Direct C3-arylation of 2H-indazole derivatives with aryl bromides using a low loading of a phosphine-free palladium-catalyst

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Abstract: The palladium-catalysed direct arylation of 2H-indazoles with aryl bromides for the preparation of 3-aryl-2H-indazoles was found to proceed in high yields using only 0.5-0.1 mol% $Pd(OAc)_2$ catalyst and KOAc as inexpensive base. A wide variety of electron-deficient and electron-rich aryl bromides and also heteroaryl bromides has been successfully employed. Both electron-withdrawing and electron-donating substituents on the 2H-indazoles are also tolerated. Moreover, the reaction can be performed in "green" solvent cyclopentyl methyl ether.

Introduction

Indazole derivatives exhibit important biological properties.[1] For example, Losoxantrone is an anticancer drug that belongs to the family of drugs called antipyrazoles; whereas, **A** exhibits anti-inflammatory properties (Figure 1).[2] Moreover, some arylated pyrazolopyrimidines also display important properties, such as Ibrutinib which is an anticancer drug. Therefore, the discovery of simple procedures allowing the easy access to C3-arylated indazole derivatives is an important research area in organic chemistry.

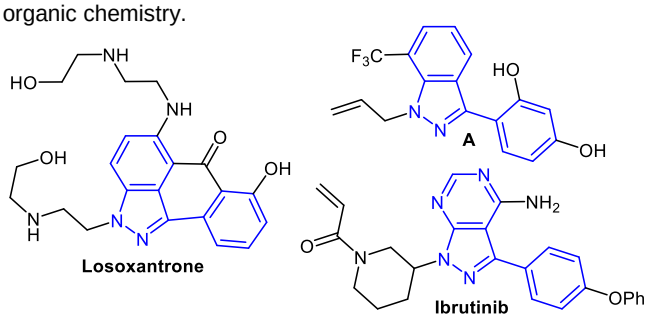
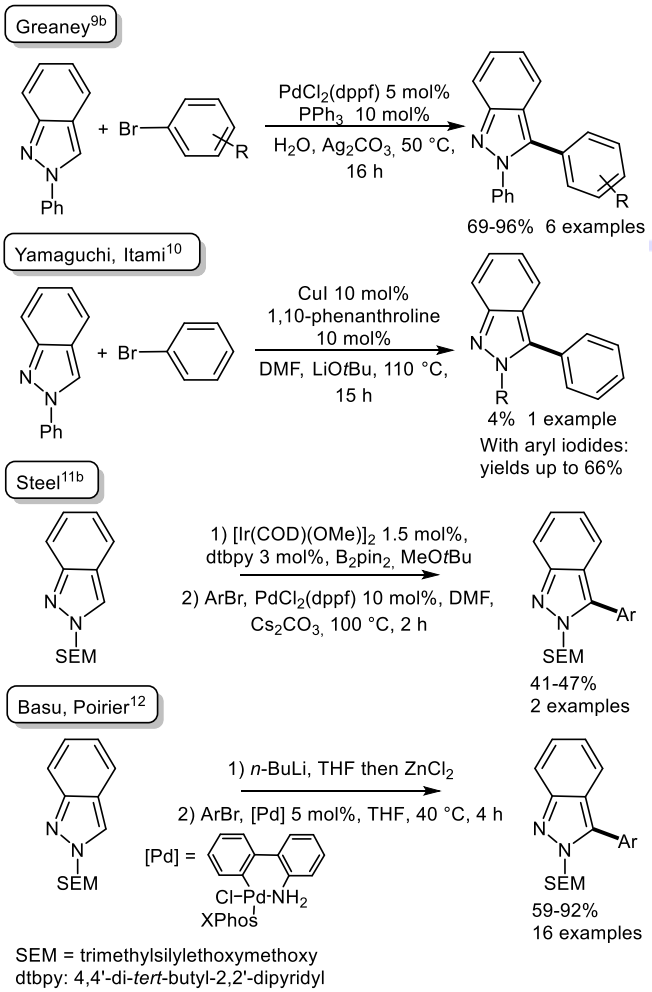


Figure 1 Examples of bioactive indazole derivatives

Nakamura, Tajima and Sakai reported in 1982, that isoxazoles could be arylated at position C4 of with aryl halides, via a C-H bond activation, using palladium catalysts.[3] Since these results, the Pd-catalysed direct arylation[4] of heteroarene derivatives, including pyrazoles, with aryl (pseudo)halides has been demonstrated to be one of the most powerful method for the synthesis of arylated heteroarenes.[4-8] For such reactions, the major by-products are a base associated to HX, instead of the metallic salts produced with other cross-coupling reactions. Since 2009, the C4- and C5-arylation of pyrazoles has been studied in details.[4r,6] On the contrary, only a few examples of Pd-catalysed direct couplings of aryl halides with 2H-indazoles have been reported so far.[9] In 2010, Greaney et al. reported that 2-phenyl-2H-indazole could be arylated at C3-position in high yields using aryl bromides as coupling partners. For this reaction, a quite high catalyst loading was employed: 5 mol% $PdCl_2(dppf)$ associated to 10 mol% PPh_3 (Scheme 1, top).[9b] Moreover, 1 equiv. of the expensive base Ag_2CO_3 was used. Yamaguchi and Itami reported in 2012 that the C3 arylation of 2H-indazoles could also be performed with a copper catalyst. However, this method is limited to the use of aryl iodides as aryl source, as with bromobenzene a very low yield of 4% was obtained (Scheme 1, middle).[10] 3-Arylindazoles can also be prepared in two steps by 1) reaction of indazoles with a boron derivative (B_2pin_2) in the presence of an iridium catalyst, 2) followed by C3-arylation via Suzuki coupling using an aryl bromide (Scheme 1, middle).[11] Very recently, Basu, Poirier et al. reported an access to a variety of 3-arylated 2H-indazoles via the formation of an indazolyl-zinc chloride intermediate prepared from indazole derivatives, followed by Negishi coupling using 5 mol% of a palladium complex containing XPhos ligand (Scheme 1, bottom).[12] Some 3-arylindazoles can also be prepared by intramolecular cyclization reactions.[13] However, the access to 3-aryl-2H-indazoles remains limited due to the relatively narrow scope of the actual synthetic methods.



Scheme 1 Reported metal-catalysed direct functionalisations and Negishi couplings of 2H-indazole derivatives with aryl bromides.

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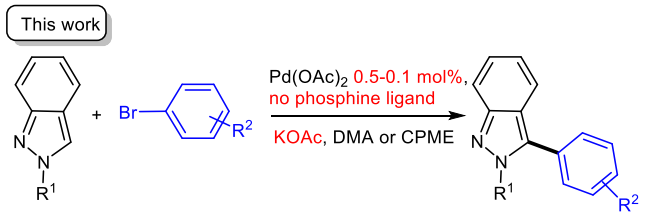
Therefore, the discovery of economically viable reaction conditions promoting the direct arylation at C3-position of 2H-indazoles with a wide variety of (hetero)aryl bromides, using a low loading of an easily available palladium catalyst, remains an important challenge.

Here, we report on the reactivity 2-benzyl-2H-indazole derivatives in the Pd-catalysed direct arylation reaction with a variety of aryl bromides using low loading of a phosphine-free palladium catalyst in the presence of an inexpensive base (Scheme 2).

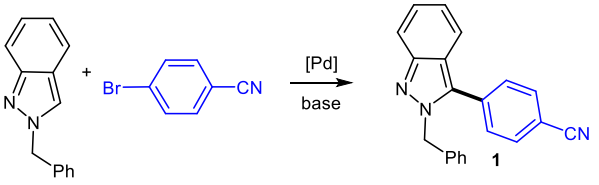


Scheme 2 Palladium-catalysed direct arylation of 2H-indazoles

Results and Discussion

We initially studied the C3-arylation of 2-benzyl-2H-indazole using 4-bromobenzonitrile as coupling partner in the presence of palladium catalysts (Table 1). The use of 2 mol% $PdCl(C_3H_5)(dppb)$ catalyst and KOAc as base at 150 °C led to the desired coupling product **1** in 85% yields, with a complete conversion of 4-bromobenzonitrile, but with the formation in low yield of [1,1'-biphenyl]-4,4'-dicarbonitrile arising from the homo-coupling of 4-bromobenzonitrile (Table 1, entry 1). In 2003, de Vries et al. reported that, when $Pd(OAc)_2$ is employed as the catalyst precursor without phosphine ligand, at elevated temperature, soluble palladium(0) colloids or nanoparticles are formed, which are very efficient catalysts in the Suzuki or Heck reactions.[14] We have recently reported that the coupling of aryl bromides with several heteroaromatics proceed nicely under the de Vries conditions.[15] Such phosphine-free conditions were found to be also very effective for the C3-arylation of 2H-indazoles. The use of 1 mol%, 0.5 mol% or even 0.1 mol% $Pd(OAc)_2$ catalyst at 150°C was found to promote efficiently the coupling of 2-benzyl-2H-indazole and 4-bromobenzonitrile, affording the target product **1** in very high yields of 88%-93% (Table 1, entries 2-4). The use of 0.5 mol% $PdCl_2$ catalyst without phosphine ligand was also very effective, as **1** was isolated in 92% yield (Table 1, entry 5). Then, the influence of some bases using these phosphine-free conditions was examined. Sodium acetate and potassium carbonate, in the presence of 0.5 mol% $Pd(OAc)_2$, afforded **1** in 72% and 85% yields, respectively (Table 1, entries 6 and 7); whereas, cesium carbonate was completely ineffective for this reaction (Table 1, entry 8). The influence of the solvent was also examined. The reaction performed in DMF, NMP or xylene gave **1** in lower yields than in DMA, due again to the formation of [1,1'-biphenyl]-4,4'-dicarbonitrile as side-product (Table 1, entries 9-11). On the contrary, cyclopentyl methyl ether (CPME) was found to be very effective for the C3-arylation of 2-benzyl-2H-indazole with 4-bromobenzonitrile, as **1** was obtained in 87% yield (Table 1, entry 12). It should be mentioned that CPME is a suitable alternative solvent to DMA,[16] due to its high hydrophobicity, low formation of peroxides (compared with THF or diisopropyl ether), relative stability under acidic and basic conditions and a narrow explosion range. CPME can be manufactured by the addition of MeOH to cyclopentene, which produces no apparent waste.[17] The reaction performed in DMA at 120°C instead of 150°C using 0.5 mol% of $Pd(OAc)_2$ catalyst afforded **1** in 80% yield (Table 1, entry 13).

Table 1. C3-arylation of 2-benzyl-2H-indazole with 4-bromobenzonitrile: influence of the reaction conditions



Entry	Solvent	Base	Catalyst (mol%)	Temp. (°C)	Conv. (%)	Yield in **1** (%)
1	DMA	KOAc	$PdCl(C_3H_5)(dppb)$ (2)	150	100	85[a]
2	DMA	KOAc	$Pd(OAc)_2$ (1)	150	100	88[a]
3	DMA	KOAc	$Pd(OAc)_2$ (0.5)	150	100	93
4	DMA	KOAc	$Pd(OAc)_2$ (0.1)	150	100	93
5	DMA	KOAc	$PdCl_2$ (0.5)	150	100	92
6	DMA	NaOAc	$Pd(OAc)_2$ (0.5)	150	100	72[a]
7	DMA	K_2CO_3	$Pd(OAc)_2$ (0.5)	150	100	85
8	DMA	Cs_2CO_3	$Pd(OAc)_2$ (0.5)	150	15	<2
9	DMF	KOAc	$Pd(OAc)_2$ (0.5)	150	100	76[a]
10	NMP	KOAc	$Pd(OAc)_2$ (0.5)	150	100	74[a]
11	xylene	KOAc	$Pd(OAc)_2$ (0.5)	140	100	71[a]
12	CPME	KOAc	$Pd(OAc)_2$ (0.5)	110	100	87
13	DMA	KOAc	$Pd(OAc)_2$ (0.5)	120	97	80

Conditions: 2-benzyl-2H-indazole (1.3 equiv.), 4-bromobenzonitrile (1 equiv.), base (2 equiv.), 20 h, conversions of 4-bromobenzonitrile determined by GC and NMR, isolated yields. [a] traces of [1,1'-biphenyl]-4,4'-dicarbonitrile were also observed.

Then, we examined the scope of the C3-arylation reaction of 2H-indazoles using various aryl bromides in the presence of 0.5 mol% $Pd(OAc)_2$ as the catalyst, KOAc as the base in DMA at 150 °C (Scheme 3). First, the coupling of 2-benzyl-2H-indazole with *para*-substituted aryl bromides was studied. Reactions with 4-bromobenzaldehyde, 4-bromoacetophenone, 4-bromopropiophenone, 4-bromobenzophenone or methyl 4-bromobenzoate afforded **2-6** in 79-93% yields.

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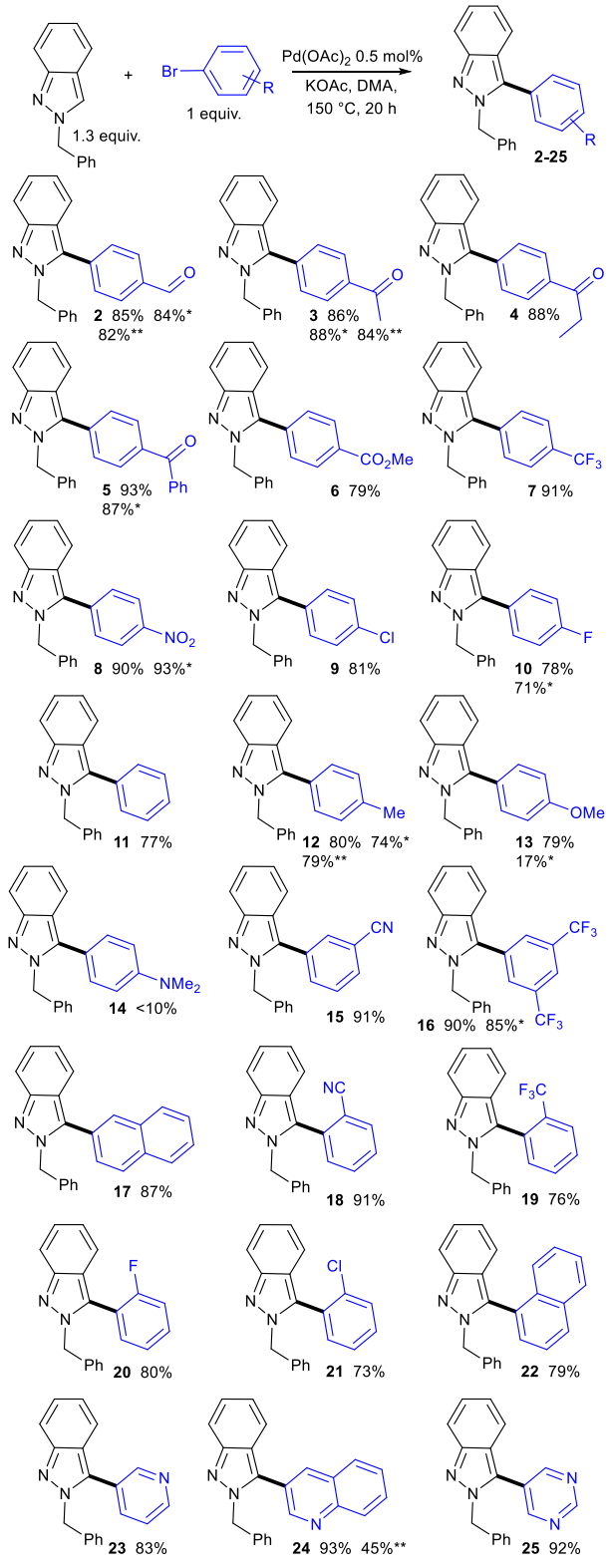

*: $Pd(OAc)_2$ 0.1 mol%
**: CMPE as solvent at 110°C

Scheme 3 Direct arylations of 2-benzyl-2H-indazole with a set of (hetero)aryl bromides.

High yields in the desired 3-arylindazoles **7**-**10** were also obtained with bromobenzenes bearing at *para*-position trifluoromethyl-, nitro-, chloro- or fluoro-substituents, in the presence of 0.5 mol% $Pd(OAc)_2$. Under these conditions, even the electron-rich 4-bromotoluene and 4-bromoanisole afforded the C3-arylated indazoles **12** and **13** in high yields; whereas, strongly electron-rich 4-*N*,*N*-dimethylaniline gave **14** in <10% yield, due to a poor conversion of this aryl bromide.

The *meta*-substituted electron-deficient aryl bromides, 3-bromobenzonitrile and 3,5-bis(trifluoromethyl)bromobenzene were also found to be suitable reactants, affording **15** and **16** in 91% and 90% yields, respectively (Scheme 3). Then, a set of *ortho*-substituted aryl bromides was reacted with 2-benzyl-2H-indazole using again 0.5 mol% $Pd(OAc)_2$ catalyst. 2-Nitrile-, 2-(trifluoromethyl)-, 2-fluoro- and 2-chloro-substituents were tolerated, affording the desired products **18**-**21** in 73-91% yields. *N*-containing heteroaryl bromides are also suitable reactants. With 3-bromopyridine, 3-bromoquinoline or 5-bromopyrimidine, under the same reaction conditions, the desired products **23**-**25** were obtained in 83-93% yields.

For several aryl bromides, the reaction yields using a lower catalyst loading of 0.1 mol% was determined (Scheme 3). With aryl bromides containing formyl, acetyl, benzoyl, nitro, trifluoromethyl, fluoro or methyl substituents, similar yields in **2**, **3** **5**, **8**, **10**, **12** and **16** than with 0.5 mol% catalyst were obtained; whereas, with electron-rich 4-bromoanisole, **13** was produced in a lower yield due to a partial conversion of this aryl bromide. A few reactions using CPME instead of DMA as solvent were also performed. Aryl bromides bearing 4-formyl-, 4-acetyl-, or 4-methyl-substituents with 0.5 mol% $Pd(OAc)_2$ at 110 °C in CPME gave **2, 3** and **12** in 79-84% yields.

Then, we investigated the influence of the nitrogen substituents on 2H-indazoles (Scheme 4). The reactivity of 2-*n*hexyl-2H-indazole was similar to 2-benzyl-2H-indazole, as its reaction with 4-bromopropiophenone, bromobenzene and 5-bromopyrimidine gave **26**-**28** in 78-93% yields. The reaction of 2-isobutyl-2H-indazole with 4-bromobenzonitrile and 4-bromonitrobenzene also gave the expected products **29** and **30** in similar yields. Even the more congested 2-isopropyl-2H-indazole reacted nicely under these low catalyst loading conditions, affording **31**-**33** in 86-93% yields.

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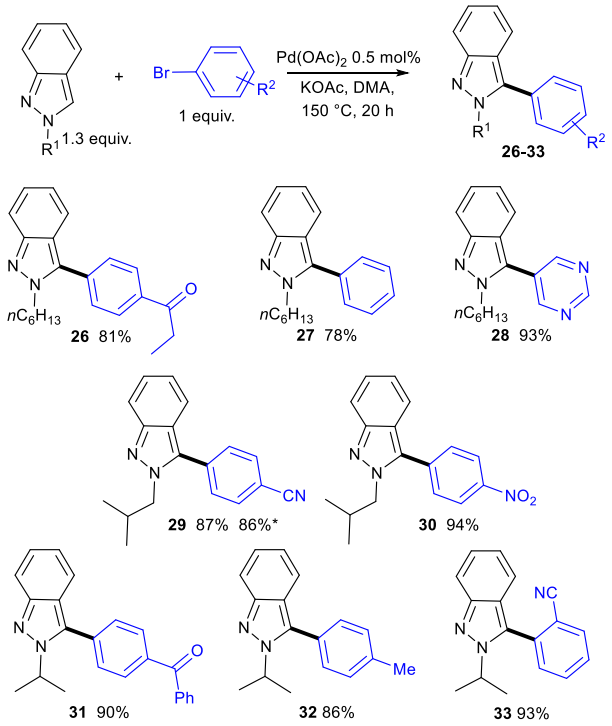
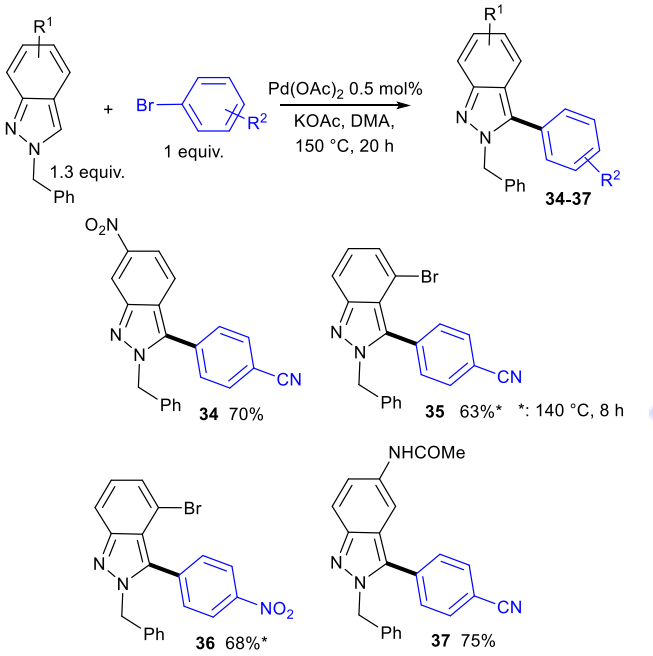


Scheme 4 Direct arylations of 2-alkyl-2H-indazoles with a set of aryl bromides.

The influence of some synthetically useful functional groups on the indazolyl moiety on the coupling was then investigated (Scheme 5). No significant influence of a nitro substituent at C6 position on indazole was observed, as the reaction of 2-benzyl-6-nitro-2H-indazole and 4-bromobenzonitrile gave **34** in 70% yield. The reaction of a 4-bromo-2*H*-indazole derivative with 4-bromobenzonitrile or 4-bromonitrobenzene at 140 °C during 8 h also proceeded nicely, without cleavage of the indazolyl C-Br bond, affording **35** and **36** in 63% and 64% yields, respectively. Under these reaction conditions, the oxidative addition of the aryl bromides to palladium is faster than the oxidative addition of the 4-bromoindazole moiety. We also examined the reactivity of an indazole bearing an acetamide substituent at C5-position. Arylation of this substrate would give an access to derivatives of Losoxantrone which is an anticancer drug (Fig. 1). Under the same reaction conditions, using 4-bromobenzonitrile as aryl source, target product **37** was obtained in 75% yield.



Scheme 5 Direct arylations of substituted 2-benzyl-2H-indazoles with aryl bromides.

N-protected 2H-indazoles can be prepared by several routes such as the reaction of a 2-nitrobenzaldehyde with an amine.[18b] They can also be obtained by reaction of indazoles with alkyl halides.[18a] However, this synthetic route sometimes affords mixtures of 1-benzyl-1H-indazoles and 2-benzyl-2H-indazoles. For example, the reaction of 5-nitroindazole with benzyl bromide in the presence of K_2CO_3 in DMF at 70 °C gave a mixture of 2-benzyl-5-nitro-2H-indazole and 1-benzyl-5-nitro-1H-indazole (ratio 1:1) which cannot be easily separated by column chromatography. We assumed that 2-benzyl-5-nitro-2H-indazole would be more reactive than 1-benzyl-5-nitro-1H-indazole in such direct arylations; therefore, we could expect to obtain selectively the C3-arylated 2-benzyl-5-nitro-2H-indazoles from a mixture of these two indazole derivatives. Indeed, from an equimolar mixture of these two indazoles and 4-bromobenzonitrile as coupling partner, the selective formation of **38** in 88% yield was observed; whereas, 1-benzyl-5-nitro-1H-indazole was recovered unreacted (Scheme 6, top). Similar results were obtained for the reaction of a mixture of these two indazoles with 3,5-bis(trifluoromethyl)bromobenzene or 3-bromoquinoline, affording the 3-arylated-2H-indazoles **39** and **40** in 79% and 77% yields, respectively. An equimolar mixture of 2-benzyl-6-nitro-2H-indazole and 1-benzyl-6-nitro-1H-indazole in the presence of 3-bromoquinoline also gave selectively the C3-arylated 2H-indazole **41** in good yield (Scheme 6, bottom).

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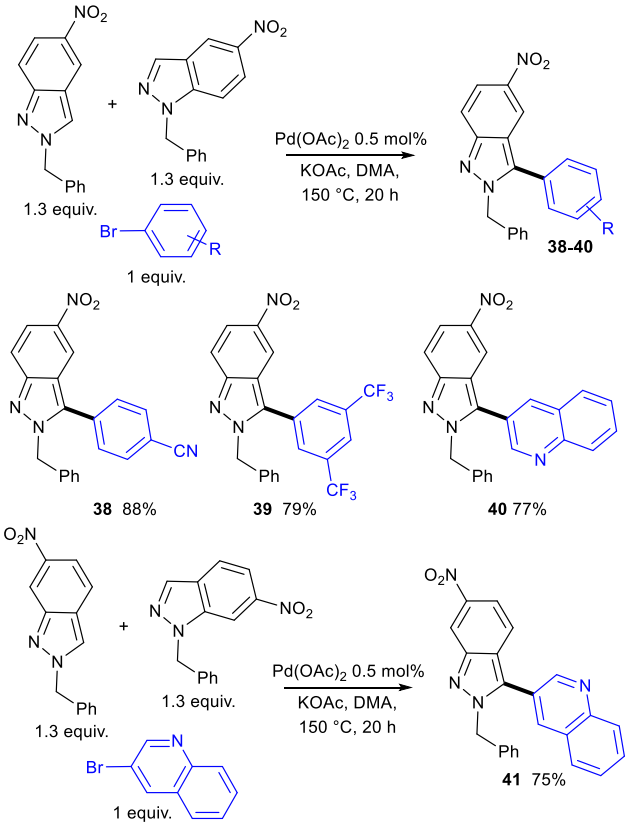
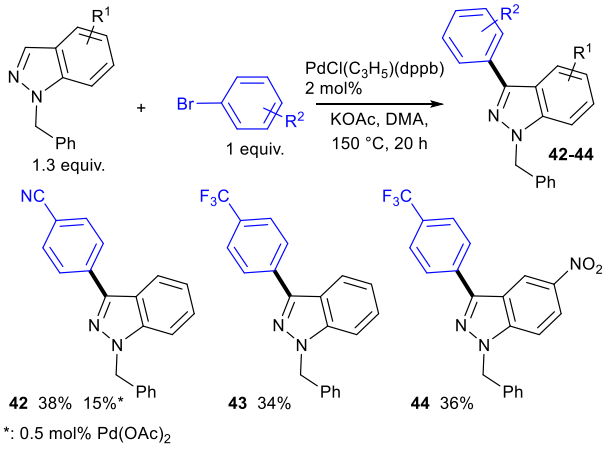


Scheme 6 Direct arylations using an equimolar mixture of nitro-substituted 2-benzyl-indazoles with a set of aryl bromides.

It should be mentioned that, despite 1H-indazoles are much less reactive than 2H-indazoles in Pd-catalysed direct arylation; however, moderate yield in 3-aryl-1H-indazoles could be obtained using 2 mol% $PdCl(C_3H_5)$(dppb) catalyst and KOAc as base in DMA at 150 °C. Under these conditions, 1-benzyl-1H-indazoles were successfully coupled with 4-bromobenzonitrile and 4-(trifluoromethyl)bromobenzene affording **42**-**44** in 34-38% yields. Product **42** was obtained in only 15% yield in the presence of 0.5 mol% $Pd(OAc)_2$ catalyst.



Scheme 7 Direct arylations of 1-benzyl-1H-indazoles with aryl bromides.

Conclusions

In summary, we demonstrated that a set of 2-benzyl-2H-indazoles reacts nicely in the presence of only 0.5-0.1 mol% of phosphine-free $Pd(OAc)_2$ catalyst and KOAc as inexpensive base to afford the C3-arylated 2H-indazoles in good to very high yields. Several functional groups on the aryl bromide such as nitro, formyl, acetyl, propionyl, benzoyl, ester, nitrile, trifluoromethyl, fluoro, chloro, methyl or methoxy are tolerated. This procedure appears to be very promising for the synthesis of 3-aryl-2H-indazoles, as the major by-products of these couplings are AcOH/KBr, as it reduces the number of steps to prepare these compounds, as there is no need to eliminate phosphine derivatives at the end of the reaction, and as it can be performed in CPME as “green” solvent.

Experimental Section

DMA (99%), was purchased from Acros. $Pd(OAc)_2$, $[Pd(C_3H_5)Cl]_2$, 1.4-bis(diphenylphosphino)butane (98%), KOAc (99%), Indazole (99%), 5-nitro-1H-indazole (98+%), and 4-bromo-1H-indazole (97+%), were purchased from Alfa Aesar. These compounds were not purified before use. 2-Benzyl-2*H*-indazole and 2-alkylindazoles were prepared according to reported procedures.[18]

Preparation of the $PdCl(C_3H_5)$(dppb) catalyst:[19] An oven-dried 40 mL Schlenk tube equipped with a magnetic stirring bar under argon atmosphere, was charged with $[Pd(C_3H_5)Cl]_2$ (182 mg, 0.5 mmol) and dppb (426 mg, 1 mmol). 10 mL of anhydrous dichloromethane was added, then the solution was stirred at room temperature for twenty minutes. The solvent was removed in vacuum. The yellow powder was used without purification. ^{31}P NMR (81 MHz, $CDCl_3$) δ = 19.3 (s).

Preparation of 2-benzyl-4-bromo-2*H*-indazole: Benzyl bromide (0.770 g, 4.5 mmol), 4-bromo-1*H*-indazole (0.591 g, 3 mmol), K_2CO_3 (1.242 g, 9 mmol) were dissolved in DMF (5 mL) under an argon atmosphere. The reaction mixture was stirred at 70 °C for 18 h. Then, the solvent was evaporated and the product was purified by silica gel column chromatography. 2-Benzyl-4-bromo-2H-indazole was obtained in 38% (0.327 g) yield as a yellow oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.91 (s, 1H), 7.68 (d, J = 8.4 Hz, 1H), 7.40-7.16 (m, 5H), 7.24 (d, J = 8.4 Hz, 1H), 7.13 (dd, J = 8.4, 8.0 Hz, 1H), 5.56 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.8, 135.2, 128.9, 128.4, 127.9, 126.6, 124.2, 124.0, 123.8, 116.7, 112.8, 57.6.

General procedure for the synthesis of compounds 1-44: In a typical experiment, the aryl bromide derivative (1 mmol), indazole derivative (1.3 mmol), KOAc (0.196 g, 2 mmol) and $PdCl(C_3H_5)$(dppb) (12.2 mg, 0.02 mmol) or $Pd(OAc)_2$ (1.1 mg, 0.005 mmol) or (0.22 mg, 0.001 mmol) (see table or schemes) were dissolved in DMA (4 mL) under an argon atmosphere. The reaction mixture was stirred at 110, 140 or 150 °C for 8 or 20 h (see tables and schemes). Then, the solvent was evaporated and the product was purified by silica gel column chromatography.

4-(2-Benzyl-2H-indazol-3-yl)benzonitrile (1): From 2-benzyl-2H-indazole (0.270 g, 1.3 mmol) and 4-bromobenzonitrile (0.182 g, 1

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mmol), **1** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 85-15) in 93% (0.287 g) yield as a yellow solid (mp: 190-192 °C). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.79 (d, *J* = 8.4 Hz, 1H), 7.75 (d, *J* = 8.3 Hz, 2H), 7.55 (d, *J* = 8.4 Hz, 1H), 7.53 (d, *J* = 8.2 Hz, 2H), 7.35 (t, *J* = 7.8 Hz, 1H), 7.31-7.22 (m, 3H), 7.15 (t, *J* = 7.8 Hz, 1H), 7.08-7.02 (m, 2H), 5.65 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.2, 136.2, 134.1, 133.9, 132.6, 129.9, 128.7, 127.9, 126.6, 126.5, 122.9, 121.4, 119.4, 118.1, 117.7, 112.3, 54.7. Elemental analysis: calcd (%) for $C_{21}H_{15}N_3$ (309.36): C 81.53, H 4.89; found: C 81.64, H 5.04.

4-(2-Benzyl-2H-indazol-3-yl)benzaldehyde (2): From 2-benzyl-2H-indazole (0.270 g, 1.3 mmol) and 4-bromobenzaldehyde (0.185 g, 1 mmol), **2** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 80-20) in 85% (0.265 g) yield as an orange solid (mp: 170-172 °C). ^1H NMR (400 MHz, $CDCl_3$): δ = 10.07 (s, 1H), 7.99 (d, *J* = 8.3 Hz, 2H), 7.80 (d, *J* = 8.4 Hz, 1H), 7.62 (d, *J* = 8.2 Hz, 2H), 7.60 (d, *J* = 8.4 Hz, 1H), 7.36 (t, *J* = 7.8 Hz, 1H), 7.31-7.22 (m, 3H), 7.13 (t, *J* = 7.8 Hz, 1H), 7.10-7.05 (m, 2H), 5.68 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.2, 148.2, 136.4, 135.8, 135.4, 134.7, 130.0, 129.9, 128.6, 127.8, 126.6, 126.5, 122.6, 121.4, 119.6, 117.6, 54.6. Elemental analysis: calcd (%) for $C_{21}H_{16}N_2O$ (312.36): C 80.75, H 5.16; found: C 80.46, H 5.02.

1-(4-(2-Benzyl-2H-indazol-3-yl)phenyl)ethan-1-one (3): From 2-benzyl-2H-indazole (0.270 g, 1.3 mmol) and 4-bromoacetophenone (0.199 g, 1 mmol), **3** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 75-25) in 88% (0.287 g) yield as a yellow solid (mp: 174-176 °C). ^1H NMR (400 MHz, $CDCl_3$): δ = 8.07 (d, *J* = 8.3 Hz, 2H), 7.79 (d, *J* = 8.4 Hz, 1H), 7.59 (d, *J* = 8.4 Hz, 1H), 7.55 (d, *J* = 8.2 Hz, 2H), 7.36 (t, *J* = 7.8 Hz, 1H), 7.31-7.22 (m, 3H), 7.12 (t, *J* = 7.8 Hz, 1H), 7.11-7.05 (m, 2H), 5.67 (s, 2H), 2.65 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.2, 148.3, 136.8, 136.5, 135.0, 134.1, 129.6, 128.8, 128.7, 127.7, 126.6, 126.4, 122.5, 121.4, 119.8, 117.6, 54.5, 26.6. Elemental analysis: calcd (%) for $C_{22}H_{18}N_2O$ (326.40): C 80.96, H 5.56; found: C 81.10, H 5.64.

1-(4-(2-Benzyl-2H-indazol-3-yl)phenyl)propan-1-one (4): From 2-benzyl-2H-indazole (0.270 g, 1.3 mmol) and 4-bromopropiophenone (0.213 g, 1 mmol), **4** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 75-25) in 88% (0.299 g) yield as a yellow solid (mp: 146-148 °C). ^1H NMR (400 MHz, $CDCl_3$): δ = 8.06 (d, *J* = 8.3 Hz, 2H), 7.79 (d, *J* = 8.4 Hz, 1H), 7.60 (d, *J* = 8.4 Hz, 1H), 7.56 (d, *J* = 8.2 Hz, 2H), 7.36 (t, *J* = 7.8 Hz, 1H), 7.31-7.22 (m, 3H), 7.13 (t, *J* = 7.8 Hz, 1H), 7.11-7.05 (m, 2H), 5.65 (s, 2H), 3.03 (q, *J* = 7.6 Hz, 2H), 1.26 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.9, 148.3, 136.7, 136.6, 135.1, 133.9, 129.6, 128.7, 128.5, 127.8, 126.7, 126.5, 122.5, 121.5, 119.9, 117.6, 54.6, 31.9, 8.2. Elemental analysis: calcd (%) for $C_{23}H_{20}N_2O$ (340.42): C 81.15, H 5.92; found: C 81.07, H 5.99.

(4-(2-Benzyl-2H-indazol-3-yl)phenyl)(phenyl)methanone (5): From 2-benzyl-2H-indazole (0.270 g, 1.3 mmol) and 4-bromobenzophenone (0.261 g, 1 mmol), **5** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 80-20) in 93% (0.361 g) yield as a brown oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.92 (d, *J* = 8.3 Hz, 2H), 7.85 (d, *J* = 8.3 Hz, 2H), 7.81 (d, *J* = 8.4 Hz, 1H), 7.61 (d, *J* = 8.4 Hz, 1H), 7.57-7.53 (m, 3H), 7.49 (t, *J* = 8.0 Hz, 2H), 7.34 (t, *J* = 7.8 Hz, 1H), 7.31-7.22 (m, 3H), 7.13 (t, *J* = 7.8 Hz, 1H), 7.11-7.08 (m, 2H), 5.67 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.4, 148.1, 137.2, 136.9, 136.4, 134.8, 133.3, 132.4, 130.3, 129.7, 129.1, 128.5, 128.1, 127.5, 126.5, 126.3, 122.3, 121.2, 119.7, 117.4, 54.3. Elemental analysis: calcd (%) for $C_{27}H_{20}N_2O$ (388.47): C 83.48, H 5.19; found: C 83.59, H 5.30.

Methyl 4-(2-benzyl-2H-indazol-3-yl)benzoate (6): From 2-benzyl-2H-indazole (0.270 g, 1.3 mmol) and methyl 4-bromobenzoate (0.215 g, 1 mmol), **6** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 70-30) in 79% (0.270 g) yield as a brown solid (mp: 178-180 °C). ^1H NMR (400 MHz, $CDCl_3$): δ = 8.16 (d, *J* = 8.3 Hz, 2H), 7.79 (d, *J* = 8.4 Hz, 1H), 7.58 (d, *J* = 8.4 Hz, 1H), 7.53 (d, *J* = 8.2 Hz, 2H), 7.35 (t, *J* = 7.8 Hz, 1H), 7.31-7.22 (m, 3H), 7.13 (t, *J* = 7.8 Hz, 1H), 7.11-7.06 (m, 2H), 5.66 (s, 2H), 3.97 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.3, 148.2, 136.4, 135.0, 134.0, 130.1, 130.0, 129.4, 128.6, 127.7, 126.6, 126.3, 122.3, 121.3, 119.7, 117.5, 54.5, 52.1. Elemental analysis: calcd (%) for $C_{22}H_{18}N_2O_2$ (342.39): C 77.17, H 5.30; found: C 77.37, H 5.17.

2-Benzyl-3-(4-(trifluoromethyl)phenyl)-2H-indazole (7): From 2-benzyl-2H-indazole (0.270 g, 1.3 mmol) and 4-(trifluoromethyl)bromobenzene (0.225 g, 1 mmol), **7** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 95-5) in 91% (0.320 g) yield as a white solid (mp: 190-192 °C). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.82 (d, *J* = 8.4 Hz, 1H), 7.77 (d, *J* = 8.3 Hz, 2H), 7.60-7.53 (m, 3H), 7.37 (t, *J* = 7.8 Hz, 1H), 7.32-7.22 (m, 3H), 7.27 (t, *J* = 7.8 Hz, 1H), 7.11-7.06 (m, 2H), 5.66 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.4, 136.5, 134.6, 133.3, 130.4 (q, *J* = 33.0 Hz), 129.9, 128.7, 127.8, 126.7, 126.5, 125.9 (q, *J* = 3.7 Hz), 123.7 (q, *J* = 272.4 Hz), 122.6, 121.5, 119.7, 117.7, 54.6. $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ = -62.8. Elemental analysis: calcd (%) for $C_{21}H_{15}F_3N_2$ (352.35): C 71.58, H 4.29; found: C 71.30, H 4.21.

2-Benzyl-3-(4-nitrophenyl)-2H-indazole (8): From 2-benzyl-2H-indazole (0.270 g, 1.3 mmol) and 4-bromonitrobenzene (0.208 g, 1 mmol), **8** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 80-20) in 93% (0.306 g) yield as a yellow solid (mp: 218-220 °C). ^1H NMR (400 MHz, $CDCl_3$): δ = 8.35 (d, *J* = 8.3 Hz, 2H), 7.82 (d, *J* = 8.4 Hz, 1H), 7.61 (d, *J* = 8.2 Hz, 2H), 7.57 (d, *J* = 8.4 Hz, 1H), 7.38 (t, *J* = 7.8 Hz, 1H), 7.31-7.24 (m, 3H), 7.18 (t, *J* = 7.8 Hz, 1H), 7.11-7.04 (m, 2H), 5.69 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.4, 147.7, 136.3, 136.1, 133.8, 130.3, 128.9, 128.1, 126.8, 126.6, 124.2, 123.3, 121.7, 119.4, 117.9, 54.9. Elemental analysis: calcd (%) for $C_{20}H_{15}N_3O_2$ (329.35): C 72.94, H 4.59; found: C 72.80, H 4.37.

2-Benzyl-3-(4-chlorophenyl)-2H-indazole (9): From 2-benzyl-2H-indazole (0.270 g, 1.3 mmol) and 4-bromochlorobenzene (0.191 g, 1 mmol), **9** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 80-20) in 81% (0.258 g) yield as a

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yellow solid (mp: 144-146 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 8.7 Hz, 1H), 7.56 (d, *J* = 8.7 Hz, 1H), 7.47 (d, *J* = 8.2 Hz, 2H), 7.42-7.21 (m, 6H), 7.17-7.04 (m, 3H), 5.63 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.2, 136.6, 134.9, 130.8, 129.2, 128.6, 128.0, 127.7, 126.7, 126.4, 122.1, 121.3, 119.8, 117.5, 54.3. Elemental analysis: calcd (%) for $C_{20}H_{15}ClN_2$ (318.80): C 75.35, H 4.74; found: C 75.70, H 5.00.

2-Benzyl-3-(4-fluorophenyl)-2H-indazole (10): From 2-benzyl-2H-indazole (0.270 g, 1.3 mmol) and 4-bromofluorobenzene (0.175 g, 1 mmol), **10** was obtained in after purification by flash chromatography on silica gel (pentane-Et_2O, 90-10) 78% (0.235 g) yield as a yellow solid (mp: 150-152 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80 (d, *J* = 8.7 Hz, 1H), 7.55 (d, *J* = 8.7 Hz, 1H), 7.44-7.23 (m, 6H), 7.20 (t, *J* = 7.6 Hz, 2H), 7.15-7.06 (m, 3H), 5.63 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.9 (d, *J* = 249.6 Hz), 148.2, 136.7, 135.2, 131.5 (d, *J* = 8.3 Hz), 128.6, 127.7, 126.7, 126.4, 125.6 (d, *J* = 3.5 Hz), 122.0, 121.4, 119.9, 117.5, 116.0 (d, *J* = 21.7 Hz), 54.3. ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ = -111.7. Elemental analysis: calcd (%) for $C_{20}H_{15}FN_2$ (302.34): C 79.45, H 5.00; found: C 79.34, H 5.12.

2-Benzyl-3-phenyl-2H-indazole (11):[10] From 2-benzyl-2H-indazole (0.270 g, 1.3 mmol) and bromobenzene (0.157 g, 1 mmol), **11** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 80-20) in 77% (0.219 g) yield as a yellow solid (mp: 120-122 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (d, *J* = 8.4 Hz, 1H), 7.64 (d, *J* = 8.4 Hz, 1H), 7.56-7.43 (m, 5H), 7.38 (t, *J* = 7.8 Hz, 1H), 7.33-7.25 (m, 3H), 7.18-7.10 (m, 3H), 5.69 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.2, 136.8, 136.3, 129.6, 129.5, 128.8, 128.7, 128.5, 127.5, 126.8, 126.2, 121.8, 121.2, 120.2, 117.3, 54.2.

2-Benzyl-3-(*p*-tolyl)-2H-indazole (12):[20] From 2-benzyl-2H-indazole (0.270 g, 1.3 mmol) and 4-bromotoluene (0.171 g, 1 mmol), **12** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 80-20) in 80% (0.238 g) yield as a yellow solid (mp: 124-126 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (d, *J* = 8.4 Hz, 1H), 7.66 (d, *J* = 8.4 Hz, 1H), 7.48-7.10 (m, 11 H), 5.70 (s, 2H), 2.50 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.3, 138.7, 136.9, 136.5, 129.6, 129.4, 128.5, 127.5, 126.8, 126.6, 126.2, 121.6, 121.2, 120.3, 117.3, 54.1, 21.2.

2-Benzyl-3-(4-methoxyphenyl)-2H-indazole (13): From 2-benzyl-2H-indazole (0.270 g, 1.3 mmol) and 4-bromoanisole (0.187 g, 1 mmol), **13** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 75-25) in 79% (0.248 g) yield as a green solid (mp: 162-164 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.78 (d, *J* = 8.4 Hz, 1H), 7.59 (d, *J* = 8.4 Hz, 1H), 7.48-7.20 (m, 6H), 7.18-7.00 (m, 5H), 5.62 (s, 2H), 3.87 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.9, 148.2, 136.9, 136.3, 130.9, 128.5, 127.5, 126.7, 126.2, 121.7, 121.5, 121.2, 120.3, 117.3, 114.3, 55.2, 54.1. Elemental analysis: calcd (%) for $C_{21}H_{18}N_2O$ (314.39): C 80.23, H 5.77; found: C 80.40, H 5.87.

4-(2-Benzyl-2H-indazol-3-yl)-*N*,*N*-dimethylaniline (14): From 2-benzyl-2H-indazole (0.270 g, 1.3 mmol) and 4-*N*,*N*-dimethylaniline (0.200 g, 1 mmol), **14** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 40-60) in 10% (0.033 g) yield in an impure form as a brown solid (mp: 190-192 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.75 (bs, 1H), 7.62 (d, *J* = 8.4 Hz, 1H), 7.35-7.23 (m, 6H), 7.20-7.02 (m, 3H), 6.81 (d, *J* = 8.2 Hz, 2H), 5.65 (s, 2H), 3.04 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.4, 148.3, 137.2, 130.5, 128.9, 128.7, 127.5, 126.9, 126.3, 121.2, 120.8, 117.3, 112.3, 54.2, 40.3.

3-(2-Benzyl-2H-indazol-3-yl)benzonitrile (15): From 2-benzyl-2H-indazole (0.270 g, 1.3 mmol) and 3-bromobenzonitrile (0.182 g, 1 mmol), **15** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 80-20) in 91% (0.281 g) yield as a yellow solid (mp: 96-98 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 8.7 Hz, 1H), 7.73 (dt, *J* = 7.5, 1.5 Hz, 1H), 7.70 (bs, 1H), 7.64 (dt, *J* = 7.9, 1.6 Hz, 1H), 7.60 (t, *J* = 7.6 Hz, 1H), 7.54 (d, *J* = 8.6 Hz, 1H), 7.37 (t, *J* = 7.8 Hz, 1H), 7.32-7.25 (m, 3H), 7.16 (t, *J* = 7.8 Hz, 1H), 7.11-7.05 (m, 2H), 5.64 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.1, 136.2, 133.6, 133.4, 132.8, 132.0, 130.9, 129.7, 128.7, 127.9, 126.6, 126.5, 122.7, 121.4, 119.2, 117.8, 117.6, 113.2, 54.6. Elemental analysis: calcd (%) for $C_{21}H_{15}N_3$ (309.36): C 81.53, H 4.89; found: C 81.40, H 5.00.

2-Benzyl-3-(3,5-bis(trifluoromethyl)phenyl)-2H-indazole (16): From 2-benzyl-2H-indazole (0.270 g, 1.3 mmol) and 3,5-bis(trifluoromethyl)bromobenzene (0.293 g, 1 mmol), **16** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 95-5) in 90% (0.378 g) yield as a yellow solid (mp: 100-102 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99 (s, 1H), 7.86 (s, 2H), 7.85 (d, *J* = 8.7 Hz, 1H), 7.54 (d, *J* = 8.6 Hz, 1H), 7.40 (t, *J* = 7.8 Hz, 1H), 7.35-7.25 (m, 3H), 7.18 (t, *J* = 7.8 Hz, 1H), 7.15-7.10 (m, 2H), 5.65 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.2, 136.1, 132.5, 132.4 (q, *J* = 33.8 Hz), 132.0, 129.7, 128.9, 128.2, 126.8, 126.7, 123.3, 122.3 (m), 122.5 (q, *J* = 273.0 Hz), 121.8, 119.0, 117.9, 55.2. ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ = -63.0. Elemental analysis: calcd (%) for $C_{22}H_{14}F_6N_2$ (420.35): C 62.86, H 3.36; found: C 62.99, H 3.47.

2-Benzyl-3-(naphthalen-2-yl)-2H-indazole (17): From 2-benzyl-2H-indazole (0.270 g, 1.3 mmol) and 2-bromonaphthalene (0.207 g, 1 mmol), **17** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 70-30) in 87% (0.291 g) yield as a yellow solid (mp: 138-140 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98 (d, *J* = 8.7 Hz, 1H), 7.96-7.80 (m, 4H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.62-7.53 (m, 3H), 7.42 (t, *J* = 7.8 Hz, 1H), 7.34-7.25 (m, 3H), 7.22-7.07 (m, 3H), 5.72 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.3, 136.9, 136.3, 133.1, 133.0, 129.2, 128.7, 128.6, 128.1, 127.7, 127.6, 126.9, 126.8, 126.7, 126.4, 122.0, 121.5, 120.2, 117.5, 54.4. Elemental analysis: calcd (%) for $C_{24}H_{18}N_2$ (334.41): C 86.20, H 5.43; found: C 86.31, H 5.31.

2-(2-Benzyl-2H-indazol-3-yl)benzonitrile (18): From 2-benzyl-2H-indazole (0.270 g, 1.3 mmol) and 2-bromobenzonitrile (0.182 g, 1 mmol), **18** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 80-20) in 91% (0.281 g) yield as a yellow solid (mp: 138-140 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 8.7 Hz, 1H), 7.80-7.77 (m, 1H), 7.65-7.58 (m, 1H), 7.55-

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7.47 (m, 1H), 7.45 (d, *J* = 8.6 Hz, 1H), 7.41-7.30 (m, 2H), 7.23-7.16 (m, 3H), 7.14 (t, *J* = 7.8 Hz, 1H), 7.00-6.94 (m, 2H), 5.71 (d, *J* = 15.3 Hz, 1H), 5.57 (d, *J* = 15.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.9, 135.8, 133.4, 133.0, 132.7, 131.6, 131.5, 129.4, 128.5, 127.7, 126.9, 126.3, 122.6, 122.1, 119.4, 117.6, 117.0, 113.5, 55.1. Elemental analysis: calcd (%) for $C_{21}H_{15}N_3$ (309.36): C 81.53, H 4.89; found: C 81.61, H 5.02.

2-Benzyl-3-(2-(trifluoromethyl)phenyl)-2H-indazole (19): From 2-benzyl-2H-indazole (0.270 g, 1.3 mmol) and 2-(trifluoromethyl)bromobenzene (0.225 g, 1 mmol), **19** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 95-5) in 76% (0.268 g) yield as a green solid (mp: 142-144 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.89 (d, *J* = 7.8 Hz, 1H), 7.80 (d, *J* = 8.8 Hz, 1H), 7.61 (t, *J* = 7.8 Hz, 1H), 7.56 (t, *J* = 7.8 Hz, 1H), 7.57-7.20 (m, 5H), 7.17 (d, *J* = 7.6 Hz, 1H), 7.10-7.02 (m, 3H), 5.57 (d, *J* = 15.1 Hz, 1H), 5.24 (d, *J* = 15.1 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.9, 136.0, 133.6, 132.2, 131.6, 130.7 (q, *J* = 30.3 Hz), 129.8, 128.5, 128.0 (m), 127.8, 127.5, 126.6 (q, *J* = 5.0 Hz), 126.1, 123.2 (q, *J* = 273.8 Hz), 122.9, 121.8, 120.0, 117.4, 54.9. ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ = -60.2. Elemental analysis: calcd (%) for $C_{21}H_{15}F_3N_2$ (352.35): C 71.58, H 4.29; found: C 71.30, H 4.18.

2-Benzyl-3-(2-fluorophenyl)-2H-indazole (20): From 2-benzyl-2H-indazole (0.270 g, 1.3 mmol) and 2-bromofluorobenzene (0.175 g, 1 mmol), **20** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 90-10) in 80% (0.242 g) yield as a yellow solid (mp: 108-110 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.82 (d, *J* = 8.6 Hz, 1H), 7.53 (d, *J* = 8.6 Hz, 1H), 7.50-7.42 (m, 1H), 7.35 (t, *J* = 7.6 Hz, 2H), 7.30-7.20 (m, 5H), 7.12 (t, *J* = 7.8 Hz, 1H), 7.08-7.03 (m, 2H), 5.62 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.7 (d, *J* = 249.0 Hz), 148.3, 136.2, 132.0 (d, *J* = 2.2 Hz), 131.2 (d, *J* = 8.1 Hz), 129.9, 128.4, 127.6, 127.1, 126.2, 124.4 (d, *J* = 3.7 Hz), 122.1, 122.0, 119.9, 117.5, 117.3, 116.2 (d, *J* = 21.6 Hz), 54.9 (d, *J* = 2.6 Hz). ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ = -112.0. Elemental analysis: calcd (%) for $C_{20}H_{15}FN_2$ (302.34): C 79.45, H 5.00; found: C 79.30, H 4.88.

2-Benzyl-3-(2-chlorophenyl)-2H-indazole (21): From 2-benzyl-2H-indazole (0.270 g, 1.3 mmol) and 2-bromochlorobenzene (0.191 g, 1 mmol), **21** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 80-20) in 73% (0.232 g) yield as a brown oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.82 (d, *J* = 8.6 Hz, 1H), 7.58 (d, *J* = 8.6 Hz, 1H), 7.47-7.29 (m, 4H), 7.25 (d, *J* = 8.0 Hz, 1H), 7.24-7.18 (m, 3H), 7.08 (t, *J* = 7.8 Hz, 1H), 7.06-7.00 (m, 2H), 5.63 (d, *J* = 15.0 Hz, 1H), 5.46 (d, *J* = 15.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.1, 136.1, 134.8, 133.0, 132.6, 130.7, 130.0, 128.7, 128.4, 127.7, 127.3, 126.8, 126.1, 122.0, 121.8, 120.0, 117.5, 55.0. Elemental analysis: calcd (%) for $C_{20}H_{15}ClN_2$ (318.80): C 75.35, H 4.74; found: C 75.50, H 4.57.

2-Benzyl-3-(naphthalen-1-yl)-2H-indazole (22): From 2-benzyl-2H-indazole (0.270 g, 1.3 mmol) and 1-bromonaphthalene (0.207 g, 1 mmol), **22** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 70-30) in 79% (0.264 g) yield as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.03 (d, *J* = 8.4 Hz, 1H), 7.98 (d, *J* = 8.4 Hz, 1H), 7.91 (d, *J* = 8.4 Hz, 1H), 7.58-7.50 (m, 2H), 7.46 (d, *J* = 8.4 Hz, 2H), 7.45-7.30 (m, 3H), 7.20-7.15 (m, 3H), 7.06 (t, *J* = 8.0 Hz, 1H), 7.01-6.95 (m, 2H), 5.61 (d, *J* = 14.9 Hz, 1H), 5.38 (d, *J* = 14.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.2, 136.2, 134.3, 133.5, 132.2, 129.7, 129.2, 128.3, 128.2, 127.5, 127.3, 126.9, 126.8, 126.3, 126.2, 125.2, 125.1, 122.6, 121.6, 120.3, 117.4, 54.7. Elemental analysis: calcd (%) for $C_{24}H_{18}N_2$ (334.41): C 86.20, H 5.43; found: C 86.14, H 5.50.

2-Benzyl-3-(pyridin-3-yl)-2H-indazole (23): From 2-benzyl-2H-indazole (0.270 g, 1.3 mmol) and 3-bromopyridine (0.158 g, 1 mmol), **23** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 60-40) in 83% (0.236 g) yield as a yellow solid (mp: 122-124 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.71 (d, *J* = 1.6 Hz, 1H), 8.70 (dd, *J* = 4.8, 1.3 Hz, 1H), 7.81 (d, *J* = 8.7 Hz, 1H), 7.70 (d, *J* = 7.9 Hz, 1H), 7.56 (d, *J* = 8.5 Hz, 1H), 7.43-7.33 (m, 2H), 7.28-7.21 (m, 3H), 7.14 (t, *J* = 7.8 Hz, 1H), 7.07 (d, *J* = 7.5 Hz, 2H), 5.65 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.0, 149.7, 148.2, 136.7, 136.3, 132.5, 128.7, 127.8, 126.6, 126.4, 125.9, 123.5, 122.5, 121.7, 119.4, 117.6, 54.6. Elemental analysis: calcd (%) for $C_{19}H_{15}N_3$ (285.34): C 79.98, H 5.30; found: C 80.12, H 5.14.

3-(2-Benzyl-2H-indazol-3-yl)quinoline (24): From 2-benzyl-2H-indazole (0.270 g, 1.3 mmol) and 3-bromoquinoline (0.208 g, 1 mmol), **24** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 55-45) in 93% (0.311 g) yield as a yellow solid (mp: 186-188 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.01 (d, *J* = 2.0 Hz, 1H), 8.20 (d, *J* = 8.4 Hz, 1H), 8.11 (d, *J* = 2.0 Hz, 1H), 7.85 (d, *J* = 8.7 Hz, 1H), 7.82-7.75 (m, 2H), 7.63-7.55 (m, 2H), 7.37 (t, *J* = 7.8 Hz, 1H), 7.30-7.18 (m, 3H), 7.17-7.10 (m, 3H), 5.68 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.2, 148.2, 147.5, 136.4, 136.3, 132.6, 130.3, 129.3, 128.6, 127.8, 127.7, 127.3, 127.2, 126.6, 126.4, 122.8, 122.5, 121.9, 119.4, 117.6, 54.6. Elemental analysis: calcd (%) for $C_{23}H_{17}N_3$ (335.40): C 82.36, H 5.11; found: C 82.40, H 4.98.

2-Benzyl-3-(pyrimidin-5-yl)-2H-indazole (25): From 2-benzyl-2H-indazole (0.270 g, 1.3 mmol) and 5-bromopyrimidine (0.159 g, 1 mmol), **25** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 55-45) in 92% (0.263 g) yield as a yellow solid (mp: 80-100 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.24 (s, 1H), 8.74 (s, 2H), 7.79 (d, *J* = 8.7 Hz, 1H), 7.50 (d, *J* = 8.7 Hz, 1H), 7.33 (t, *J* = 7.8 Hz, 1H), 7.30-7.20 (m, 3H), 7.13 (t, *J* = 7.8 Hz, 1H), 7.30-6.99 (m, 2H), 5.60 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.1, 156.5, 148.1, 135.8, 128.7, 128.6, 128.0, 126.5, 126.4, 124.5, 123.2, 122.0, 118.7, 117.8, 54.8. Elemental analysis: calcd (%) for $C_{18}H_{14}N_4$ (286.33): C 75.50, H 4.93; found: C 75.66, H 5.11.

1-(4-(2-Hexyl-2H-indazol-3-yl)phenyl)propan-1-one (26): From 2-hexyl-2H-indazole (0.263 g, 1.3 mmol) and 4-bromopropiophenone (0.213 g, 1 mmol), **26** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 75-25) in 81% (0.270 g) yield as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.11 (d, *J* = 8.4 Hz, 2H), 7.72 (d, *J* = 8.4 Hz, 1H), 7.58 (d, *J* = 8.4 Hz, 2H), 7.51 (d, *J* = 8.4 Hz, 1H), 7.28 (t, *J* = 7.8 Hz, 1H), 7.06 (t, *J* = 7.8 Hz, 1H), 4.40 (t, *J* = 7.4 Hz, 2H), 3.04 (q, *J* = 7.4 Hz,

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2H), 2.00-1.88 (m, 2H), 1.30-1.15 (m, 9H), 0.79 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.7, 147.9, 136.4, 134.3, 134.2, 129.5, 128.5, 126.1, 122.1, 121.1, 119.6, 117.2, 50.8, 31.8, 31.0, 30.5, 26.1, 22.2, 13.7, 8.0. Elemental analysis: calcd (%) for $C_{22}H_{26}N_2O$ (334.46): C 79.00, H 7.84; found: C 79.14, H 7.74.

2-*n*Hexyl-3-phenyl-2H-indazole (27): From 2-*n*hexyl-2H-indazole (0.263 g, 1.3 mmol) and bromobenzene (0.157 g, 1 mmol), **27** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 85-15) in 78% (0.217 g) yield as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69 (d, *J* = 8.4 Hz, 1H), 7.65-7.45 (m, 6H), 7.32 (t, *J* = 7.8 Hz, 1H), 7.07 (t, *J* = 7.8 Hz, 1H), 4.42 (t, *J* = 7.4 Hz, 2H), 2.05-1.90 (m, 2H), 1.30-1.15 (m, 6H), 0.83 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.9, 135.7, 129.9, 129.7, 128.9, 128.6, 126.1, 121.5, 121.2, 120.1, 117.1, 50.7, 31.1, 30.7, 26.2, 22.4, 13.9. Elemental analysis: calcd (%) for $C_{19}H_{22}N_2$ (278.40): C 81.97, H 7.97; found: C 82.04, H 7.87.

2-*n*Hexyl-3-(pyrimidin-5-yl)-2H-indazole (28): From 2-*n*hexyl-2H-indazole (0.263 g, 1.3 mmol) and 5-bromopyrimidine (0.159 g, 1 mmol), **28** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 65-35) in 93% (0.260 g) yield as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.28 (s, 1H), 8.88 (s, 2H), 7.71 (d, *J* = 8.4 Hz, 1H), 7.46 (d, *J* = 8.4 Hz, 1H), 7.28 (t, *J* = 7.8 Hz, 1H), 7.08 (t, *J* = 7.8 Hz, 1H), 4.34 (t, *J* = 7.4 Hz, 2H), 2.00-1.88 (m, 2H), 1.30-1.15 (m, 6H), 0.78 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.1, 156.7, 148.0, 128.1, 126.4, 124.9, 122.9, 121.7, 118.6, 117.6, 51.0, 31.0, 30.7, 26.1, 22.2, 13.7. Elemental analysis: calcd (%) for $C_{17}H_{20}N_4$ (280.38): C 72.83, H 7.19; found: C 72.70, H 7.00.

4-(2-Isobutyl-2H-indazol-3-yl)benzonitrile (29): From 2-isobutyl-2H-indazole (0.226 g, 1.3 mmol) and 4-bromobenzonitrile (0.182 g, 1 mmol), **29** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 85-15) in 87% (0.239 g) yield as a white solid (mp: 114-116 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.82 (d, *J* = 8.3 Hz, 2H), 7.72 (d, *J* = 8.4 Hz, 1H), 7.60 (d, *J* = 8.3 Hz, 2H), 7.48 (d, *J* = 8.4 Hz, 1H), 7.30 (t, *J* = 7.8 Hz, 1H), 7.09 (t, *J* = 7.8 Hz, 1H), 4.22 (d, *J* = 7.6 Hz, 2H), 2.43-2.29 (m, 1H), 0.78 (d, J = 7.6 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.8, 134.4, 133.8, 132.6, 130.1, 126.2, 122.4, 121.1, 119.2, 118.1, 117.3, 112.0, 57.9, 29.7, 19.6. Elemental analysis: calcd (%) for $C_{18}H_{17}N_3$ (275.36): C 78.52, H 6.22; found: C 78.67, H 5.99.

2-Isobutyl-3-(4-nitrophenyl)-2H-indazole (30): From 2-isobutyl-2H-indazole (0.226 g, 1.3 mmol) and 4-bromonitrobenzene (0.208 g, 1 mmol), **30** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 75-25) in 94% (0.277 g) yield as a yellow solid (mp: 138-140 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.40 (d, *J* = 8.3 Hz, 2H), 7.75 (d, *J* = 8.4 Hz, 1H), 7.69 (d, *J* = 8.3 Hz, 2H), 7.52 (d, *J* = 8.4 Hz, 1H), 7.33 (t, *J* = 7.8 Hz, 1H), 7.13 (t, *J* = 7.8 Hz, 1H), 4.27 (d, *J* = 7.6 Hz, 2H), 2.46-2.32 (m, 1H), 0.80 (d, *J* = 7.6 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.0, 147.5, 136.6, 133.6, 130.4, 126.4, 124.2, 122.8, 121.4, 119.2, 117.6, 58.2, 29.9, 19.8. Elemental analysis: calcd (%) for $C_{17}H_{17}N_3O_2$ (295.34): C 69.14, H 5.80; found: C 69.00, H 5.78.

(4-(2-Isopropyl-2H-indazol-3-yl)phenyl)(phenyl)methanone (31): From 2-isopropyl-2H-indazole (0.208 g, 1.3 mmol) and 4-bromobenzophenone (0.261 g, 1 mmol), **31** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 85-15) in 90% (0.306 g) yield as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00 (d, *J* = 8.4 Hz, 2H), 7.88 (d, *J* = 8.4 Hz, 2H), 7.81 (d, *J* = 8.3 Hz, 1H), 7.62-7.59 (m, 3H), 7.58 (d, *J* = 8.4 Hz, 1H), 7.50 (t, *J* = 8.0 Hz, 2H), 7.31 (t, *J* = 7.8 Hz, 1H), 7.08 (t, *J* = 7.8 Hz, 1H), 4.93 (sept., *J* = 7.4 Hz, 1H), 1.65 (d, *J* = 7.4 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.6, 147.9, 137.3, 137.0, 133.8, 133.4, 132.5, 130.5, 129.8, 129.4, 128.3, 125.9, 122.0, 121.0, 119.6, 117.4, 51.5, 23.2. Elemental analysis: calcd (%) for $C_{23}H_{20}N_2O$ (340.43): C 81.15, H 5.92; found: C 81.43, H 5.99.

2-Isopropyl-3-(*p*-tolyl)-2H-indazole (32): From 2-isopropyl-2H-indazole (0.208 g, 1.3 mmol) and 4-bromotoluene (0.171 g, 1 mmol), **32** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 90-10) in 86% (0.215 g) yield as a white solid (mp: 112-114 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.77 (d, *J* = 8.3 Hz, 1H), 7.52 (d, *J* = 8.4 Hz, 1H), 7.42-7.38 (m, 4H), 7.30 (t, *J* = 7.8 Hz, 1H), 7.05 (t, *J* = 7.8 Hz, 1H), 4.89 (sept., *J* = 7.4 Hz, 1H), 2.48 (s, 3H), 1.63 (d, *J* = 7.4 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.9, 138.7, 134.9, 129.7, 129.6, 127.0, 125.9, 121.3, 131.0, 120.2, 117.2, 51.2, 23.3, 21.3. Elemental analysis: calcd (%) for $C_{17}H_{18}N_2$ (250.35): C 81.56, H 7.25; found: C 81.31, H 7.27.

2-(2-Isopropyl-2H-indazol-3-yl)benzonitrile (33): From 2-isopropyl-2H-indazole (0.208 g, 1.3 mmol) and 2-bromobenzonitrile (0.182 g, 1 mmol), **33** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 85-15) in 93% (0.243 g) yield as a yellow solid (mp: 150-152 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86 (d, *J* = 8.3 Hz, 1H), 7.79 (d, *J* = 8.3 Hz, 1H), 7.70 (t, *J* = 8.0 Hz, 1H), 7.58 (t, *J* = 8.0 Hz, 1H), 7.50 (d, *J* = 8.4 Hz, 1H), 7.38 (d, *J* = 8.4 Hz, 1H), 7.33 (t, *J* = 7.8 Hz, 1H), 7.10 (t, *J* = 7.8 Hz, 1H), 4.63 (sept., *J* = 7.4 Hz, 1H), 1.71 (d, *J* = 7.4 Hz, 3H), 1.53 (d, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.0, 133.7, 133.6, 133.1, 131.8, 130.4, 129.5, 126.1, 122.3, 121.8, 119.4, 117.7, 117.2, 113.9, 52.3, 23.6, 22.5. Elemental analysis: calcd (%) for $C_{17}H_{15}N_3$ (261.33): C 78.13, H 5.79; found: C 78.20, H 5.70.

4-(2-Benzyl-6-nitro-2H-indazol-3-yl)benzonitrile (34): From 2-benzyl-6-nitro-2H-indazole (0.329 g, 12 mmol) and 4-bromobenzonitrile (0.182 g, 1 mmol), **34** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 65-35) in 70% (0.248 g) yield as a yellow solid (mp: 172-174 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.77 (s, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.83 (d, *J* = 8.6 Hz, 2H), 7.62 (d, *J* = 8.0 Hz, 1H), 7.54 (d, *J* = 8.6 Hz, 2H), 7.33-7.27 (m, 3H), 7.13-7.04 (m, 2H), 5.69 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.0, 146.3, 135.3, 135.2, 133.0, 132.9, 130.3, 129.0, 128.4, 126.9, 123.8, 121.0, 117.9, 116.7, 115.8, 113.4, 55.6. Elemental analysis: calcd (%) for $C_{21}H_{14}N_4O_2$ (354.37): C 71.18, H 3.98; found: C 71.27, H 3.04.

4-(2-Benzyl-4-bromo-2H-indazol-3-yl)benzonitrile (35): From 2-benzyl-4-bromo-2*H*-indazole (0.373 g, 1.3 mmol) and 4-bromobenzonitrile (0.182 g, 1 mmol), **35** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O,

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80-20) in 63% (0.244 g) yield as a yellow solid (mp: 136-138 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.82-7.65 (m, 3H), 7.43 (d, *J* = 8.4 Hz, 2H), 7.30-7.10 (m, 5H), 7.00-6.90 (m, 2H), 5.45 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.6, 135.7, 134.7, 134.2, 132.4, 131.5, 128.7, 128.1, 127.0, 126.9, 126.1, 120.9, 118.2, 117.3, 113.3, 112.9, 55.1. Elemental analysis: calcd (%) for $C_{21}H_{14}BrN_3$ (388.27): C 64.96, H 3.63; found: C 65.10, H 3.47.

2-Benzyl-4-bromo-3-(4-nitrophenyl)-2H-indazole (36): From 2-benzyl-4-bromo-2*H*-indazole (0.373 g, 1.3 mmol) and 4-bromonitrobenzene (0.208 g, 1 mmol), **36** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 70-30) in 68% (0.277 g) yield as a yellow solid (mp: 140-142 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.27 (d, *J* = 8.6 Hz, 2H), 7.77 (d, *J* = 8.4 Hz, 1H), 7.50 (d, *J* = 8.6 Hz, 2H), 7.31-7.21 (m, 4H), 7.18 (t, J = 8.0 Hz, 1H), 7.01-6.65 (m, 2H), 5.47 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.5, 148.3, 136.0, 135.6, 134.2, 132.7, 128.7, 128.1, 126.9, 126.2, 122.8, 120.9, 117.3, 112.9, 55.1. Elemental analysis: calcd (%) for $C_{20}H_{14}BrN_3O_2$ (408.26): C 58.84, H 3.46; found: C 58.98, H 3.30.

***N*-(2-Benzyl-3-(4-cyanophenyl)-2H-indazol-5-yl)acetamide (37)** From *N*-(2-benzyl-2H-indazol-5-yl)acetamide (0.344 g, 1.3 mmol) and 4-bromobenzonitrile (0.182 g, 1 mmol), **37** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 85-15) in 75% (0.274 g) yield as an orange solid (mp: 218-220 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.07 (s, 1H), 7.73-7.63 (m, 4H), 7.50 (d, *J* = 8.6 Hz, 2H), 7.29-7.22 (m, 3H), 7.15 (d, *J* = 8.0 Hz, 1H), 7.05-6.99 (m, 2H), 5.61 (s, 2H), 2.15 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.6, 146.0, 136.2, 134.2, 134.1, 133.0, 132.7, 130.0, 128.8, 128.0, 126.6, 122.4, 121.4, 118.4, 118.2, 112.2, 108.8, 54.8, 24.4. Elemental analysis: calcd (%) for $C_{23}H_{18}N_4O$ (366.42): C 75.39, H 4.95; found: C 75.50, H 4.81.

4-(2-Benzyl-5-nitro-2H-indazol-3-yl)benzonitrile (38): From a mixture of 2-benzyl-5-nitro-2H-indazole and 1-benzyl-5-nitro-1H-indazole (ratio 1:1) (0.658 g, 2.6 mmol) and 4-bromobenzonitrile (0.182 g, 1 mmol), **38** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 65-35) in 88% (0.311 g) yield as a brown solid (mp: 204-206 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.54 (s, 1H), 8.10 (d, *J* = 9.4 Hz, 1H), 7.84 (d, *J* = 8.1 Hz, 2H), 7.79 (d, *J* = 9.4 Hz, 1H), 7.58 (d, *J* = 8.1 Hz, 2H), 7.33-7.28 (m, 3H), 7.09 (d, *J* = 8.0 Hz, 2H), 5.67 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.1, 143.7, 138.4, 135.2, 132.9, 132.3, 130.1, 128.9, 128.3, 126.8, 120.7, 120.0, 118.8, 118.7, 117.7, 113.6, 55.3. Elemental analysis: calcd (%) for $C_{21}H_{14}N_4O_2$ (354.36): C 71.18, H 3.98; found: C 71.04, H 4.17.

2-Benzyl-3-(3,5-bis(trifluoromethyl)phenyl)-5-nitro-2H-indazole (39): From a mixture of 2-benzyl-5-nitro-2H-indazole and 1-benzyl-5-nitro-1H-indazole (ratio 1:1) (0.658 g, 2.6 mmol) and 3,5-bis(trifluoromethyl)bromobenzene (0.293 g, 1 mmol), **39** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 90-10) in 79% (0.367 g) yield as a brown oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.50 (s, 1H), 8.16 (d, *J* = 9.4 Hz, 1H), 8.06 (s, 1H), 7.88 (d, *J* = 9.4 Hz, 1H), 7.81 (s, 2H), 7.34-7.28 (m, 3H), 7.15-7.10 (m, 2H), 5.63 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.9, 143.9, 136.9, 135.1, 132.7 (q, *J* = 33.8 Hz), 130.2, 129.8 (m), 128.9, 128.5, 127.0, 123.5 (m), 122.6 (q, *J* = 273.0 Hz), 120.8, 120.4, 118.9, 118.2, 55.8. ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ = -62.9. Elemental analysis: calcd (%) for $C_{22}H_{13}F_6N_3O_2$ (465.36): C 56.78, H 2.82; found: C 56.89, H 2.67.

3-(2-Benzyl-5-nitro-2H-indazol-3-yl)quinolone (40): From a mixture of 2-benzyl-5-nitro-2H-indazole and 1-benzyl-5-nitro-1H-indazole (ratio 1:1) (0.658 g, 2.6 mmol) and 3-bromoquinoline (0.208 g, 1 mmol), **40** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 55-45) in 77% (0.293 g) yield as a brown oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.89 (s, 1H), 8.62 (s, 1H), 8.26-8.15 (m, 3H), 7.92-7.84 (m, 3H), 7.73-7.65 (m, 1H), 7.35-7.25 (m, 3H), 7.17-7.11 (m, 2H), 5.71 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.4, 149.1, 148.0, 143.5, 137.4, 137.1, 135.4, 131.1, 129.4, 128.9, 128.3, 128.1, 127.8, 127.0, 126.9, 121.2, 120.7, 120.5, 118.9, 118.6, 55.3. Elemental analysis: calcd (%) for $C_{23}H_{16}N_4O_2$ (380.41): C 72.62, H 4.24; found: C 72.80, H 4.14.

3-(2-Benzyl-6-nitro-2H-indazol-3-yl)quinolone (41): From a mixture of 2-benzyl-6-nitro-2H-indazole and 1-benzyl-6-nitro-1H-indazole (ratio 1:1) (0.658 g, 2.6 mmol) and 3-bromoquinoline (0.208 g, 1 mmol), **41** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 55-45) in 75% (0.285 g) yield as a yellow solid (mp: 198-200 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.97 (s, 1H), 8.78 (s, 1H), 8.22 (d, *J* = 8.0 Hz, 1H), 8.17 (s, 1H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.88-7.80 (m, 2H), 7.70-7.63 (m, 2H), 7.32-7.26 (m, 3H), 7.17-7.10 (m, 2H), 5.72 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.8, 147.9, 146.9, 146.2, 137.1, 135.5, 134.0, 131.0, 129.4, 128.9, 128.4, 128.0, 127.8, 127.2, 127.0, 124.3, 121.7, 121.0, 116.4, 115.8, 55.6. Elemental analysis: calcd (%) for $C_{23}H_{16}N_4O_2$ (380.41): C 72.62, H 4.24; found: C 72.87, H 4.30.

4-(1-Benzyl-1H-indazol-3-yl)benzonitrile (42): From 1-benzyl-1H-indazole (0.270 g, 1.3 mmol) and 4-bromobenzonitrile (0.182 g, 1 mmol), **42** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 85-15) in 38% (0.117 g) yield as a yellow solid (mp: 126-128 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14 (d, *J* = 8.3 Hz, 2H), 8.01 (d, *J* = 8.2 Hz, 1H), 7.78 (d, *J* = 8.3 Hz, 2H), 7.42-7.23 (m, 8H), 5.68 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.9, 141.2, 138.2, 136.3, 132.5, 128.8, 127.9, 127.6, 127.1, 126.7, 122.0, 121.9, 120.8, 119.0, 111.0, 110.0, 53.3. Elemental analysis: calcd (%) for $C_{21}H_{15}N_3$ (309.36): C 81.53, H 4.89; found: C 81.47, H 5.10.

1-Benzyl-3-(4-(trifluoromethyl)phenyl)-1H-indazole (43): From 1-benzyl-1H-indazole (0.270 g, 1.3 mmol) and 4-(trifluoromethyl)bromobenzene (0.225 g, 1 mmol), **43** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 95-5) in 34% (0.120 g) yield as a brown solid (mp: 84-86 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14 (d, *J* = 8.1 Hz, 2H), 8.03 (d, *J* = 8.2 Hz, 1H), 7.77 (d, *J* = 8.1 Hz, 2H), 7.42-7.26 (m, 8H), 5.68 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.5, 141.1, 137.2, 136.5, 129.5 (q, *J* = 32.4 Hz), 128.7, 127.8, 127.5, 127.1, 126.6, 125.7 (q, *J* = 3.8 Hz), 124.4 (q, *J* = 272.0 Hz), 122.0, 121.7, 121.0, 109.9,

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53.2. $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ = -62.5. Elemental analysis: calcd (%) for $C_{21}H_{15}F_3N_2$ (352.35): C 71.58, H 4.29; found: C 71.37, H 4.14.

1-Benzyl-5-nitro-3-(4-(trifluoromethyl)phenyl)-1H-indazole (44): From 2-benzyl-5-nitro-2H-indazole (0.329 g, 1.3 mmol) and 4-(trifluoromethyl)bromobenzene (0.225 g, 1 mmol), **44** was obtained after purification by flash chromatography on silica gel (pentane-Et_2O, 95-5) in 36% (0.143 g) yield as a yellow solid (mp: 212-214 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.97 (d, J = 1.8 Hz, 1H), 8.27 (dd, J = 9.2, 1.8 Hz, 1H), 8.11 (d, J = 8.1 Hz, 2H), 7.81 (d, J = 8.1 Hz, 2H), 7.44 (d, J = 9.2 Hz, 1H), 7.40-7.23 (m, 5H), 5.71 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.5, 143.1, 142.7, 135.4, 135.3, 130.7 (q, J = 30.6 Hz), 129.0, 128.4, 127.7, 127.2, 126.1 (q, J = 3.8 Hz), 123.9 (q, J = 273.0 Hz), 121.8, 121.2, 118.9, 110.2, 53.8. $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ = -62.7. Elemental analysis: calcd (%) for $C_{21}H_{14}F_3N_3O_2$ (397.35): C 63.48, H 3.55; found: C 63.19, H 3.67.

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Keywords: palladium • C-H bond activation • 2H-indazoles • aryl bromides • coupling

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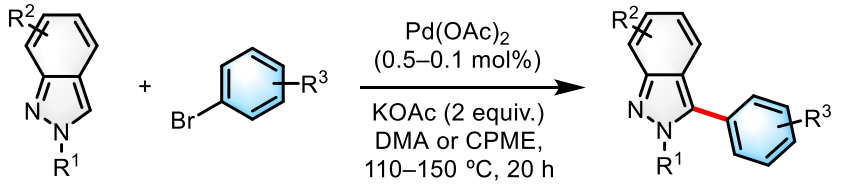

High yields 41 examples

The palladium-catalysed direct arylation of 2H-indazoles with both electron-deficient and electron-rich aryl bromides for the preparation of 3-aryl-2H-indazoles was found to proceed in high yields using only 0.5-0.1 mol% of phosphine-free $Pd(OAc)_2$ catalyst and KOAc as inexpensive base.

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Direct C3-arylation of 2H-indazole derivatives with aryl bromides using a low loading of a phosphine-free palladium-catalyst

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