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Palladium-Catalyzed Direct C7-Arylation of Substituted Indazoles

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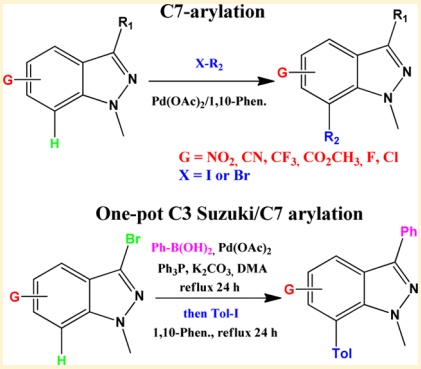
Supporting Information

ABSTRACT: A novel direct C7-arylation of indazoles with iodoaryls is described using $Pd(OAc)_2$ as catalyst, 1,10-phenanthroline as ligand, and K_2CO_3 as base in refluxing DMA. Direct C7-arylation of 3-substituted 1*H*-indazole containing an EWG on the arene ring gave the expected products in good isolated yields. In addition, a one-pot Suzuki–Miyaura/arylation procedure leading to C3,C7-diarylated indazoles has been developed.



INTRODUCTION

The C–H activation of heteroarenes, a very useful reaction in the field of organic synthesis, represents today a powerful approach for the preparation of new and promising bioactive aryl–heteroaryl systems.[1] In addition, the arylation of six-membered rings in 6,5-bicyclic systems containing no heteroatom on the six-membered ring and at least one heteroatom on the five-membered ring is quite rare. As far as we know, only one example of the C–H arylation of the benzene ring of quinolones has been reported.[2] The reported examples are usually related to the five-membered rings (examples: indole,[3] azaindole,[4] imidazo[1,2-*a*]pyridine,[5] imidazo[1,2-*a*]pyrimidine,[6] benzimidazole,[7] benzothiophene,[8] benzofuran,[8] and indazole,[9,10] among others). Unluckily, the arylation of the arene systems depends on directing groups such as amides,[11] carboxylic acids,[12] phosphoramidates,[13] cyano,[14] aldehyde,[15] purine,[16] and nitro groups,[17] among others.[18] In these cases, unfortunately, the reaction is limited by regioselectivity because most of the directing groups act on the ortho or meta position.[19] It should also be noted that new examples have been reported on the use of directing groups for the arylation of heteroaenes.[20]

Recently, we and others[9] developed C3-arylation of low reactive 1*H*-indazoles using $Pd(OAc)_2$ as catalyst and 1,10-phenanthroline as ligand. We and others have also reported that nitroindazoles, which are commercially available materials, can be transformed in a few steps into very interesting bioactive molecules.[21] Pursuing our effort to develop direct arylation, we wish to present herein the results of the regioselective C7-arylation of indazoles. To our knowledge, this is the first example of direct arylation at the six-membered ring of 6,5-bicyclic systems containing one or more heteroatoms on the five-membered ring.

RESULTS AND DISCUSSION

Guided by our previous reaction conditions developed for the C3-arylation of 1*H*-indazoles,[9b] we started our investigation using 4-nitro-, 5-nitro-, 6-nitro-, and 7-nitroindazoles as starting materials (**1a–d**)[9b] and iodobenzene as the coupling partner (Table 1). After initial optimization, we found that the use of K_3PO_4 as an additive to the previous reaction conditions improved both reaction yields and times. Thus, using the conditions 1 equiv of iodobenzene in the presence of 0.2 equiv of $Pd(OAc)_2$, 0.4 equiv of 1,10-phenanthroline, 3 equiv of K_2CO_3, and 2 equiv of K_3PO_4 in refluxing DMA, both 5-nitro- and 6-nitroindazoles (**1a,b**, respectively) gave mixtures of C3-arylated products (**2a,b**, respectively) and C3/C7-double-arylated products (**3a,b**, respectively). In both cases, when the amount of iodobenzene was increased (2 or 6 equiv), the ratios of C3-arylated products decreased while the ratios of C3/C7-double-arylated products increased (entries 1 and 2, Table 1). Interestingly, the reaction using 4-nitroindazole gave exclusively the C7-arylated product **4c**; no trace of the C3-

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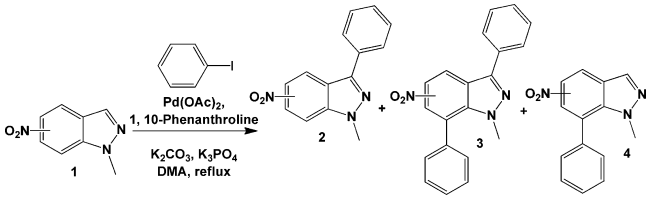
Table 1. Results of C3-Arylation versus C3/C7-Arylation

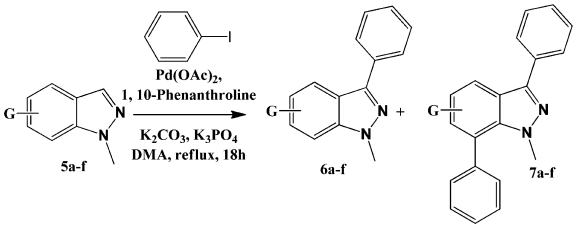


Entry	1	Ph-I (equiv.)	Reaction time	Yields 1/2/3/4
1		1	18	traces/61/21/0
		2	18	0/41/38/0
	1a	6	18	0/36/45/0
2		1	18	traces/53/19/0
		2	18	0/45/32/0
	1b			
3		1	24	45/0/0/12
		1	48	32/0/0/17
	1c	3	24	9/0/0/43
		5	24	0/0/0/**45**
4		1	18	traces/69/0/0
		2	18	0/**71**/0/0
	1d			

arylated product was observed. This is probably due to the steric demands of the nitro group in position 4 of compound **1c**. Total conversion was obtained when 5 equiv of iodobenzene was used (entry 3, Table 1). As expected, only the C3-arylated product **2d** was isolated in the case of 7-nitroindazole **1d**; here, the desired product was isolated in 71% yield (entry 4, Table 1).

Pleased by our preliminary results, we decided to apply the reaction conditions to indazoles **5a–e**, containing various substituents at either the 5- or 6-positions[9b] (Table 2). In the case of **5a–c** results similar to those obtained with 5-nitro- and 6-nitroindazoles were found. Explicitly, mixtures of the C3-arylated products **6a–c** and C3/C7-double-arylated products **7a–c** were obtained. In the case of 5-fluoro-1-methyl-1*H*-indazole (**5d**) as starting material, when 1 equiv of iodobenzene was used, the C3-arylated product **6d** was isolated in 69% yield,

Table 2. Results of C3-Arylation versus C3/C7-Arylation

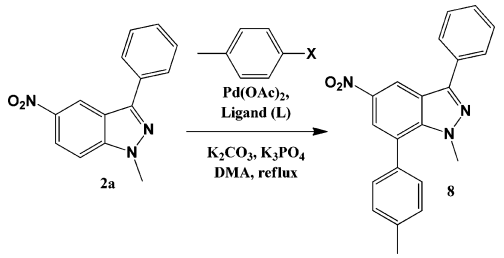


Entry	5	Ph-I (equiv.)	Yields 6/7
1		1	55/20
	5a	2	42/34
2		1	49/20
	5b	2	45/30
3		1	43/17
		2	39/26
	5c		
4		1	69/5
	5d	2	62/9
5		2	59/traces
	5e		
6		2	65/0
	5f		

and a very low amount of the C3/C7-double-arylated product **7d** was obtained (5%, entry 4, Table 2). A similar result was obtained when using **5e** as starting material: in this case, only the C3-arylated product **6e** was isolated in 59% yield (entry 5. Table 2). As expected, the reaction between **5f** and iodobenzene (2 equiv) led exclusively to the C3-arylated product **6f** in 65% yield (entry 6. Table 2). We noticed that, in the cases of starting materials **5a–d**, the same phenomenon was observed when increasing the amount of iodobenzene (2 equiv): the ratios of C3-arylated products **6a–d** dropped while the ratios of C3/C7-double-arylated products **7a–d** increased (entries 1–4, Table 2).

In order to optimize the C7-arylation reaction, we decided to use 1-methyl-5-nitroindazole **2a**, containing a phenyl group at the 3-position, as the starting material and 4-iodotoluene or 4-bromotoluene as the coupling partner (Table 3). In addition,

Table 3. Optimization of C7-Arylation of Indazole 2a



entry	X	amt of Pd (mol %)	L (amt (mol %))	base	time (h)	yield (%)
1	I	20	Phen (40)	K_2CO_3	48	61[a]
2	**I**	**20**	**Phen (40)**	**K_2CO_3**	**24**	**64**
3	I	20	Phen (40)	none	48	48 (17)[b]
4	I	20	Phen (40)	Ag_2CO_3	48	57
5	I	20	Phen (40)	Cs_2CO_3	24	58
6	I	20	Phen (40)	K_2CO_3	24	62[c]
7	I	20	Phen (40)	Ag_2CO_3	24	59[c]
8	I	20	Ph_3P (40)	K_2CO_3	24	0 (38)[b]
9	I	20	Xantphos (40)	K_2CO_3	24	0 (24)[b]
10	I	20	Phen (40)	K_2CO_3	24	49[d]
11	I	20	none	K_2CO_3	24	41[e]
12	I	20	Davephos (40)	K_2CO_3	24	traces (34)[b]
13	I	20	X-Phos (40)	K_2CO_3	24	traces (26)[b]
14	I	20	$PCy_3{\cdot}HBF_4$ (40)	K_2CO_3	24	15 (23)[b]
15	I	10	Phen (20)	K_2CO_3	36	62
16	I	5	Phen (10)	K_2CO_3	24	16 (47)[b]
17	I	20	Phen .(40)	Et_3N	24	12 (69)[b]
18	Br	20	Phen (40)	K_2CO_3	24	42 (13)[b]
19	Br	20	Phen (40)	K_2CO_3	48	47

[a]In this case the reaction was carried out without K_3PO_4. [b]The amount of recovered starting material **2a** is given in parentheses. [c]In this case $PdCl_2$ was used instead of $Pd(OAc)_2$. [d]In this case 0.3 equiv of PivOH as additive was added to the reaction mixture. [e]In this case the reaction was conducted without ligand in the presence of 0.3 equiv of PivOH as additive.

various reaction conditions were investigated using different bases (organic and inorganic), catalysts, ligands, amounts of catalysts and ligands, and reaction times.

K_3PO_4 has a significant impact on the reaction time (entries 1 and 2, Table 3). Thus, when K_3PO_4 was added to the reaction mixture, the reaction time was improved (24 h instead of 48 h).

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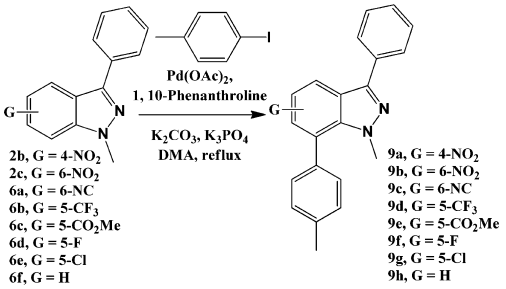
We also observed that the reaction yield was slightly enhanced (64% instead of 61%). K_2CO_3 was found to be the best base in comparison to Ag_2CO_3, Cs_2CO_3, and Et_3N, (entries 2, 4, 5, and 17, Table 3). $PdCl_2$ was also effective, giving the desired arylated product **8** in similar yields in comparison to those obtained when using $Pd(OAc)_2$ (entries 6 and 7, Table 3). Bromobenzene showed low reactivity in comparison to iodobenzene (entries 18 and 19, Table 3), and 1,10-phenanthroline proved to be the most effective ligand in comparison to all the ligands investigated in this study (entries 8−14, Table 3).

In order to examine the scope and limitation of the C7-arylation reaction, we decided to prepare a series of 7-substituted indazoles using the optimized reaction conditions. Various 3-phenyl-1-methylindazoles substituted with NO_2, CN, CF_3, CO_2Me, F, Cl, and H (**2b,c** and **6a−f**) were prepared starting from the substituted 1-methylindazoles **1b,c** and **5a−f** under standard Suzuki−Miyaura conditions.[22] Intermediates **2b,c** and **6a−f** were then used as starting materials, and 4-iodotoluene was used as the coupling partner (Table 4). In the case of EWG-substituted indazoles, the desired compounds **9a−e** were isolated in acceptable yields ranging between 63 and 66% (Table 4). In contrast, when 5-fluoro-3-phenyl-1-methylindazole was used as the starting material, the yield of the C7-arylated product **9f** was relatively low (43%, Table 4). The C7-arylation dropped when 5-chloro-1-methyl-3-phenyl-1*H*-indazole (**6e**) was used as the starting material, and only low yields were obtained when using either 2 or 5 equiv of 4-iodotoluene: the yields of the isolated product **9g** were 8 and 17%, respectively. In this case large amounts of starting material **6e** were recovered (Table 4). As expected, the reaction between 3-phenyl-1-methylindazole (**6f**) and 4-iodotoluene gave no trace of the desired product **9h**; only starting material **6f** was recovered in 74% yield (Table 4). This first study of the scope and limitation demonstrated that the presence of strong electron-withdrawing groups on positions 4, 5, and 6 is crucial for the achievement of a C7-arylation reaction in good reaction yields.

We then decided to introduce various aryls and heteroaryls at the 7-position of 5-nitro-1-methylindazole **2a**. To this end, we used various iodo(hetero)aryls as coupling partners (Table 5).

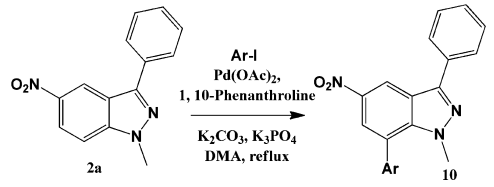
Table 4. Results of C7-Arylation of 1*H*-Indazoles 2b,c and 6a−f by 4-Iodotoluene



entry	starting material	product	yield (%)
1	**2b**	**9a**[a]	65
2	**2c**	**9b**[a]	63
3	**6a**	**9c**	66
4	**6b**	**9d**	65
5	**6c**	**9e**	64
6	**6d**	**9f**	43
7	**6e**	**9g**	8 (59),[b] 17[c] (31)[b]
8	**6f**	**9h**	0 (74)[d]

[a]NOESY experiments for compounds **9a,b** confirmed their structures (see the Supporting Information). [b]The amount of recovered starting material **6e** is given in parentheses. [c]In this case 5 equiv of 4-iodotoluene were used. [d]The amount of recovered starting material **6f** is given in parentheses.

Table 5. Results of C7-Arylation of 1*H*-Indazole 2a



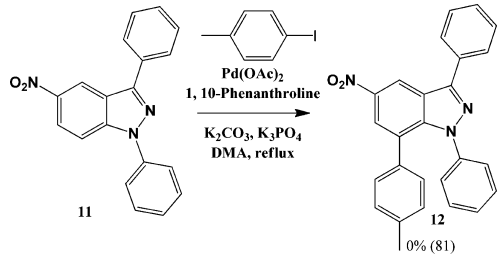
Entry	Aryl	Product	Yield (%)
1		**10a**[a]	67
2		**10b**	65
3		**10c**	69
4		**10d**	65
5		**10e**	66
6		**10f**	67
7		**10g**	0 (81)[b]
8		**10h**	0 (73)
9		**10i**	0 (75)

[a]A NOESY experiment for compound **10a** confirmed the structure (see the Supporting Information). [b]The amounts of recovered **2a** are given in parentheses.

As desired, the arylation reactions between **2a** and iodoaryls led to the expected products **10a−f** in yields ranging between 65 and 69%. Surprisingly, no reaction between **2a** and iodoheteroaryls was observed. In all cases only starting material **2a** was recovered.

For a mechanistic study, we decided to verify whether the reaction is influenced by the nature of the substituent at N1. For this reason we used 5-nitro-1,3-diphenyl-1*H*-indazole (**11**)[9b] as the starting material instead of **2a**. When **11** was treated with 4-iodotoluene no C7-arylation reaction was observed; only starting material **11** was recovered in 81% yield (Scheme 1). On the basis of this result we assume that the single lone pair of nitrogen (*N1*-methyl) plays the role of a directing group for regioselective C7-arylation by coordination with the palladium or by the inductive effect of the N1 nitrogen

Scheme 1. Reaction between 1*H*-Indazole 11 and 4-Iodotoluene



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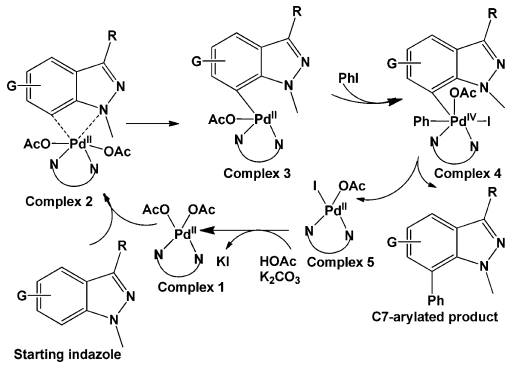
atom to stabilize the C−Pd bond. When the single lone pair of N1 is conjugated with a phenyl group, no coordination occurred, resulting in no C7-arylation, which might be attributed to the formation of an N2,C2′(phenyl ring)-palladacycle that inhibits the catalytic activity of Pd. We also think that the presence of an EWG at the 4-, 5-, or 6-position significantly enhances the reactivity at the C7-position of the six-membered ring.

A plausible mechanism is proposed in Scheme 2. The *N1*-indazole (starting material) coordinated to the catalyst

Scheme 2. Plausible Mechanism of C7-Arylation Reaction



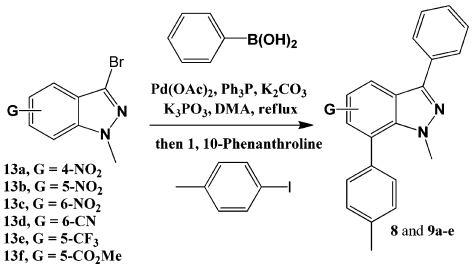
(complex 2) generated in situ from $Pd(OAc)_2$ and 1,10-phenanthroline (complex 1). Complex 2 led to complex 3 through C−H activation of the C7-position of indazole. Oxidative addition of I-Ph led to complex 4. Reductive elimination furnished the C7-arylated product and complex 5.

We then decided to develop a one-pot Suzuki/arylation sequence for the synthesis of C3,C7-diarylated indazoles. For this reason, we first developed new reaction conditions for Suzuki−Miyaura coupling similar to those found for the C7-arylation reaction. Accordingly, we found that adding Ph_3P as ligand to the reaction conditions previously developed for C7-arylation ($Pd(OAc)_2$ as catalyst, K_2CO_3 as base, and K_3PO_4 as additive in refluxing DMA for 24 h) was crucial for the achievement of total reaction conversions. Having optimized reaction conditions for Suzuki−Miyaura coupling on the one hand, we decided on the other hand to develop the one-pot Suzuki/arylation sequence. To accomplish this goal, 3-bromoindazoles **13a−f**, used as starting materials, and phenylboronic acid, used as coupling partner, were treated under Suzuki−Miyaura conditions for 24 h (first cross-coupling reactions) and then 1,10-phenanthroline and iodotoluene were added and the reaction mixture was heated again for 24 h (second cross-coupling reactions). This sequence led to the one-pot synthesis of C3,C7-diarylated products **8** and **9a−e** in yields ranging between 50 and 58% (Table 6).

CONCLUSIONS

In conclusion, the first example of regioselective direct C7-arylation of a 3-substituted 1*H*-indazole containing an EWG on the arene ring was reported. The optimal reaction conditions were found leading to the preparation of various C7-arylated indazole derivatives. We have shown that direct arylation of 1-methyl-4-nitroindazole gave exclusively the C7-arylated product, while the direct arylation of 1-methyl-7-nitroindazole led to the C3-arylated product. We then extended our study to the synthesis of C3,C7-diarylated products using a new one-pot Suzuki−Miyaura/arylation sequence. We believe that the N1 of

Table 6. Results of One-Pot Suzuki/C7-Arylation



entry	starting material	product	one-pot yield (%)
1	**13a**	**9a**	55
2	**13b**	**8**	58
3	**13c**	**9b**	53
4	**13d**	**9c**	56
5	**13e**	**9d**	50
6	**13f**	**9e**	51

1-methylindazole via the lone pair of *N1*-methyl acts as a directing group and that the presence of electron-withdrawing groups (EWG) on positions 4, 5, and 6 improves the C7-arylation reaction yields. We think that this interesting reactivity of substituted 1*H*-indazoles may open new avenues for the development of direct arylation reactions of several heteroaromatic systems.

EXPERIMENTAL SECTION

All reagents were purchased from commercial suppliers and were used without further purification. Microwave-assisted reactions were carried out with a microwave synthesis instrument, and temperatures were measured by an IR sensor. The reactions were monitored by thin-layer chromatography (TLC) analysis. Compounds were visualized by UV irradiation, Flash column chromatography was performed on silica gel 60 (230−400 mesh, 0.040 0.063 mm). Melting points (mp, °C) were taken on samples in open capillary tubes and are uncorrected. ^1H and ^{13}C NMR spectra were recorded on a spectrometer at 250 MHz (^{13}C, 62.9 MHz) or 400 MHz (^{13}C, 100 MHz). Chemical shifts are given in parts per million from tetramethylsilane (TMS) as internal standard. The following abbreviations are used for the proton spectra multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; qt, quintuplet; m, multiplet. Coupling constants (*J*) are reported in hertz (Hz). High-resolution mass spectra (HRMS) were performed on a Q-TOF mass spectrometer.

Synthesis of 1-Methyl-1*H*-indazole: 1a and 5f. In a 50 mL flask was dissolved 1 g of indazole in 10 mL of acetone at 0 °C, and then 3 equiv of KOH was added and the contents of the flask, sealed with a septum, were stirred for 60 min. Then, 1.5 equiv of CH_3I was added using a syringe and the reaction mixture was warmed to room temperature and this temperature maintained for 18 h. The inorganic base was removed by filtration, and the mixture was separated by flash chromatography on silica gel.

Synthesis of 1-Methyl-1*H*-indazole: 1b−d and 5a−e. Sodium hydride (55.0 mmol) was added to a solution of 1*H*-indazole (18.40 mmol) in *N*,*N*-dimethylformamide (50 mL), and the mixture was maintained for 60 min at 0 °C. Then, methyl iodide (22.12 mmol) was added and the reaction mixture. The reaction mixture was warmed to room temperature and this temperature maintained for 18 h. The reaction mixture was quenched with water (60 mL) and filtered through Celite, and the filtrate was concentrated. Purification by flash chromatography on silica gel led to the desired products **2a−d** and **5a−e**. This procedure gave exclusively *N*-methylation at the N1 position.

General Suzuki Procedure for the Preparation of 2b,c and 6a−f.[22a] A microwave vial containing a stirring bar was loaded with 3-bromoindazoles in 1,4-dioxane/EtOH/H_2O (3/1/0.5), phenylboronic

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acid (1.5 equiv) and cesium carbonate (1.3 equiv). The microwave vial was evacuated and back-filled twice with dry argon. Tetrakis-(triphenylphosphine)palladium (0.10 equiv) was then added, and the mixture was submitted to microwave irradiation with stirring at 140 °C for 100 min. After it was cooled, the mixture was filtered and the organic phase was extracted three times with ethyl acetate and dried over magnesium sulfate and then concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel.

Synthesis of 5-Nitro-1-phenyl-1*H*-indazole 11. In a microwave tube, 1 g (0.0041 mol) of the 5-nitro-1*H*-indazole was dissolved with stirring in 10 mL of *N*-methylpyrrolidine (NMP); then CuI (0.23 g, 0.0012 mol, 0.2 equiv), bipyridine (0.48 g, 0.003 mol, 0.5 equiv), K_2CO_3 (2.54 g, 0.018 mol, 3 equiv), and iodophenyl (1.3 g, 0.0061 mol, 1.5 equiv) were added. The microwave tube was sealed with a silicon septum and subjected to microwave irradiation at 200 °C with stirring for 45 min. Then, the reaction mixture was diluted with ethyl acetate and extracted (three times). The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (ether/CH_2Cl_2).

General Procedure of C7-Arylation. In a 10 mL flask, a solution of phenanthroline (57 mg, 0.31 mmol, 0.4 equiv) in DMA (2 mL) was degassed by bubbling argon, and then palladium acetate (0.14 mmol, 31 mg, 0.2 equiv) was added. The solution was stirred at room temperature for 3 min, and then K_2CO_3 (2.1 mmol, 290 mg, 3 equiv), K_3PO_4 (1.3 mmol, 297 mg, 2 equiv), 1-methylindazole (96 mg, 0.7 mmol), and 4-iodotoluene (0.9 mmol, 1 equiv) were successively added. The reaction mixtures were refluxed under argon for 24 h. After it was cooled, the mixture was filtered through Celite and the organic phase was extracted three times with ethyl acetate, dried over magnesium sulfate, and then concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel.

General Protocol of One-Pot Suzuki/Arylation. A flask containing a stirring bar was charged with 3-bromoindazoles, phenylboronic acid (1.5 equiv), K_2CO_3 (1.5 equiv), K_3PO_4 (1.5 equiv), and PPh_3 (0.2 equiv) in DMA (2 mL). The flask was degassed and back-filled with dry argon twice. $Pd(OAc)_2$ (0.1 equiv) was added. After the mixture was refluxed for 24 h, phenanthroline (0.4 equiv) and 4-iodotoluene (1 equiv) were added, and then, the reaction mixture was continuously refluxed under argon for 24 h. After it was cooled, the mixture was filtered through Celite and the organic phase was extracted three times with ethyl acetate, dried over magnesium sulfate, and then concentrated under reduced pressure. The residue was purified by flash chromatography to provide the desired products.

*1-Methyl-5-nitro-1H-indazole (**1a**).* Yield: 0.69 g, 70%. Beige solid. Mp: 160−162 °C (lit.[23] mp 161−162 °C).

*1-Methyl-6-nitro-1H-indazole (**1b**).* Yield: 2.5 g, 85%. Yellow solid. Mp: 124−126 °C. (lit.[24] mp 125−126 °C).

*1-Methyl-4-nitro-1H-indazole (**1c**).* Yield: 2.3 g, 79%. Yellow solid. Mp: 132−134 °C. (lit.[21a] mp 145 °C, lit.[25] mp 123−125 °C).

*1-Methyl-7-nitro-1H-indazole (**1d**).* Yield: 2.6 g, 88%. Yellow solid. Mp: 104−106 °C. (lit.[26] mp 99−100 °C).

*1-Methyl-5-nitro-3-phenyl-1H-indazole (**2a**).* Yield: 0.1 g, 61%. Yellow solid. Mp: 123 °C. IR (neat): ν_{max} 3093.83, 2945.67, 1614.36, 1515.03, 1328.96, 1276,99, 1078.12, 746.17, 662.52 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.95 (s, 1H), 8.29 (d, J = 9.5 Hz, 1H), 7.92 (d, J = 7.6 Hz, 2H), 7.50 (dt, J = 18.6, 8.2 Hz, 4H), 4.16 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 146.8, 142.9, 142.5, 131.8, 129.0 (2C), 128.8, 127.4 (2C), 121.4, 120.7, 119.3, 109.4, 35.9.HRMS (ESI): m/z calcd for $C_{14}H_{11}N_3O_2$ $[M + H]^+$: 254.0926, found 254.0924.

*1-Methyl-6-nitro-3-phenyl-1H-indazole (**2b**).* Yield: 0.36 g, 73%. Yellow solid. Mp: 109−111 °C. IR (neat): ν_{max} 3085.94, 1514.65, 1339.64, 1286.48, 1116.32, 962.66, 781.42734.56, 689.96 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.39 (d, J = 1.7 Hz, 1H), 8.10 (d, J = 8.9 Hz, 1H), 8.05 (dd, J = 8.9, 1.8 Hz, 1H), 7.93 (d, J = 8 Hz, 2H), 7.53 (t, J = 7.5 Hz, 2H), 7.45 (t, J = 7.4 Hz, 1H), 4.23 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 146.8, 144.8, 140.5, 132.6, 129.3 (2C), 128.9, 127.7 (2C), 124.9, 122.5, 115.9, 106.3, 36.46. HRMS (ESI): m/z calcd for $C_{14}H_{11}N_3O_2$ $[M + H]^+$ 254.0926, found 254.0924.

*1-Methyl-4-nitro-3-phenyl-1H-indazole (**2c**).* Yield: 0.35 g, 71%. Yellow solid. Mp: 109−111 °C. IR (neat): ν_{max} 32011.22, 2947.09, 1521.41, 1340.21, 978.82, 829.18, 729.19, 700.15, 666.52 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.83 (d, J = 7.5 Hz, 1H), 7.72 (d, J = 8.5 Hz, 1H), 7.52−7.39 (m, 6H), 4.19 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 143.5, 143.0, 142.5, 133.1, 128.3 (2C), 128.0, 127.8 (2C), 125.2, 117.5, 112.6, 114.6, 35.8. HRMS (ESI): m/z calcd for $C_{14}H_{11}N_3O_2$ $[M + H]^+$ 254.0927, found 254.0924.

*1-Methyl-7-nitro-3-phenyl-1H-indazole (**2d**).* Yield: 0.34 g, 71%. Yellow solid. Mp: 76−78 °C. IR (neat): ν_{max} 3035.61, 2956.10, 1617.41, 1525.76, 1389.59, 1363.12, 1256.99, 985.90, 897.63, 728.19, 691.09 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ 8.27 (dd, J = 8.0, 1.0 Hz, 1H), 8.14 (dd, J = 7.8, 1.0 Hz, 1H), 7.89−7.85 (m, 1H), 7.58−7.43 (m, 1H), 7.27 (t, J = 8.0 Hz, 1H), 4.29 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 145.6, 132.8, 132.2, 130.2, 129.3 (2C), 129.1, 128.4, 128.2 (2C), 127.0, 124.9, 120.3, 41.2. HRMS (ESI): m/z calcd for $C_{14}H_{11}N_3O_2$ $[M + H]^+$ 254.0927, found 254.0924.

*1-Methyl-5-nitro-3,7-diphenyl-1H-indazole (**3a**).* Yield: 20 mg, 21%. Yellow solid. Mp: 156 °C. IR (neat): ν_{max} 3055.57, 2947.11, 1597.89, 1524.87, 1330.78, 1074.29, 780.22, 699.54, cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.94 (d, J = 2.1 Hz, 1H), 8.15 (d, J = 2.1 Hz, 1H), 7.95−7.91 (m, 2H), 7.58−7.47 (m, 8H), 3.70 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 146.9, 142.0, 140.9, 136.5, 131.8, 129.6 (2C), 129.1 (2C), 128.9, 128.75, 128.4 (2C), 127.6 (2C), 126.6, 122.7, 121.9, 118.0, 39.4. HRMS (ESI): m/z calcd for $C_{20}H_{15}N_3O_2$ $[M + H]^+$ 330.1239, found 330.1237.

*1-Methyl-6-nitro-3,7-diphenyl-1H-indazole (**3b**).* Yield: 18 mg, 19%. Yellow solid. Mp: 123−125 °C. IR (neat): ν_{max} 3051.26, 2947.91, 1522.67, 1356.22, 1263.94, 1025.84, 758.96, 695.88 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.06 (d, J = 8.8 Hz, 1H), 7.89 (d, J = 7.0 Hz, 2H), 7.67 (d, J = 8.8 Hz, 1H), 7.55−7.49 (m, 5H), 7.46−7.42 (m, 3H), 3.48 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 147.9, 144.1, 138.9, 132.5, 132.5, 130.0 (2C), 129.2, 129.1 (2C), 128.6, 128.4 (2C), 127.7 (2C), 123.9, 121.4, 120.7, 116.4, 39.3. HRMS (ESI): m/z calcd for $C_{20}H_{15}N_3O_2$ $[M + H]^+$ 330.1239, found 330.1237.

*1-Methyl-4-nitro-7-phenyl-1H-indazole (**4**).* Yield: 44 mg, 45%. Yellow oil. IR (neat): ν_{max} 2918.39, 2849.86, 1518.20, 1336.02, 963.25, 838.08, 699.42 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ 8.70 (s, 1H), 8.17 (d, J = 7.9 Hz, 1H), 7.54−7.51 (m, 3H), 7.45 (m, 2H), 7.33 (d, J = 7.8 Hz, 1H), 3.67 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 139.8, 139.3, 136.9, 133.6, 132.8, 129.4 (2C), 129.0, 128.8, 128.5 (2C), 127.3, 118.3, 39.6. HRMS (ESI): m/z calcd for $C_{14}H_{11}N_3O_2$ $[M + H]^+$ 253.0859, found 253.0856.

*1-Methyl-1H-indazole-6-carbonitrile (**5a**).* Yield: 2.2 g, 73%. Yellow solid. Mp: 261−263 °C. IR (neat): ν_{max} 3072.28, 2942.20, 2222.74, 1475.11, 1380.95, 1293.27, 1229.00, 763.70, 875.58, 828.96, 763.70, 623.14 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.07 (s, 1H), 7.82 (dd, J = 8.3, 0.7 Hz, 1H), 7.79 (d, J = 0.7 Hz, 1H), 7.36 (dd, J = 8.3, 1.1 Hz, 1H), 4.14 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 138.5, 133.1, 125.9, 122.5, 122.3, 119.2, 114.3, 109.3, 35.8. HRMS (ESI): m/z calcd for $C_9H_7N_3$ $[M + H]^+$ 158.0719, found 158.0712.

*5-(Trifluoromethyl)-1-methyl-1H-indazole (**5b**).* Yield: 2.5 g, 81%. Yellow solid. Mp: 49−51 °C. IR (neat): ν_{max} 2945.57, 1633.21, 1332.56, 1179.24, 1093.31, 933.97, 804.94, 716,92, 613.83 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.08 (s, 1H), 8.05 (s, 1H), 7.60 (d, J = 8.8 Hz, 1H), 7.48 (d, J = 8.8 Hz, 1H), 4.11 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 140.6, 133.8, 124.7 ($q_{Cq\text{-}F}$, J^1= 273 Hz), 123.3 ($q_{Cq\text{-}CF}$, J^2= 32.3 Hz), 123.1, 122.7 ($q_{Cq\text{-}CF}$, J^2= 32.3 Hz), 122.8 ($q_{CH\text{-}F}$, J^3= 3.8 Hz), 119.3 ($q_{CH\text{-}F}$, J^3= 4 Hz), 109.5, 35.7. HRMS (ESI): m/z calcd for $C_9H_7F_3N_2$ $[M + H]^+$ 201.0638, found 201.0634.

*Methyl 1-Methyl-1H-indazole-5-carboxylate (**5c**).* Yield: 2.3 g, 75%. White solid. Mp: 117 °C. IR (neat): ν_{max} 2957.87, 1697.76, 1618.19, 1423.55, 1250.71, 1192.44, 981.95, 825.08, 766.18, 630.16 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.51 (s, 1H), 8.07 (d, J = 8.8 Hz, 2H), 7.40 (d, J = 8.8 Hz, 1H), 4.10 (s, 3H), 3.95 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 167.2, 141.5, 134.4, 127.0, 124.5, 123.6, 122.7, 108.5, 52.0, 35.6. HRMS (ESI): m/z calcd for $C_{10}H_{10}N_2O_2$ $[M + H]^+$ 191.0820, found 191.0815.

*5-Fluoro-1-methyl-1H-indazole (**5d**).* Yield: 2.6 g, 83%. Yellow oil. IR (neat): ν_{max} 3068.19, 1500.41, 1249.55, 1143.29, 802.39, 761.04

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cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (d, J = 0.6 Hz, 1H), 7.32 (dt, J = 7.8, 3.6 Hz, 2H), 7.16 (td, J = 9.0, 2.3 Hz, 1H), 4.06 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 158.9, 156.6, 136.9, 132.3 (d, J = 5 Hz), 123.8 (d, J = 10,1 Hz), 115.8 (d, J = 28.2 Hz), 109.9 (d, J = 9.1 Hz), 104.8 (d, J = 24.3 Hz), 35.7. HRMS (ESI): m/z calcd for $C_8H_7FN_2$ $[M + H]^+$ 151.0671, found 151.0666.

*5-Chloro-1-methyl-1H-indazole (**5e**).* Yield: 2.7 g, 86%. Orange solid. Mp: 65−67 °C. IR (neat): ν_{max} 3076.88, 2934.75, 1482.56, 1219.40, 880.81, 802.58, 746.66 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (s, 1H), 7.70 (d, J = 1.0 Hz, 1H), 7.33 (d, J = 1.6 Hz, 2H), 4.07 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 138.5, 132.2, 127.0, 126.3, 124.9, 120.3, 110.1, 35.8. HRMS (ESI): m/z calcd for $C_8H_7ClN_2$ $[M + H]^+$ 167.0376, found 167.0371.

*1-Methyl-1H-indazole (**5f**).* Yield: 0.78 g, 70%. White solid; mp 58−59 °C (lit.[9b] mp 57−59 °C).

*1-Methyl-3-phenyl-1H-indazole-6-carbonitrile (**6a**).* Yield: 0.34 g, 70%. Yellow solid. Mp: 99−101 °C. IR (neat): ν_{max} 3068.49, 2941.89, 2224.85, 1519.28, 1247.58, 965.81, 805.10, 699.02, 660.17, 628.62 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (d, J = 8.4 Hz, 1H), 7.91 (d, J = 7.1 Hz, 2H), 7.80 (s, 1H), 7.52 (t, J = 7.5 Hz, 2H), 7.47−7.39 (m, 2H), 4.18 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 144.4, 140.0, 132.4, 128.9 (2C), 128.4, 127.3 (2C), 123.5, 122.8, 122.6, 119.2, 114.5, 109.4, 35.8. HRMS (ESI): m/z calcd for $C_{15}H_{11}N_3$ $[M + H]^+$ 234.1028, found 234.1025.

*5-(Trifluoromethyl)-1-methyl-3-phenyl-1H-indazole (**6b**).* Yield: 0.33 g, 68%. Yellow solid. Mp: 74 °C. IR (neat): ν_{max} 2929.32, 1622.99, 1316.89, 1277.91, 1138.40, 1097.23, 805.25, 685.74, 623.32 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30 (s, 1H), 7.93 (d, J = 7.2 Hz, 2H), 7.64 (dd, J = 8.8, 1.2 Hz, 1H), 7.57−7.41 (m, 4H), 4.15 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 145.0, 142.1, 132.6, 128.9 (2C), 128.3, 127.4 (2C), 124.7 ($q_{Cq\text{-}F}$, J^1= 273 Hz), 123.6 ($q_{Cq\text{-}CF}$, J^2= 32.3 Hz),, 123.1, 122.8 ($q_{CH\text{-}F}$, J^3= 3.6 Hz), 120.7, 119.5 ($q_{CH\text{-}F}$, J^3= 4 Hz), 109.7, 35.7. HRMS (ESI): m/z calcd for $C_{15}H_{11}F_3N_2$ $[M + H]^+$ 277.0950, found 277.0947.

*Methyl 1-Methyl-3-phenyl-1H-indazole-5-carboxylate (**6c**).* Yield: 0.37 g, 75%. White solid. Mp: 95−97 °C. IR (neat): ν_{max} 2947.93, 1700.43, 1611.79, 1292.87, 1238.36, 1087.15, 780.02, 696,57, 669.26 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.75 (d, J = 0.6 Hz, 1H), 8.08 (dd, J = 8.9, 1.4 Hz, 1H), 7.96 (d, J = 7.1 Hz, 2H), 7.52 (t, J = 7.5 Hz, 2H), 7.41 (dd, J = 17.8, 8.1 Hz, 2H), 4.11 (s, 3H), 3.95 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 167.2, 145.5, 143.0, 132.7, 128.8 (2C), 128.2, 127.4 (2C), 127.0, 124.8, 123.0, 121.3, 108.8, 52.0, 35.6. HRMS (ESI): m/z calcd for $C_{16}H_{14}N_2O_2$ $[M + H]^+$: 267.1132, found 267.1128.

*5-Fluoro-1-methyl-3-phenyl-1H-indazole (**6d**).* Yield: 0.37 g, 76%. Yellow oil. IR (neat): ν_{max} 3065.54, 2938.05, 1497.25, 1410.43, 1278.02, 1253.52, 1134.19, 878.02, 771.60, 696.29 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (dd, J = 9.3, 4.6 Hz, 1H), 7.59−7.52 (m, 2H), 7.51−7.44 (m, 3H), 7.18−7.06 (m, 2H), 4.16 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 160.0, 157.6, 145.4, 136.3 (d, J = 8.1 Hz), 129.5, 129.2, 128.9, 120.5 (d, J = 12,1 Hz), 119.1 (d, J = 9.1 Hz), 117.6 (d, J = 29.3 Hz), 102.7 (d, J = 24.2 Hz), 38.8. HRMS (ESI): m/z calcd for $C_{14}H_{11}FN_2$ $[M + H]^+$ 227.0983, found 227.0979.

*5-Chloro-1-methyl-3-phenyl-1H-indazole (**6e**).* Yield: 0.36 g, 73%. Colorless oil. IR (neat): ν_{max} 3060.09, 2926.69, 2848.73, 1724.70, 1486.24, 1275.36, 821.35, 696.08 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (d, J = 0.9 Hz, 1H), 7.91(d, J = 1.3 Hz, 2H), 7.51 (t, J = 7.5 Hz, 2H), 7.43−7.34 (m, 3H), 4.12 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 143.4, 140.0, 133.2, 129.0 (2C), 128.2, 127.4 (2C), 127.1, 126.8, 122.5, 120.7, 110.4, 35.9. HRMS (ESI): m/z calcd for $C_{14}H_{11}ClN_2$ $[M + H]^+$ 243.0685, found 243.0683.

*1-Methyl-3-phenyl-1H-indazole (**6f**).* Yield: 0.35 g, 72%. Yellow solid. Mp: 72−73 °C (lit.[9b] mp 71−73 °C).

*1-Methyl-3,7-diphenyl-1H-indazole-6-carbonitrile (**7a**).* Yield: 66 mg, 34%. White solid. Mp: 119−121 °C. IR (neat): ν_{max} 3064.22, 2949.53, 2225.07, 1727.07, 1463.69, 1444.89, 1267.46, 758.07, 698.64 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.06 (d, J = 8.5 Hz, 1H), 7.90 (dd, J = 8.3, 1.4 Hz, 2H), 7.58−7.45 (m, 9H), 3.59 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 144.4, 138.7, 134.5, 132.6, 131.3, 130.0, 129.6, 129.1, 128.7, 128.6, 127.7, 124.4, 123.7, 121.5, 118.5, 110.9, 39.3. HRMS (ESI): m/z calcd for $C_{21}H_{15}N_3$ $[M + H]^+$ 310.1341, found 310.1338.

*5-(Trifluoromethyl)-1-methyl-3,7-diphenyl-1H-indazole (**7b**).* Yield: 52 mg, 30%. White solid. Mp: 102−104 °C. IR (neat): ν_{max} 3062.00, 1617.76, 1316.13, 1302.48, 1260.16, 1107.32, 889.74, 758.43, 696.69, 649.33 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.28 (s, 2H), 7.93 (d, J = 7.1 Hz, 4H), 7.52 (ddd, J = 11.4, 8.7, 4.8 Hz, 16H), 3.70 (s, 5H).^{13}C NMR (101 MHz, $CDCl_3$): δ 145.1, 140.1, 137.3, 132.5, 129.7 (2C), 128.9 (2C), 128.4, 128.3, 128.2 (2C), 127.6 (2C), 126.9, 124.6 ($q_{Cq\text{-}F}$, J^1 = 273 Hz), 124.4 ($q_{CH\text{-}F}$, J^3 = 3.1 Hz), 123.2 ($q_{Cq\text{-}CF}$, J^2 = 32.7 Hz), 121.9, 118.7 ($q_{Cq\text{-}CF}$, J^2 = 32 Hz), 118.4 ($q_{CH\text{-}F}$, J^3 = 4.04 Hz), 39.2. HRMS (ESI): m/z calcd for $C_{21}H_{15}F_3N_2$ $[M + H]^+$ 353.1262, found 353.1260.

*Methyl 1-Methyl-3,7-diphenyl-1H-indazole-5-carboxylate (**7c**).* Yield: 46 mg, 26%. White solid. Mp: 151−153 °C. IR (neat): ν_{max} 3061.75, 2947.20, 2849.50, 1707.30, 1601.78, 1244.89, 1209.06, 761.64, 698.41 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.74 (d, J = 1.5 Hz, 1H), 7.94 (d, J = 1.4 Hz, 2H), 7.59−7.43 (m, 9H), 3.95 (s, 3H), 3.69 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 167.4, 145.8, 141.1, 138.0, 132.8, 130.0 (2C), 129.1 (2C), 128.9, 128.5, 128.3 (2C), 128.3, 127.9 (2C), 126.1, 123.9, 123.2, 122.7, 52.2, 39.4. HRMS (ESI): m/z calcd for $C_{22}H_{18}N_2O_2$ $[M + H]^+$ 343.1442, found 343.1441.

*5-Fluoro-1-methyl-3,7-diphenyl-1H-indazole (**7d**).* Yield: 18 mg, 9%. White solid. Mp: 142−144 °C. IR (neat): ν_{max} 3054.50, 2959.93, 1961.95, 1491.48, 1385.79, 1140.44, 860.98, 756.66, 697.41 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.05 (dd, J = 8.53, 2 Hz, 2H), 7.59−7.39 (m, 8H), 7.26 (dd, J = 8.9, 2.4 Hz, 1H), 7.15 (dd, J = 8.7, 2.4 Hz, 1H), 4.20 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 158.7, 156.3, 143.6 (d, J = 6.06 Hz), 138.0, 136.5, 134.5, 133.1, 129.4 (2C), 128.8 (2C), 127.8 (2C), 127.5 (d, J = 9.09 Hz), 127.2 (2C), 122.4 (d, J = 10.1 Hz), 117.4 (d, J = 27.3 Hz), 104.0 (d, J = 24.2 Hz), 39.2. HRMS (ESI): m/z calcd for $C_{20}H_{15}FN_2$ $[M + H]^+$ 303.1290, found 303.1292.

*1-Methyl-5-nitro-3-phenyl-7-p-tolyl-1H-indazole (**8**).* Yield: 86 mg, 64%. Yellow solid. Mp: 157 °C. IR (neat): ν_{max} 2925.78, 1727.70, 1596.61, 1333.16, 1073.21, 820.24, 745.87, 695.10 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.92 (d, J = 2.1 Hz, 1H), 8.12 (d, J = 2.1 Hz, 1H), 7.92 (d, J = 6.7 Hz, 2H), 7.59−7.29 (m, 7H), 3.71 (s, 3H), 2.47 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 144.2, 140.1, 135.1, 135.1, 128.5, 125.9 (2C), 125.3, 125.2 (2C), 125.1 (2C), 124.6, 123.7 (2C), 119.8, 117.2, 116.8, 112.4, 35.4, 17.5.HRMS (ESI): m/z calcd for $C_{21}H_{17}N_3O_2$ $[M + H]^+$ 344.1395, found 344.1393.

*1-Methyl-4-nitro-3-phenyl-7-p-tolyl-1H-indazole (**9a**).* Yield: 86 mg, 65%. Yellow oil. IR (neat): ν_{max} 2918.66, 2850.12, 1519.07, 1337.16, 1036.77, 1020.35, 815.37, 698.90 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.87 (d, J = 7.5 Hz, 1H), 7.49−7.46 (m, 5H), 7.40−7.36 (m, 4H), 7.32 (d, J = 7.7 Hz, 1H), 3.74 (s, 3H), 2.51 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 143.6, 142.3, 140.6, 138.8, 133.9, 133.4, 132.1, 129.3 (2C), 129.1 (2C), 128.4 (2C), 128.2, 128.0 (2C), 127.2, 117.7, 113.8, 39.7, 21.3. HRMS (ESI): m/z calcd for $C_{21}H_{17}N_3O_2$ $[M + H]^+$ 344.1393, found 344.1393.

*1-Methyl-6-nitro-3-phenyl-7-p-tolyl-1H-indazole (**9b**).* Yield: 85 mg, 63%. Yellow solid. Mp: 177 °C. IR (neat): ν_{max} 2922.64, 1525.30, 1357.28, 1264.34, 792.55, 818.30, 693.89 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, J = 8.8 Hz, 1H), 7.89 (dd, J = 8.3, 1.2 Hz, 2H), 7.64 (d, J = 8.8 Hz, 1H), 7.54 (t, J = 7.4 Hz, 2H), 7.45 (t, J = 7.4 Hz, 1H), 7.31 (s, 4H), 3.52 (s, 3H), 2.46 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 148.0, 143.9, 138.9, 138.91, 132.3, 129.7 (2C), 129.1, 129.0 (2C), 128.9 (2C), 128.4, 127.5 (2C), 123.6, 121.0, 120.6, 116.2, 39.2, 21.3. HRMS (ESI): m/z calcd for $C_{21}H_{17}N_3O_2$ $[M + H]^+$ 344.1396, found 344.1393.

*1-Methyl-3-phenyl-7-p-tolyl-1H-indazole-6-carbonitrile (**9c**).* Yield: 91 mg, 66%. White solid. Mp: 149 °C. IR (neat): ν_{max} 3027.82, 2921.54, 2225.34, 1463.28, 1262.181019.73, 817.62, 764.23, 697.81 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.04 (d, J = 8.5 Hz, 1H), 7.89 (d, J = 7.0 Hz, 2H), 7.56−7.35 (m, 8H), 3.68−3.56 (s, 3H), 2.48 (s, 3H). ^{13}C NMR (63 MHz, $CDCl_3$): δ 144.3, 139.5, 132.6, 131.5, 131.4, 129.9 (2C), 129.4 (2C), 129.1 (2C), 128.5, 127.7 (2C), 127.5, 124.3, 123.7, 121.3, 118.7, 111.0, 39.4, 21.6. HRMS (ESI): m/z calcd for $C_{22}H_{17}N_3$ $[M + H]^+$ 324.1498, found 324.1495.

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*5-(Trifluoromethyl)-1-methyl-3-phenyl-7-p-tolyl-1H-indazole (**9d**).* Yield: 86 mg, 65%. White solid. Mp: 136 °C. IR (neat): ν_{max} 2945.35, 1613.54, 1318.89, 1301.08, 1108.59, 888.50, 760.39, 699.69 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.28 (s, 1H), 7.94 (d, J = 7.1 Hz, 2H), 7.57 (t, J = 7.5 Hz, 2H), 7.51−7.45 (m, 2H), 7.41−7.32 (m, 4H), 3.74 (s, 3H), 2.50 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 146.0, 141.2, 139.2, 135.3, 133.6, 130.6 (2C), 129.9 (2C), 129.3 (2C), 128.6 (2C), 127.9, 125.6 ($q_{Cq\text{-}F}$, J^1 = 273 Hz), 125.4 ($q_{CH\text{-}F}$, J^3 = 3.03 Hz), 124.2 ($q_{Cq\text{-}CF}$, J^2 = 32.3 Hz), 123.9 ($q_{Cq\text{-}CF}$, J^2 = 32 Hz), 122.9, 119.1 ($q_{CH\text{-}F}$, J^3 = 4.04 Hz), 40.2, 22.2. HRMS (ESI): m/z calcd for $C_{22}H_{17}F_3N_2$ $[M + H]^+$ 367.1418, found 367.1416.

*Methyl 1-Methyl-3-phenyl-7-p-tolyl-1H-indazole-5-carboxylate (**9e**).* Yield: 85 mg, 64% White solid. Mp: 138−140 °C. IR (neat): ν_{max} 2918.96, 2849.63, 1706.94, 1433.22, 1247.08, 1209.16, 762.91, 695.47 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ 8.72 (d, J = 1.8 Hz, 1H), 7.94 (m, 3H), 7.48−7.38 (m, 7H), 3.94 (s, 3H), 3.70 (s, 3H), 2.46 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 167.3, 145.6, 144.6, 137.9, 134.9, 132.7, 129.7 (2C), 128.9 (2C), 128.9 (2C), 128.8, 128.38, 127.7(2C), 126.0, 123.62, 123.06, 122.54, 52.12, 39.30, 21.30. HRMS (ESI): m/z calcd for $C_{23}H_{20}N_2O_2$ $[M + H]^+$ 357.1599, found 357.1597.

*5-Fluoro-1-methyl-3-phenyl-7-p-tolyl-1H-indazole (**9f**).* Yield: 60 mg, 43%. White solid. Mp: 135−137 °C. IR (neat): ν_{max} 3066.64, 2921.78, 1489.14, 1262.94, 993.98, 823.45, 698.87 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.88 (d, J = 7.2 Hz, 2H), 7.60 (dd, J = 8.8, 2.3 Hz, 1H), 7.50 (t, J = 7.6 Hz, 2H), 7.42−7.24 (m, 5H), 7.03 (dd, J = 9.3, 2.4 Hz, 1H), 3.66 (s, 3H), 2.45 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 158.5, 156.2, 143.5 (d, J = 6.06 Hz), 137.9, 137.7, 136.3, 134.3, 133.0, 130.1, 129.3 (2C), 128.6 (2C), 127.8, 127.7 (2C), 127.4 (d, J = 9.09 Hz), 127.1 (2C), 126.5, 122.4 (d, J = 10.1 Hz), 117.2 (d, J = 27.2 Hz), 103.8 (d, J = 24.2 Hz), 39.1, 21.0. HRMS (ESI): m/z calcd for $C_{21}H_{17}FN_2$ $[M + H]^+$ 317.1449, found 317.1448.

*5-Chloro-1-methyl-3-phenyl-7-p-tolyl-1H-indazole (**9g**).* Yield: 23 mg, 17%. Colorless oil. IR (neat): ν_{max} 2922.10, 2851.19, 2388.26, 1728.20, 1482.53, 1261.03, 826.65, 698.95 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ 7.94 (d, J = 2.0 Hz, 1H), 7.89 (dd, J = 8.3, 1.3 Hz, 2H), 7.55−7.49 (m, 3H), 7.43 (d, J = 7.1 Hz, 1H), 7.36−7.31 (m, 3H), 7.21 (d, J = 1.9 Hz, 1H), 3.66 (s, 3H), 2.46 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 143.5, 138.3, 138.2, 134.6, 133.1, 131.0, 129.7 (2C), 129.0 (2C), 128.6, 128.2 (2C), 127.6 (2C), 126.4, 125.2, 123.5, 119.4, 39.4, 21.4. HRMS (ESI): m/z calcd for $C_{21}H_{17}ClN_2$ $[M + H]^+$ 333.1451, found 333.1453.

*7-(4-Methoxyphenyl)-1-methyl-5-nitro-3-phenyl-1H-indazole (**10a**).* Yield: 95 mg, 67%. Yellow solid. Mp: 148−150 °C. IR (neat): ν_{max} 2960.90, 1596.52, 1507.82, 1284.87, 1704.93, 1024.50, 790.32, 692.85 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.92 (d, J = 2.1 Hz, 1H), 8.13 (d, J = 2.1 Hz, 1H), 7.93 (d, J = 7.1 Hz, 2H), 7.56 (t, J = 7.4 Hz, 2H), 7.48 (t, J = 8 Hz,1H), 7.39 (d, J = 8.7 Hz, 2H), 7.05 (d, J = 8.7 Hz, 2H), 3.91 (s, 3H), 3.73 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 159.9, 146.9, 142.1, 141.3, 131.8, 130.8 (2C), 129.1 (2C), 128.8, 128.6, 127.6 (2C), 126.4, 122.8, 121.9, 117.7, 113.8 (2C), 55.3, 39.4. HRMS (ESI): m/z calcd for $C_{21}H_{17}N_3O_3$ $[M + H]^+$ 360.1342, found 360.1343.

*7-(4-(Trifluoromethyl)phenyl)-1-methyl-5-nitro-3-phenyl-1H-indazole (**10b**).* Yield: 100 mg, 65%. Green solid. Mp: 165−167 °C. IR (neat): ν_{max} 3093.02, 2946.32, 1596.14, 1323.76, 1121.81, 1065.12, 842.30, 780.83 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.98 (d, J = 2.1 Hz, 1H), 8.16 (d, J = 2.1 Hz, 1H), 7.93 (d, J = 7.2 Hz, 2H), 7.82 (d, J = 8 Hz, 2H), 7.64 (d, J = 8 Hz, 2H), 7.58 (t, J = 7.2 Hz, 2H), 7.50 (t, J = 7.4 Hz, 1H), 3.72 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 147.2, 142.0, 140.5, 140.2, 131.5, 131.3, 130.1 (2C), 129.1 (2C), 129.0 (2C), 127.6 (2C), 125.5 ($q_{CH\text{-}F}$, J^3= 4.04 Hz), 125.0 ($q_{Cq\text{-}CF}$, J^2= 32 Hz), 123.8 ($q_{Cq\text{-}F}$, J^1= 273 Hz), 122.8, 122.2, 118.7, 39.6. HRMS (ESI): m/z calcd for $C_{21}H_{14}F_3N_3O_2$ $[M + H]^+$ 398.1110, found 398.1111.

*Ethyl 4-(1-Methyl-5-nitro-3-phenyl-1H-indazol-7-yl)benzoate (**10d**).* Yield: 100 mg, 65%. Yellow solid. Mp: 197 °C. IR (neat): ν_{max} 3054.39, 2979.68, 1702.27, 1458.69, 1289.58, 1098.04, 870.14, 774.78, 689.72 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.97 (d, J = 2.1 Hz, 1H), 8.22 (d, J = 8.3 Hz, 2H), 8.17 (d, J = 2.1 Hz, 1H), 7.93 (d, J = 7.1 Hz, 2H), 7.57 (dd, J = 7.8, 6.1 Hz, 4H), 7.53−7.47 (m, 1H), 4.46 (q, J = 7.1 Hz, 2H), 3.70 (s, 3H), 1.46 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 165.9, 147.1, 142.0, 140.9, 140.6, 131.6, 130.9, 129.7 (2C), 129.6 (2C), 129.1 (2C), 129.0, 127.6 (2C), 125.4, 122.6, 122.2, 118.5, 61.3, 39.5, 14.3. HRMS (ESI): m/z calcd for $C_{23}H_{19}N_3O_4$ $[M + H]^+$ 401.1376, found 401.1380.

*1-Methyl-5-nitro-3-phenyl-7-o-tolyl-1H-indazole (**10e**).* Yield: 89 mg, 66%. Yellow oil. IR (neat): ν_{max} 3065.97, 2945.32, 1597.87, 1527.01, 1330.10, 897.94, 694.02 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.94 (dd, J = 9.7, 2.2 Hz, 2H), 8.14 (dd, J = 8.7, 2.1 Hz, 1H), 8.10 (d, J = 2.1 Hz, 1H), 7.95−7.92 (m, 2H), 7.59−7.28 (m, 5H), 3.71 (s, 3H), 3.58 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 147.1, 142.4, 141.2, 138.4, 136.9, 133.7, 130.5, 130.3, 129.74, 129.3 (2C), 129.1, 128.4, 127.8 (2C), 126.9, 126.1, 122.4, 118.3, 39.6, 20.3. HRMS (ESI): m/z calcd for $C_{21}H_{17}N_3O_2$ $[M + H]^+$ 344.1397, found 344.1393.

*1-Methyl-5-nitro-3-phenyl-7-m-tolyl-1H-indazole (**10f**).* Yield: 90 mg, 67%. Yellow oil. IR (neat): ν_{max} 3055.47, 2918.88, 1598.36, 1525.29, 1330.58, 1077.53, 743.80, 680.61 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ 8.89 (d, J = 2.1 Hz, 1H), 8.10 (d, J = 2.1 Hz, 1H), 7.89 (dd, J = 8.4, 2.1 Hz, 2H), 7.59−7.43 (m, 1H), 7.42−7.23 (m, 1H), 3.68 (s, 3H), 2.44 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 147.1, 142.2, 141.1, 138.4, 136.6, 132.0, 130.5, 129.6, 129.2 (2C), 129.0, 128.4, 127.8 (2C), 127.0, 126.9, 122.8, 122.1, 118.0, 39.6, 21.6. HRMS (ESI): m/z calcd for $C_{21}H_{17}N_3O_2$ $[M + H]^+$ 344.1396, found 344.1393.

*5-Nitro-1-phenyl-1H-indazole (**11**).* Yield: 0.88 g, 88%. Yellow solid. Mp: 180 °C (lit.[27] mp 178−180 °C).

*5-Nitro-1,3-diphenyl-1H-indazole (**12**).* Yield: 89 mg, 68%. Yellow solid. Mp: 158 °C. IR (neat): ν_{max} 3063.11, 2621.11, 2283.20, 2162.63, 2049.56, 1498.38, 1336.29, 1079.08, 749.97, 690.58 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ 9.04 (dd, J = 2.2, 0.6 Hz, 1H), 8.32 (td, J = 9.3, 2.1 Hz, 1H), 8.03 (dd, J = 8.2, 1.6 Hz, 2H), 7.83−7.76 (m, 2H), 7.62−7.44 (m, 5H), 7.09 (dd, J = 2.1, 4.6 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 148.7, 143.2, 142.2, 139.1, 131.7, 129.9 (2C), 129.4, 129.3 (2C), 128.1, 127.9 (2C), 125.9, 123.5 (2C), 122.4, 119.6, 111.1. HRMS (ESI): m/z calcd for $C_{19}H_{13}N_3O_2$ $[M + H]^+$ 316.1081, found 316.1080.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Figures giving proton and carbon NMR spectra of the reported compounds, NOESY NMR spectra of **9a**,**b** and **10a**, and IR spectra of reported 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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