. Probably the coupling reactions were influenced with steric bulky effect of benzothiophene.

**Table 5.** Synthesis of 1,3-dialkylated indazoles by palladium-catalyzed heck reaction with *N*-benzyl 3-iodoindazoles and alkenes.




To introduce double bond to indazole moiety, we finally examined Heck coupling conditions with *N*-benzyl 3-iodoindazoles with functional group containing terminal alkenes. The optimal Heck reaction conditions were 1 mol % $Pd(PPh_3)_2Cl_2$, 2 equiv TEA, and DMF at 120°C. The alkene coupled products and yields are shown in Table 5.

The reaction using various different electronic substituted *N*-benzyl 3-iodoindazole and terminal double bond substrates provided 80–99% yields of 1,3-dialkyl indazoles. The aryl -alkene coupling reactions proceeded excellent yields without any electronic effects for benzyl or functionalized alkene substrates, such as methyl acrylate, styrene, and vinyl ketones.

## Conclusion

Diverse aryl, vinyl, and *N*-aryl coupling reactions with indazoles were performed with arylboronic acids, functionalized terminal alkenes, and aryl halides by microwave-assisted palladium or copper catalysis. Diverse isomeric mono or disubstituted indazoles were easily prepared within 60 min with excellent yields. This microwave-assisted bond formation could be extended to prepare diversely functionalized indazoles for drug discovery research.

## Experimental Section

**Instrumentation and Analysis.** Bruker Fourier 300 (Billerica, MA, USA), 500 MHz spectrometers were used for recording $^1H$ and $^{13}C$ NMR spectra of products. Waters ACQVI (UPLC) SQD 2 (Milford, MA, USA) was used to obtain LC–MS spectra. All microwave-assisted reactions were performed with an initiator instrument (EXP EU, Biotage, 400 W, 2450 MHz). Flash column chromatography on 230-400-mesh ASTM 60 silica gel was used for products purification. All chemical species were purchased from Sigma-Aldrich Chemical Co (St. Louis, USA), TCI (Tokyo, Japan), and Alfa Aesar (Lancs, UK).

**General Procedure for Microwave-assisted Palladium-catalyzed Aryl-Aryl Coupling Reactions[27].** *tert*-Butyl 3-bromo 1*H*-indazole-1-carboxylate (0.5 mmol), $Na_2CO_3$ (0.5 mmol), boronic acid (1.0 mmol), $Pd(PPh_3)_2Cl_2$ (1 mol %), and 1,4-dioxane: ethanol = 4:1 (5 mL) were added to 10 mL vial. The vial was sealed with a crimp cap and placed in a Biotage initiator microwave cavity. After the reaction vial was irradiated at 140 °C for 30 min, the microwave reactor was cooled with air. Product was separated with ethyl acetate and saturated aqueous $NH_4Cl$ solution. The organic layer was dried with anhydrous sodium sulfate, filtered, and concentrated. Products were purified by silica gel column chromatography using a hexane: ethyl acetate = 4:1.

**3-Phenyl-1*H*-indazole (1a).** Yield (92%), brown oil, $^1H$ NMR (300 MHz, $CDCl_3$) δ 11.63 (s, 1H), 8.05–7.99

(m, 3H), 7.57–7.48 (m, 2H), 7.48–7.40 (m, 1H), 7.35 (ddd, *J* = 7.9, 6.7, 1.0 Hz, 1H), 7.26–7.21 (m, 1H), 7.21–7.14 (m, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 145.7, 141.7, 133.6, 129.0, 128.2, 127.8, 126.8, 121.4, 121.1, 121.0, 110.3; MS(*m*/*z*): 194.62 (M + 1).

**3-(Thiophen-3-yl)-1*H*-indazole (1b)**. Yield (92%), brown solid, mp: 90–94°C; $^1$H NMR (300 MHz, $CDCl_3$) δ 11.77 (s, 1H), 7.96 (dd, *J* = 8.2, 1.1 Hz, 1H), 7.84 (dd, *J* = 3.0, 1.1 Hz, 1H), 7.78–7.71 (m, 1H), 7.45 (dd, *J* = 5.0, 3.0 Hz, 1H), 7.36–7.29 (m, 1H), 7.25–7.10 (m, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 141.7, 141.5, 134.6, 127.0, 127.0, 126.3, 122.4, 121.4, 120.9, 120.9, 110.4; MS(*m*/*z*): 200.73 (M + 1).

**3-(Benzo[*b*]thiophen-3-yl)-1*H*-indazole (1c)**. Yield (93%), brown solid, mp: 120–122°C; $^1$H NMR (300 MHz, $CDCl_3$) δ 11.86 (s, 1H), 8.44 (dt, *J* = 7.1, 3.5 Hz, 1H), 8.01–7.90 (m, 1H), 7.90–7.81 (m, 2H), 7.38 (tt, *J* = 7.1, 3.5 Hz, 2H), 7.31–7.22 (m, 1H), 7.14 (ddd, *J* = 8.1, 6.9, 1.0 Hz, 1H), 7.02 (dd, *J* = 8.1, 1.0 Hz, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 141.3, 141.1, 140.4, 138.0, 129.2, 127.0, 125.5, 124.9, 124.7, 124.4, 122.7, 122.0, 121.3, 120.9, 110.3; MS(*m*/*z*): 250.70 (M + 1).

**3-(6-Methoxypyridin-3-yl)-1*H*-indazole (1d)**. Yield (82%), pale yellow solid, mp: 138–139°C; $^1$H NMR (500 MHz, $CDCl_3$) δ 10.84 (s, 1H), 8.83 (d, *J* = 2.4 Hz, 1H), 8.22 (dd, *J* = 8.6, 2.4 Hz, 1H), 8.00 (d, *J* = 8.2 Hz, 1H), 7.50 (d, *J* = 8.2 Hz, 1H), 7.44 (ddd, *J* = 8.1, 6.7, 1.0 Hz, 1H), 7.26 (ddd, *J* = 8.1, 6.7, 1.0 Hz, 1H), 6.93 (d, *J* = 8.6 Hz, 1H), 4.06 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 164.0, 145.5, 143.1, 141.6, 137.9, 127.6, 127.0, 123.1, 121.6, 120.9, 111.3, 110.0, 53.7; MS(m/z): 225.68 (M + 1).

**4-(Benzo[*b*]thiophen-3-yl)-1*H*-indazole (1e)**. Yield (98%), purple solid, mp: 150–151°C; $^1$H NMR (300 MHz, $CDCl_3$) δ 8.05 (s, 1H), 8.02–7.92 (m, 1H), 7.89–7.79 (m, 1H), 7.60 (s, 1H), 7.56–7.46 (m, 2H), 7.39 (m, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 140.6, 138.0, 135.5, 134.9, 129.3, 127.2, 124.8, 124.7, 124.4, 123.2, 122.9, 121.5, 109.1; MS(*m*/*z*): 250.32 (M + 1).

**4-(Thiophen-3-yl)-1*H*-indazole (1f)**. Yield (78%), brown oil; $^1$H NMR (300 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.65 (dd, *J* = 3.0, 1.4 Hz, 1H), 7.54 (dd, *J* = 5.0, 1.3 Hz, 1H), 7.52–7.49 (m, 1H), 7.49–7.44 (m, 2H), 7.34 (dd, *J* = 6.6, 1.3 Hz, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 140.6, 138.0, 135.5, 127.2, 124.8, 124.7, 124.4, 123.2, 122.9, 121.5, 109.1; MS(*m*/*z*): 200.26 (M + 1).

**Methyl 4-(1*H*-indazol-4-yl)benzoate (1g)**. Yield (88%), pink oil; $^1$H NMR (500 MHz, $CDCl_3$) δ 7.55–7.43 (m, 3H), 7.36–7.25 (m, 3H), 7.06–6.98 (m, 1H), 3.92 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 159.9, 141.2, 132.1, 129.9, 128.6, 127.2, 121.0, 120.6, 114.1, 113.4, 55.4, 29.7, 23.2; MS(*m*/*z*): 252.38 (M + 1).

**4-(3-Methoxyphenyl)-1*H*-indazole (1h)**. Yield (79%), white solid, mp: 180–181°C; $^1$H NMR (500 MHz, $CDCl_3$) δ 10.48 (s, 1H), 8.28–8.19 (m, 3H), 7.84–7.78 (m, 2H), 7.60–7.55 (m, 1H), 7.51 (dd, *J* = 8.4, 7.0 Hz, 1H), 7.32 (dd, *J* = 7.1, 0.9 Hz, 1H), 4.00 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 167.0, 144.3, 140.6, 134.2, 134.2, 130.2, 129.4, 128.5, 127.1, 121.7, 120.8, 115.3, 109.6, 52.3; MS(*m*/*z*): 224.26 (M + 1).

**5-(Thiophen-3-yl)-1*H*-indazole (1i)**. Yield (99%), brown solid, mp: 245–247 °C; $^1$H NMR (300 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.96 (s, 1H), 7.68 (dd, *J* = 8.7, 1.6 Hz, 1H), 7.53 (d, *J* = 8.7 Hz, 1H), 7.46–7.40 (m, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 142.5, 133.1, 132.3, 126.7, 126.6, 126.4, 114.0, 102.7, 99.4, 93.2, 87.8; MS(*m*/*z*): 200.26 (M + 1).

**5-(Benzo[*b*]thiophen-3-yl)-1*H*-indazole (1j)**. Yield (99%), brown solid, mp: 179°C; $^1$H NMR (300 MHz, $CDCl_3$) δ 8.17 (s, 1H), 8.00–7.84 (m, 3H), 7.69–7.56 (m, 2H), 7.46–7.35 (m, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 140.7, 139.5, 138.2, 138.0, 135.2, 129.2, 128.5, 124.5, 124.4, 123.7, 123.3, 123.0, 122.9, 120.7, 110.0; MS(*m*/*z*): 250.32 (M + 1).

**5-(6-Methoxypyridin-3-yl)-1*H*-indazole (1k)**. Yield (97%), white solid, mp: 184–185 °C; $^1$H NMR (300 MHz, $CDCl_3$) δ 10.35 (s, 1H), 8.45 (d, *J* = 2.6 Hz, 1H), 8.17 (s, 1H), 7.90 (t, *J* = 1.2 Hz, 1H), 7.86 (dd, *J* = 8.5, 2.6 Hz, 1H), 7.60 (d, *J* = 1.2 Hz, 2H), 6.87 (d, *J* = 8.5 Hz, 1H), 4.03 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 163.4, 145.1, 137.8, 135.3, 131.3, 130.4, 126.6, 118.7, 110.9, 110.3, 106.3, 53.6, 29.7; MS(*m*/*z*): 225.25 (M + 1).

**5-(Benzo[*d*][*1,3*]dioxol-5-yl)-1*H*-indazole (1l)**. Yield (93%), white solid, mp: 207–209°C; $^1$H NMR (300 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.79 (s, 1H), 7.49 (q, *J* = 8.8 Hz, 2H), 7.06–6.98 (m, 2H), 6.83 (d, *J* = 7.9 Hz, 1H), 5.94 (s, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 148.2, 146.9, 146.4, 135.9, 135.6, 134.7, 127.1, 120.8, 110.2, 108.7, 108.0, 101.2, 31.0, 30.0; MS(*m*/*z*): 238.25 (M + 1).

**6-Phenyl-1*H*-indazole (1m)**. Yield (99%), yellow solid, mp: 128–131°C; $^1$H NMR (300 MHz, $CDCl_3$) δ 10.19 (s, 1H), 8.18 (s, 1H), 7.84 (d, *J* = 8.4 Hz, 1H), 7.67 (d, *J* = 7.4 Hz, 3H), 7.53–7.39 (m, 4H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 141.2, 140.9, 140.7, 134.4, 128.9, 127.8, 127.6, 127.6, 121.8, 121.3, 107.9, MS(*m*/*z*): 194.24 (M + 1).

**6-(3-Methoxyphenyl)-1*H*-indazole (1n)**. Yield (96%), yellow solid, mp: 68–72°C; $^1$H NMR (300 MHz, $CDCl_3$) δ 10.99 (s, 1H), 8.17 (d, *J* = 1.1 Hz, 1H), 7.83 (dd, *J* = 8.4, 0.9 Hz, 1H), 7.68 (q, *J* = 1.1 Hz, 1H), 7.51–7.35 (m, 2H), 7.30–7.25 (m, 1H), 7.21 (d, *J* = 1.9 Hz, 1H), 6.96 (ddd, *J* = 8.2, 2.6, 1.0 Hz, 1H), 3.91 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 160.0, 142.9, 140.8, 140.3, 134.6, 129.9, 122.6, 121.4, 121.1, 120.2, 113.5, 112.9, 108.0, 55.4, MS(*m*/*z*): 244.26 (M + 1).

**6-(6-Methoxypyridin-3-yl)-1*H*-indazole (1o).** Yield (97%), yellow solid, mp: 166–167°C; $^1$H NMR (300 MHz, $CDCl_3$) δ 11.26 (s, 1H), 8.50 (d, *J* = 2.5 Hz, 1H), 8.15 (s, 1H), 7.91–7.79 (m, 2H), 7.63 (s, 1H), 7.36 (dd, *J* = 8.4, 1.5 Hz, 1H), 6.87 (d, *J* = 8.6 Hz, 1H), 4.05 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3\delta$ 163.8, 145.3, 140.8, 137.9, 136.9, 134.9, 130.3, 122.5, 121.5, 120.8, 111.0, 107.45, 53.7; MS(*m*/*z*): 225.25 (M + 1).

**6-(4-Methoxyphenyl)-1*H*-indazole (1p).** Yield (93%), white solid, mp: 178–179°C; $^1$H NMR (300 MHz, $CDCl_3$) δ 10.36 (s, 1H), 8.10 (s, 1H), 7.79 (d, *J* = 8.4 Hz, 1H), 7.63–7.54 (m, 3H), 7.40 (d, *J* = 8.4 Hz, 1H), 7.00 (d, *J* = 8.4 Hz, 2H), 3.86 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 159.4, 140.10, 138.4, 135.0, 133.8, 128.6, 121.3, 121.0, 114.3, 107.1, 104.2, 55.4; MS(*m*/*z*): 244.26 (M + 1).

**Synthesis of Diarylated Indazoles (2a-2i) with Microwave-assisted Palladium-catalyzed Aryl-Aryl Coupling reactions[27].** *tert*-Butyl 3,6-dibromo 1*H*-indazole-1-carboxylate (0.5 mmol), $Na_2CO_3$ (2.0 mmol), arylboronic acid (2.0 mmol), $Pd(PPh_3)_2Cl_2$ (10 mol %), and 1,4-dioxane: ethanol:water = 6:2:1 (5 mL) were added to 10 mL vial. After the reaction mixture was heated at 120 °C for 40 min, product was purified with same work-up procedure for monoaryl coupling reaction conditions.

**3,6-Bis(6-methoxypyridi-3-yl)-1*H*-indazole (2a).** Yield (91%), yellow oil, $^1$H NMR (500 MHz, $CDCl_3$) δ 8.84 (d, *J* = 2.3 Hz, 1H), 8.52–8.46 (m, 1H), 8.23 (dd, *J* = 8.6, 2.4 Hz, 1H), 8.06 (dd, *J* = 8.5, 0.8 Hz, 1H), 7.90 (dd, *J* = 8.6, 2.6 Hz, 1H), 7.66 (d, *J* = 1.2 Hz, 1H), 7.45 (dd, *J* = 8.5, 1.5 Hz, 1H), 6.95 (d, *J* = 8.6 Hz, 1H), 6.90 (dd, *J* = 8.6, 0.8 Hz, 1H), 4.06 (s, 3H), 4.04 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 176.04, 172.14, 158.61, 155.51, 152.35, 143.82, 140.25, 137.86, 136.37, 135.13, 132.57, 131.08, 122.52, 121.14, 120.61, 111.32, 102.17, 30.08, 29.68; MS(*m*/*z*): 332.36 (M + 1).

**3,6-Bis(2-methoxypyridin-4-yl)-1*H*-indazole (2b).** Yield (83%), pale yellow oil; $^1$H NMR (500 MHz, $CDCl_3$) δ 8.30 (dd, *J* = 5.0, 1.9 Hz, 1H), 8.23 (dd, *J* = 5.0, 1.9 Hz, 1H), 8.04 (dd, *J* = 7.3, 2.0 Hz, 1H), 7.90–7.83 (m, 1H), 7.78–7.68 (m, 2H), 7.41 (dd, *J* = 8.5, 1.4 Hz, 1H), 7.12–6.99 (m, 2H), 4.08 (s, 3H), 4.02 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 160.96, 155.43, 154.13, 146.88, 145.99, 138.93, 136.87, 133.92, 132.13, 121.74, 120.03, 117.16, 112.44, 111.49, 107.58, 106.07, 96.89, 11.82, 11.42; MS(*m*/*z*): 332.36 (M + 1).

**6-(Thiophen-2-yl)-3-(thiophen-3-yl)-1*H*-indazole (2c).** Yield (65%), brown oil; $^1$H NMR (300 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.5 Hz, 1H), 7.88 (dd, *J* = 2.9, 1.2 Hz, 1H), 7.78–7.75 (m, 1H), 7.73 (d, *J* = 4.0 Hz, 1H), 7.71 (s, 1H), 7.56 (dq, *J* = 7.0, 2.9, 2.3 Hz, 3H), 7.49 (ddt, *J* = 8.0, 5.0, 2.5 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) 151.01, 143.85, 137.15, 134.84, 129.31, 128.84, 127.39, 121.87, 121.66, 121.17, 112.43, 109.92, 109.04, 107.81, 107.63; MS(*m*/*z*): 282.38 (M + 1).

**3,6-Bis(benzo[*d*][*1,3*]dioxol-5-yl)-1*H*-indazole (2d).** Yield (61%), yellow solid, mp: 182.1–183.3°C; $^1$H NMR (300 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.5 Hz, 1H), 7.79 (d, *J* = 7.8 Hz, 1H), 7.61 (s, 1H), 7.53–7.50 (m, 3H), 7.42 (dd, *J* = 8.5, 1.5 Hz, 1H), 7.16–7.11 (m, 2H), 7.02–6.98 (m, 1H), 6.94 (d, *J* = 8.7 Hz, 1H), 6.06 (s, 4H), 6.04 (s, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 149.45, 149.28, 148.21, 148.15, 147.72, 147.36, 146.21, 146.10, 145.56, 144.45, 143.48, 142.96, 129.61, 129.45, 127.52, 127.33, 121.32, 121.13, 108.74, 108.67, 108.02, 107.98, 107.61, 101.26, 101.21; MS(*m*/*z*): 385.35 (M + 1).

**Diethyl 4,4′-(1*H*-indazole-3,6-diyl)dibenzoate (2e).** Yield (64%), yellow oil; $^1$H NMR (300 MHz, $CDCl_3$) δ 8.72 (s, 1H), 8.36 (d, *J* = 10.0 Hz, 1H), 8.22 (d, *J* = 7.9 Hz, 1H), 8.16–8.08 (m, 2H), 7.85 (d, *J* = 7.8 Hz, 1H), 7.73 (s, 1H), 7.66–7.53 (m, 3H), 7.27 (d, *J* = 2.3 Hz, 1H), 4.53–4.38 (m, 4H), 1.44 (qd, *J* = 8.1, 7.6, 4.2 Hz, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 151.54, 141.67, 141.18, 134.56, 133.59, 131.78, 131.27, 131.12, 129.31, 128.91, 128.64, 128.52, 128.12, 127.24, 121.62, 119.36, 115.73, 112.53, 110.56, 61.16, 61.05, 14.37, 14.30; MS(*m*/*z*): 414.46 (M + 1).

**Dimethyl 4,4′-(1*H*-indazole-3,6-diyl)dibenzoate (2f).** Yield (78%), colorless oil; $^1$H NMR (300 MHz, $CDCl_3$) δ 8.23 (d, *J* = 8.2 Hz, 2H), 8.12 (d, *J* = 7.7 Hz, 2H), 7.98–7.89 (m, 3H), 7.77 (d, *J* = 9.5 Hz, 1H), 7.63 (s, 1H), 7.27–7.22 (m, 2H), 3.99 (s, 3H), 3.93 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 173.98, 173.74, 148.30, 146.82, 145.68, 145.16, 140.01, 137.87, 130.26, 130.17, 129.97, 129.40, 127.26, 123.25, 121.43, 121.22, 119.56, 119.34, 109.09, 108.52, 108.20, 103.78, 102.16, 37.56, 36.13; MS(*m*/*z*): 386.41 (M + 1).

**3,6-Bis(3-methoxyphenyl)-1*H*-indazole (2g).** Yield (67%), yellow solid, mp: 150.8–151.3°C; $^1$H NMR (300 MHz, $CDCl_3$) δ 7.85 (dt, *J* = 7.2, 1.1 Hz, 2H), 7.77 (d, *J* = 2.7 Hz, 2H), 7.47 (t, *J* = 7.8 Hz, 3H), 7.28 (d, *J* = 1.0 Hz, 1H), 7.23–7.12 (m, 3H), 3.95 (s, 3H), 3.94 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 160.05, 159.97, 146.14, 143.07, 141.17, 135.15, 134.63, 129.97, 129.84, 127.22, 121.63, 120.18, 120.03, 119.47, 114.29, 113.42, 112.79, 112.21, 110.29, 55.39, 55.29; MS(*m*/*z*): 330.14 (M + 1).

**3,6-Di-*p*-tolyl-1H-indazole (2h).** Yield (67%), yellow oil; $^1$H NMR (300 MHz, $CDCl_3$) δ 8.06 (t, *J* = 8.5 Hz, 1H), 7.96 (d, *J* = 7.8 Hz, 2H), 7.53 (d, *J* = 7.8 Hz, 2H), 7.48 (d, *J* = 10.2 Hz, 1H), 7.37 (d, *J* = 8.0 Hz, 2H), 7.33–7.28 (m, 2H), 7.07 (d, *J* = 4.3 Hz, 1H), 2.46 (s, 3H), 2.43 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 145.77, 142.43, 140.19, 138.24, 138.08, 137.37, 130.65, 130.05, 129.85, 129.65, 129.55, 128.58, 127.50, 127.40, 121.47, 121.37, 120.10, 115.10, 107.85, 21.34, 21.15; MS(*m*/*z*): 298.15 (M + 1).

**3,6-Bis(3-fluoro-4-methoxyphenyl)-1*H*-indazole (2i).** Yield (77%), yellow solid, mp: 194.5–195.8°C; $^1$H NMR (300 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.5 Hz, 1H), 7.80–7.71 (m, 2H), 7.52 (s, 1H), 7.46–7.40 (m, 1H), 7.40–7.35 (m, 1H), 7.10 (dt, *J* = 12.2, 8.6 Hz, 2H), 6.88 (dd, *J* = 5.4, 3.0 Hz, 1H), 3.98 (s, 3H), 3.96 (d, *J* = 2.9 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 165.58, 165.00, 153.82, 143.86, 143.26, 141.76, 137.46, 137.11, 136.72, 130.25, 130.22, 129.73, 128.92, 127.34, 127.13, 125.82, 123.84, 119.86, 113.81, 113.20, 111.97, 45.72, 45.01; MS(*m*/*z*): 366.37 (M + 1).

**General Procedure for Microwave-promoted Copper-catalyzed *N*-Arylation Reaction[24,26,27].** 3-(Thiophen-

3-yl)-1*H*-indazole (0.5 mmol), bromobenzene (0.55 mmol), $Cs_2CO_3$ (0.75 mmol), $Cu_2O$ (10 mol %), and DMA (5 mL) were added to a 10 mL vial. The vial was sealed with a crimp cap and placed in a Biotage initiator microwave cavity. After the reaction vial was heated at 200 °C for 1 h, product was purified with same work-up procedure for monoaryl coupling reaction conditions using a hexane: ethyl acetate = 50:1 solvent.

**1-Phenyl-3-(thiophen-3-yl)-1*H*-indazole (3a)** was obtained with 71% yields as a pink solid. mp: 81–82°C;$^1$H NMR (300 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.1 Hz, 1H), 7.90 (dd, *J* = 2.9, 1.3 Hz, 1H), 7.83–7.72 (m, 4H), 7.55 (t, *J* = 7.8 Hz, 2H), 7.50–7.42 (m, 2H), 7.42–7.26 (m, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 142.3, 140.1, 134.3, 129.5, 127.2, 127.1, 126.7, 126.0, 123.2, 123.0, 122.5, 122.0, 121.4, 110.7, 29.8; MS(*m*/*z*): 276.36 (M + 1).

**1-(3-Methoxyphenyl)-3-(thiophen-3-yl)-1*H*-indazole (3b)**. Yield (59%), brown oil; $^1$H NMR (500 MHz, $CDCl_3$) δ 8.09 (dd, *J* = 8.1, 1.0 Hz, 1H), 7.93 (dd, *J* = 3.0, 1.2 Hz, 1H), 7.86–7.80 (m, 2H), 7.54–7.42 (m, 3H), 7.44–7.26 (m, 3H), 6.95 (dd, *J* = 8.1, 2.5 Hz, 1H), 3.93 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 160.5, 142.2, 141.2, 140.1, 134.2, 130.2, 127.3, 127.1, 126.0, 123.2, 122.5, 122.0, 121.3, 115.1, 112.5, 110.9, 108.8, 55.6; MS(*m*/*z*): 306.39 (M + 1).

**3-(Thiophen-3-yl)-1-(*p*-tolyl)-1*H*-indazole (3c)**. Yield (65%), white solid, mp: 95°C; $^1$H NMR (300 MHz, $CDCl_3$) δ 8.05 (dt, *J* = 8.2, 1.1 Hz, 1H), 7.88 (dt, *J* = 2.5, 1.2 Hz, 1H), 7.79 (dd, *J* = 5.0, 1.1 Hz, 1H), 7.73 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.69–7.61 (m, 2H), 7.50–7.40 (m, 2H), 7.38–7.27 (m, 3H), 2.44 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 141.9, 140.1, 137.6, 136.6, 134.4, 131.8, 130.0, 127.0, 125.9, 123.0, 122.9, 122.3, 121.7, 121.3, 110.7, 21.1; MS(*m*/*z*): 290.39 (M + 1).

**1-(3,4-Dimethoxyphenyl)-3-(thiophen-3-yl)-1*H*-indazole (3d)**. Yield (39%), brown oil; $^1$H NMR (300 MHz, $CDCl_3$) δ 8.05 (d, *J* = 8.2 Hz, 1H), 7.91–7.87 (m, 1H), 7.80 (d, *J* = 5.0 Hz, 1H), 7.68 (d, *J* = 8.5 Hz, 1H), 7.52–7.38 (m, 2H), 7.30 (d, *J* = 7.6 Hz, 3H), 7.03 (d, *J* = 8.2 Hz, 1H), 3.96 (s, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 149.7, 148.1, 141.8, 140.4, 134.3, 133.3, 127.1, 127.0, 126.0, 122.7, 122.4, 121.8, 121.3, 115.4, 111.3, 110.6, 107.9, 56.2, 56.2; MS(*m*/*z*): 336.42 (M + 1).

**1-(6-Methylpyridin-2-yl)-3-phenyl-1*H*-indazole (3e)**. Yield (61%), brown solid, mp: 93–94°C; $^1$H NMR (300 MHz, $CDCl_3$) δ 8.96 (dt, *J* = 8.6, 1.0 Hz, 1H), 8.10–7.99 (m, 3H), 7.95 (d, *J* = 8.2 Hz, 1H), 7.69 (t, *J* = 7.9 Hz, 1H), 7.60–7.49 (m, 3H), 7.49–7.39 (m, 1H), 7.36–7.29 (m, 1H), 6.98 (d, *J* = 7.5 Hz, 1H), 2.65 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 156.9, 153.8, 146.9, 140.4, 138.5, 133.1, 128.9, 128.6, 128.0, 127.7, 124.0, 122.7, 121.0, 119.1, 115.9, 110.5, 24.3; MS(*m*/*z*): 285.35 (M + 1).

**1-(Benzo[*b*]thiophen-3-yl)-3-phenyl-1*H*-indaz-ole (3f)**. Yield (43%), yellow oil; $^1$H NMR (300 MHz, $CDCl_3$) δ 8.13 (d, *J* = 8.1 Hz, 1H), 8.11–8.05 (m, 2H), 7.98–7.90 (m, 2H), 7.68 (s, 1H), 7.60–7.50 (m, 3H), 7.49–7.40 (m, 4H), 7.32 (dd, *J* = 7.9, 6.9 Hz, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 146.1, 141.9, 139.0, 134.5, 133.2, 132.4, 128.9, 128.4, 127.8, 127.2, 125.5, 124.9, 123.0, 122.9, 122.3, 122.1, 121.6, 119.6, 110.7; MS(*m*/*z*): 326.42 (M + 1).

**1-(3-Methoxyphenyl)-3-(6-methoxypyridin-3-yl)-1*H*-indazole (3g)**. Yield (53%), white solid, mp: 89–91°C; $^1$H NMR (300 MHz, $CDCl_3$) δ 8.87 (q, *J* = 2.2 Hz, 1H), 8.28 (dq, *J* = 7.2, 2.2 Hz, 1H), 8.07–8.02 (m, 1H), 7.87–7.82 (m, 1H), 7.49 (m, 2H), 7.43–7.36 (m, 2H), 7.36–7.30 (m, 1H), 7.00–6.91 (m, 2H), 4.06 (s, 3H), 3.93 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 164.1, 160.6, 145.7, 145.7, 143.3, 141.1, 140.3, 138.1, 130.2, 127.3, 123.0, 122.2, 121.2, 115.0, 112.6, 111.3, 111.0, 108.8, 55.6, 53.7; MS(*m*/*z*): 331.38 (M + 1).

**3-(6-Methoxypyridin-3-yl)-1-(*p*-tolyl)-1*H*-indazole (3h)**. Yield (55%), red solid, mp: 102°C; $^1$H NMR (300 MHz, $CDCl_3$) δ 8.83 (dd, *J* = 2.4, 0.8 Hz, 1H), 8.25 (dd, *J* = 8.6, 2.4 Hz, 1H), 8.01 (dt, *J* = 8.2, 1.0 Hz, 1H), 7.74 (dt, *J* = 8.6, 0.9 Hz, 1H), 7.70–7.59 (m, 2H), 7.45 (dd, *J* = 8.4, 6.9 Hz, 1H), 7.40–7.24 (m, 3H), 6.90 (dd, *J* = 8.6, 0.8 Hz, 1H), 4.02 (s, 3H), 2.44 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 164.0, 145.6, 143.0, 140.3, 138.1, 137.5, 136.8, 130.1, 127.1, 123.0, 122.9, 122.7, 122.0, 121.2, 111.3, 110.8, 53.7, 21.1; MS(*m*/*z*): 315.38 (M + 1).

**1-(6-Methoxynaphthalen-2-yl)-3-(6-methoxypyridin-3-yl)-1*H*-indazole (3i)**. Yield (42%), brown solid, mp: 109–110°C; $^1$H NMR (300 MHz, $CDCl_3$) δ 8.89 (d, *J* = 2.4 Hz, 1H), 8.31 (dd, *J* = 8.6, 2.4 Hz, 1H), 8.14 (s, 1H), 8.08 (d, *J* = 8.2 Hz, 1H), 7.98–7.91 (m, 2H), 7.86 (t, *J* = 8.2 Hz, 2H), 7.53–7.49 (m, 1H), 7.38–7.32 (m, 1H), 7.29–7.24 (m, 2H), 6.95 (d, *J* = 8.6 Hz, 1H), 4.07 (s, 3H), 3.99 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 164.0, 158.0, 145.7, 143.3, 140.5, 138.1, 135.6, 133.3, 129.4, 129.0, 128.2, 127.3, 122.9, 122.8, 122.6, 122.1, 121.3, 120.6, 119.9, 111.3, 110.8, 105.9, 55.4, 53.7; MS(*m*/*z*): 381.44 (M + 1).

**3-(Benzo[*b*]thiophen-3-yl)-1-(3-methoxyphenyl)-1*H*-indazole (3j)**. Yield (48%), yellow oil; $^1$H NMR (300 MHz, $CDCl_3$) δ 8.61 (dt, *J* = 7.6, 1.6 Hz, 1H), 8.02 (d, *J* = 8.1 Hz, 1H), 7.99–7.91 (m, 2H), 7.86 (d, *J* = 8.4 Hz, 1H), 7.53–7.38 (m, 6H), 7.33–7.23 (m, 1H), 6.94 (m, 1H), 3.91 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 160.5, 142.0, 141.3, 140.3, 139.7, 137.8, 130.2, 128.7, 127.4, 125.6, 124.9, 124.8, 124.7, 124.2, 122.6, 122.0, 121.5, 115.0, 112.3, 110.9, 108.8, 55.6; MS(*m*/*z*): 356.45 (M + 1).

**3-(Benzo[*b*]thiophen-3-yl)-1-(*p*-tolyl)-1*H*-indazole (3k)**. Yield (45%), white solid, mp: 173–175°C; $^1$H NMR (500 MHz, $CDCl_3$) δ 8.64 (d, *J* = 7.8 Hz, 1H), 8.05 (d, *J* = 8.3 Hz, 1H), 7.98 (d, *J* = 7.8 Hz, 2H), 7.83 (d, *J* = 8.3 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 2H), 7.55–7.43 (m, 3H), 7.41 (d, *J* = 8.0 Hz, 2H), 7.33 (t, *J* = 7.5 Hz, 1H), 2.49 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 141.7, 136.6, 134.3, 130.0, 129.9, 129.2, 129.1, 127.2, 125.3, 124.8, 124.7, 124.6, 124.5, 122.9, 122.5, 121.8, 121.4, 110.7, 68.7, 21.1; MS(*m*/*z*): 340.45 (M + 1).

**3-(Benzo[*b*]thiophen-3-yl)-1-(3-isopropoxyphenyl)-1*H*-indazole (3l)**. Yield (42%), colorless oil; $^1$H NMR (300 MHz, $CDCl_3$) δ 8.62–8.44 (m, 1H), 7.93 (dt, *J* = 8.2, 1.0 Hz, 1H), 7.88–7.84 (m, 2H), 7.81–7.75 (m, 1H), 7.44–7.35 (m, 3H), 7.35–7.30 (m, 3H), 7.22–7.15 (m, 1H), 6.83 (dt, *J* = 7.6, 2.1 Hz, 1H), 4.57 (h, *J* = 6.0 Hz, 1H), 1.32 (d, *J* = 6.0 Hz, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 158.9, 141.9, 141.3, 140.3, 139.7, 137.8, 130.2, 128.8, 127.4, 125.5, 124.9, 124.8, 124.7, 124.2, 122.5, 122.0, 121.5, 114.8, 114.1, 111.0, 110.6, 70.3, 22.1; MS(*m*/*z*): 384.50 (M + 1).

**General Procedure for Microwave-assisted Palladium-catalyzed Alkene Coupling reaction[27].** *N*-Benzyl-3-iodo-1*H*-indazole (0.5 mmol), methyl acrylate (1.5 mmol), $Pd(PPh_3)_2Cl_2$(1 mol %), TEA (1.0 mmol), and DMF (3 mL) were added to a 5 mL vial. After the reaction vial was heated at 120 °C for 30 min, product was purified with same work-up procedure for monoaryl coupling reaction conditions using a hexane: ethyl acetate = 10:1.

**(*E*)-Methyl 3-(1-benzyl-1*H*-indazol-3-yl)acrylate (4a).** Yield (99%) white solid; mp: 89–90°C; $^1$H NMR (500 MHz, $CDCl_3$) δ 8.07 (d, *J* = 16.2 Hz, 1H), 7.96 (dt, *J* = 8.1, 1.0 Hz, 1H), 7.44–7.37 (m, 2H), 7.37–7.22 (m, 6H), 6.83 (d, *J* = 16.2 Hz, 1H), 5.64 (s, 2H), 3.87 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 167.6, 140.9, 140.1, 136.1, 128.8, 128.0, 127.2, 126.9, 123.0, 122.3, 120.8, 118.8, 110.0, 53.5, 51.8, 29.7; MS(*m*/*z*): 292.34 (M + 1).

**(*E*)-Ethyl 3-(1-benzyl-1*H*-indazol-3-yl)acrylate (4b).** Yield (89%), white solid, mp: 82–83°C; $^1$H NMR (300 MHz, $CDCl_3$) δ 8.03 (d, *J* = 16.3 Hz, 1H), 7.94 (dt, *J* = 8.2, 1.0 Hz, 1H), 7.39–7.33 (m, 2H), 7.31–7.17 (m, 6H), 6.78 (d, *J* = 16.3 Hz, 1H), 5.60 (s, 2H), 4.29 (q, *J* = 7.1 Hz, 2H), 1.35 (t, *J* = 7.1 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 167.1, 140.9, 140.2, 136.1, 135.9, 128.8, 128.0, 127.2, 126.9, 123.0, 122.2, 120.8, 119.4, 110.0, 60.5, 53.4, 14.4; MS(*m*/*z*): 306.37 (M + 1).

**(*E*)-1-(3-Methoxybenzyl)-3-styryl-1*H*-indazole (4c)**. Yield (81%), white solid, mp: 70–71°C; $^1$H NMR (500 MHz, $CDCl_3$) δ 8.08 (d, *J* = 8.2 Hz, 1H), 7.67–7.60 (m, 2H), 7.59–7.48 (m, 2H), 7.45–7.36 (m, 4H), 7.34–7.30 (m, 1H), 7.25 (td, *J* = 8.0, 2.3 Hz, 2H), 6.86–6.82 (m, 2H), 6.80 (t, *J* = 1.9 Hz, 1H), 5.61 (s, 2H), 3.77 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 159.9, 142.7, 141.0, 138.3, 137.4, 130.7, 129.8, 128.7, 127.8, 126.7, 126.5, 122.4, 121.2, 120.2, 119.4, 113.1, 112.9, 109.7, 60.4, 55.2, 53.0; MS(*m*/*z*): 340.43 (M + 1).

**(*E*)-4-(1-(3-Methoxybenzyl)-1*H*-indazol-3-yl)but-3-en-2-one (4d).** Yield (80%), yellow oil; $^1$H NMR (500 MHz, $CDCl_3$) δ 7.98 (dq, *J* = 8.3, 0.8 Hz, 1H), 7.89 (d, *J* = 16.6 Hz, 1H), 7.43–7.39 (m, 2H), 7.30–7.26 (m, 1H), 7.24 (d, *J* = 7.9 Hz, 1H), 7.07 (d, *J* = 16.6 Hz, 1H), 6.85–6.80 (m, 2H), 6.77 (t, *J* = 2.1 Hz, 1H), 5.61 (s, 2H), 3.76 (s, 3H), 2.45 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 198.7, 160.0, 141.1, 140.2, 137.5, 135.2, 129.9, 128.3, 127.0, 123.0, 122.5, 120.9, 119.4, 113.2, 113.1, 110.1, 55.2, 53.4, 27.0; MS(*m*/*z*): 367.37 (M + 1).

**(*E*)-Benzyl 3-(1-(3-fluorobenzyl)-1*H*-indazol-3-yl)-acrylate (4e).** Yield (93%), white solid, mp: 85–86°C; $^1$H NMR (500 MHz, $CDCl_3$) δ 8.06 (d, *J* = 16.3 Hz, 1H), 7.97–7.92 (m, 1H), 7.47–7.31 (m, 7H), 7.29–7.21 (m, 2H), 7.00–6.88 (m, 3H), 6.84 (d, *J* = 16.3 Hz, 1H), 5.59 (s, 2H), 5.29 (s, 2H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 166.9, 164.0, 162.0, 140.9, 140.4, 138.6 (d, $J_{CF}$ = 6.6 Hz), 136.3, 136.1, 130.5 (d, $J_{CF}$ = 8.3 Hz), 128.6, 128.3, 128.3, 127.1, 123.0, 122.7 (d, $J_{CF}$ = 2.7 Hz), 122.4, 120.9, 119.2, 115.0 (d, $J_{CF}$ = 21.1 Hz), 114.0 (d, $J_{CF}$ = 22.0 Hz), 109.8, 66.4, 52.8; MS(*m*/*z*): 386.43 (M + 1).

**(*E*)-Ethyl 3-(1-(3-fluorobenzyl)-1*H*-indazol-3-yl)acrylate (4f).** Yield (99%), white solid, mp: 73–74°C; $^1$H NMR (500 MHz, $CDCl_3$) δ 8.05 (d, *J* = 16.3 Hz, 1H), 7.98 (dt, *J* = 8.2, 1.0 Hz, 1H), 7.46–7.33 (m, 2H), 7.33–7.24 (m, 2H), 7.04–6.94 (m, 2H), 6.91 (dt, *J* = 9.4, 2.1 Hz, 1H), 6.82 (d, *J* = 16.3 Hz, 1H), 5.62 (s, 2H), 4.33 (q, *J* = 7.1 Hz, 2H), 1.39 (t, *J* = 7.1 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 167.1, 164.0, 162.0, 140.7 (d, $J_{CF}$ = 53.6 Hz), 138.6 (d, $J_{CF}$ = 6.7 Hz), 135.7, 130.4 (d, $J_{CF}$ = 8.3 Hz), 127.1, 123.0, 122.7 (d, $J_{CF}$ = 2.8 Hz), 122.4, 120.9, 119.7, 115.0 (d, $J_{CF}$ = 21.2 Hz), 114.2 (d, $J_{CF}$ = 22.2 Hz), 109.7, 60.6, 52.8, 14.4; MS(*m*/*z*): 324.36 (M + 1).

**(*E*)-Ethyl 3-(1-(3-methylbenzyl)-1*H*-indazol-3-yl)acrylate (4g).** Yield (89%), colorless oil; $^1$H NMR (500 MHz, $CDCl_3$) δ 8.06 (d, *J* = 16.3 Hz, 1H), 7.98 (dt, *J* = 8.2, 1.0 Hz, 1H), 7.41 (d, *J* = 3.8 Hz, 2H), 7.30–7.26 (m, 1H), 7.22 (t, *J* = 7.6 Hz, 1H), 7.13–7.02 (m, 3H), 6.81 (d, *J* = 16.3 Hz, 1H), 5.60 (s, 2H), 4.33 (q, *J* = 7.1 Hz, 2H), 2.32 (s, 3H), 1.39 (t, *J* = 7.1 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 167.2, 140.9, 140.1, 138.6, 136.0, 128.8, 128.7, 127.9, 126.8, 124.3, 123.0, 122.2, 121.1, 120.8, 119.3, 110.0, 60.5, 53.5, 21.4, 14.4; MS(*m*/*z*): 320.39 (M + 1).

**(*E*)-Methyl 3-(1-(4-(*tert*-butyl)benzyl)-1*H*-indazol-3-yl)acrylate (4h).** Yield (99%), yellow oil; $^1$H NMR (300 MHz, $CDCl_3$) δ 8.03 (d, *J* = 16.2 Hz, 1H), 7.93 (d, *J* = 8.1 Hz, 1H), 7.42–7.28 (m, 4H), 7.28–7.21 (m, 1H), 7.16 (d, *J* = 8.4 Hz, 2H), 6.78 (d, *J* = 16.2 Hz, 1H), 5.58 (s, 2H), 3.84 (s, 3H), 1.27 (s, 9H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 167.6, 151.0, 140.9, 140.0, 136.2, 133.1, 127.0, 126.8, 125.7, 123.0, 122.2, 120.7, 118.7, 110.1, 53.1, 51.7, 34.5, 31.3; MS(*m*/*z*): 348.45 (M + 1).

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