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Rh(III)-Catalyzed C–H Cyanation of 2*H*-Indazole with *N*-Cyano-*N*-phenyl-*p*-toluenesulfonamide

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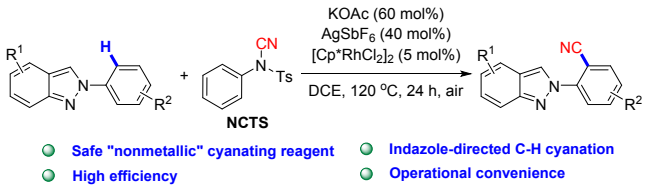


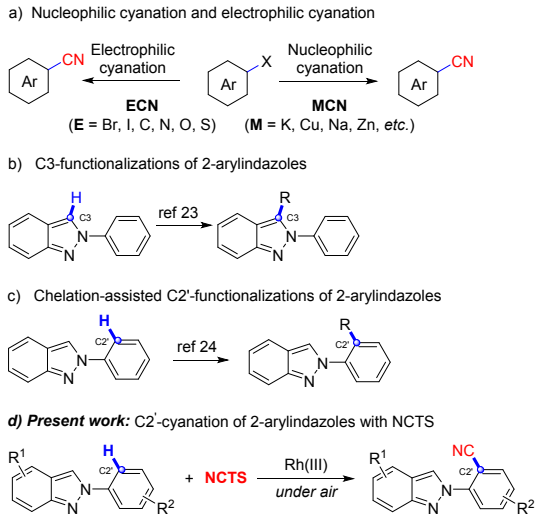
ABSTRACT: A Rh(III)-catalyzed direct cyanation of 2*H*-indazoles with *N*-Cyano-*N*-phenyl-*p*-toluenesulfonamide has been realized via chelation-assisted strategy. The methodology enables regioselective access to various *ortho*-cyanated phenylindazoles in good yields with broad substrate scope and good functional group compatibility. The obtained cyanated indazoles could further be converted into other value-added chemicals. Importantly, the current protocol is featured with several characteristics, including novel cyanating agent, good regioselectivity, and operational convenience.

INTRODUCTION

Aromatic nitriles are versatile in nature products with diverse applications in pharmaceuticals, dyes, agrochemicals, and materials.[1] In particular, the nitrile group allows multiple transformations to other important functional groups, such as amines, amidines, tetrazoles, aldehydes, and amides.[2] Traditionally, Rosenmund-von Braun reaction of aryl halides and Sandmeyer reaction of aryldiazonium salts with a stoichiometric amount of copper cyanide salt were the two most employed methods to access aromatic nitriles.[3] To date, various cyanide anion sources, including KCN, CuCN, NaCN, $Zn(CN)_2$, TMSCN, and $K_4Fe(CN)_6$ have been reported via nucleophilic cyanation (Scheme 1a).[4] However, prefunctionalized substrates and potential toxic metal cyanating reagents are required. Alternatively, the utilization of non-metallic organic cyano-group sources, including cyanogen halides,[5] cyanamides,[6] cyanates,[7] thiocyanates,[8] and alkyl nitriles,[9] would provide a complementary synthetic route via electrophilic cyanation (Scheme 1a).[10] In addition, in situ generated cyano units from readily available organic precursors have also been successfully achieved for cyanation reactions.[11]

Very recently, transition-metal-catalyzed C–H activation has emerged as a powerful approach to construct various chemical bonds via a chelation-assisted strategy.[12] In this context, *N*-cyano-*N*-phenyl-*p*-methylbenzenesulfonamide (NCTS) have attracted much attention in C–H cyanation reactions as a representative non-toxic, bench-stable, and readily accessible electrophilic cyanamide.[13] Inspired by the pioneering work of Beller and Wang,[14] the groups of Fu,[15] Anbarasan,[16] Ackermann,[17] Chang,[18] Glorius,[19] and others[20] have successfully developed C–H cyanation of (hetero)arenes assisted by oxime, pyridine, pyrimidine, pyrazole, ketone, and other directing groups. Despite the above progress, deprotection of such directing groups is usually required for further applications. It is thus highly advisable to develop a cyanation methodology assisted by an auxiliary moiety suitable for other utility.

Scheme 1. C–H functionalization of 2-arylindazoles



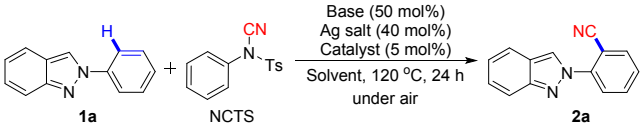
Indazoles have been recognized as an important class of *N*-heterocycles due to their prevalence in natural products, pharmaceutics, and bioactive compounds.[21] Consequently, great efforts have been made to synthesize and functionalize 2*H*-indazole derivatives.[22,23] However, most elaborations of 2*H*-indazoles are reported at the C3 position (Scheme 1b).[23] Recently, chelation-assisted strategy has also been utilized for the selective functionalization of 2-arylindazole moiety (Scheme 1c).[24] For example, the groups of Punniyamurthy and Fan have independently developed annulation of 2-arylindazoles with alkynes,[24a] azabenzonorbornadienes,[24b] maleimides,[24c] and *α*-diazo

carbonyl compounds[24d] to access polyaromatic structures. Hajra and co-workers have reported *ortho*-C–H functionalization of 2-arylindazoles with dioxazolones and maleimides.[24e,f] On the other hand, our group has developed N,O-bidentate directing group-assisted C-H alkoxylation and alkynylation/annulation.[25] Meanwhile, chelation-assisted C-H allylation and sulfonylation of indolines have also been successfully achieved.[26] As a continuation of our previous work,[25-27] we herein firstly report Rh-catalyzed indazole-directed C-H cyanation using NCTS as the cyanating agent (Scheme 1d). Importantly, as an intrinsic pharmacophore, deprotection of indazole might be not required, which is more atom economy.[28]

RESULTS AND DISCUSSION

Our initial investigation started with reaction of 2-phenyl-2*H*-indazole **1a** and NCTS using $[Cp^*RhCl_2]_2/AgSbF_6$ as the catalyst and NaOAc as the base (Table 1). To our delight, the desired cyanated product **2a** was isolated in 27% yield in MeCN at 120 °C for 24 h (Table 1, entry 1). Subsequently, the effect of solvent was investigated, and DCE displayed the best activity to afford **2a** in 81% yield (Table 1, entry 4). Next, other base and base loading were systematically employed (Table 1, entries 6-10). When 60 mmol% KOAc was employed, product **2a** could be obtained in 90% yield (Table 1, entry 10). In addition, replacement of $[Cp^*RhCl_2]_2$ and $AgSbF_6$ by other catalysts all gave inferior results (Table 1, entries 11-14). Moreover, when the catalyst loading was modulated, cyanated product **2a** was also isolated in in decreased yield (Table 1, entries 15 and 16). Finally, either elevating or lowering temperature was detrimental to the reaction efficiency (see the Supporting Information). The molecular structure of **2a** was further confirmed by X-ray diffraction (see the supporting information).

Table 1. Optimization of reaction conditions[a]

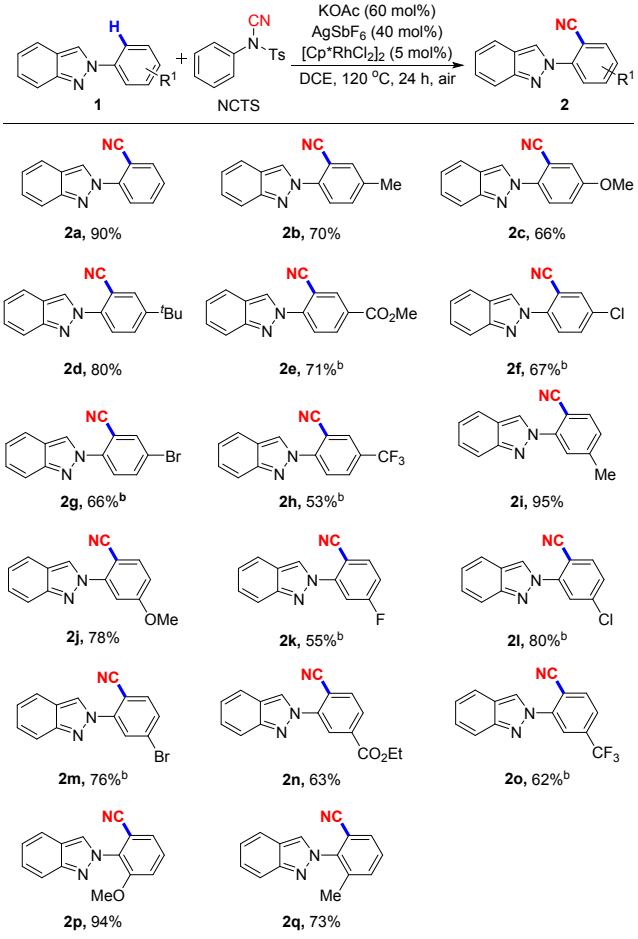


Entry	Catalyst/Ag salt	Base	Solvent	Yield(%)
1	$[Cp^*RhCl_2]_2/AgSbF_6$	NaOAc	MeCN	27
2	$[Cp^*RhCl_2]_2/AgSbF_6$	NaOAc	Dioxane	65
3	$[Cp^*RhCl_2]_2/AgSbF_6$	NaOAc	DMF	14
4	$[Cp^*RhCl_2]_2/AgSbF_6$	NaOAc	DCE	81
5	$[Cp^*RhCl_2]_2/AgSbF_6$	NaOAc	TCP	74
6	$[Cp^*RhCl_2]_2/AgSbF_6$	NaOH	DCE	18
7	$[Cp^*RhCl_2]_2/AgSbF_6$	DABCO	DCE	55
8	$[Cp^*RhCl_2]_2/AgSbF_6$	$NaCO_3$	DCE	37
9	$[Cp^*RhCl_2]_2/AgSbF_6$	KOAc	DCE	84
10[b]	**$[Cp^*RhCl_2]_2/AgSbF_6$**	**KOAc**	**DCE**	**90**
11[b]	$[Cp^*IrCl_2]_2/AgSbF_6$	KOAc	DCE	N.R.
12[b]	$[Cp^*RuCl_2]_2/AgSbF_6$	KOAc	DCE	N.R.
13[b]	$RhCl_3/AgSbF_6$	KOAc	DCE	N.R.
14[b]	$[Cp^*RhCl_2]_2/AgOTf$	KOAc	DCE	83
15[bc]	$[Cp^*RhCl_2]_2/AgSbF_6$	KOAc	DCE	80
16[bd]	$[Cp^*RhCl_2]_2/AgSbF_6$	KOAc	DCE	86

[a]Reaction conditions: **1a** (0.1 mmol), NCTS (0.25 mmol), Catalyst (5 mol%), Ag salt (40 mol%), Base (50 mol%), Solvent (1.0 mL), 24 h, 120 °C. Isolated yield. [b]Base (60 mmol%). [c]$[Cp^*RhCl_2]_2$ (3 mmol%). [d]$[Cp^*RhCl_2]_2$ (7 mmol%). TCP = 1,2,3-Trichloropropane.

With optimized conditions in hand (Table 1, entry 10), the substrate scope of 2-phenyl-2*H*-indazoles was investigated (Table 2). Initially, *N*2-substituted 2-arylindazoles were systematically examined. Both electron-donating (Me, OMe and ^{t}Bu,) and electron-withdrawing (CO_2Me, Br, Cl, and CF_3) groups at the *para*-position were well tolerated to afford the corresponding products **2a-h** in 53-90% yields. For meta-substituted 2-phenyl-2H-indazoles, regioselective cyanation took place at the sterically less hindered position to provide cyanated products **2i-2o** in 55-95% yields. When Me or OMe substituents locate at the *ortho* position, the desired cyanated product **2p** and **2q** could also be obtained in 94% and 73% yield, respectively. Overall, compared with electron-deficient 2-arylindazoles, the ones bearing electron-donating groups exhibited increased reactivity. Nevertheless, when 2-arylindazoles bearing electron-withdrawing groups were heated in TCP at 130 °C using t-BuOK as the base, satisfied yields could still be obtained, probably due to the comparable reactivity and high boiling point of TCP (Table 1, entry 5).

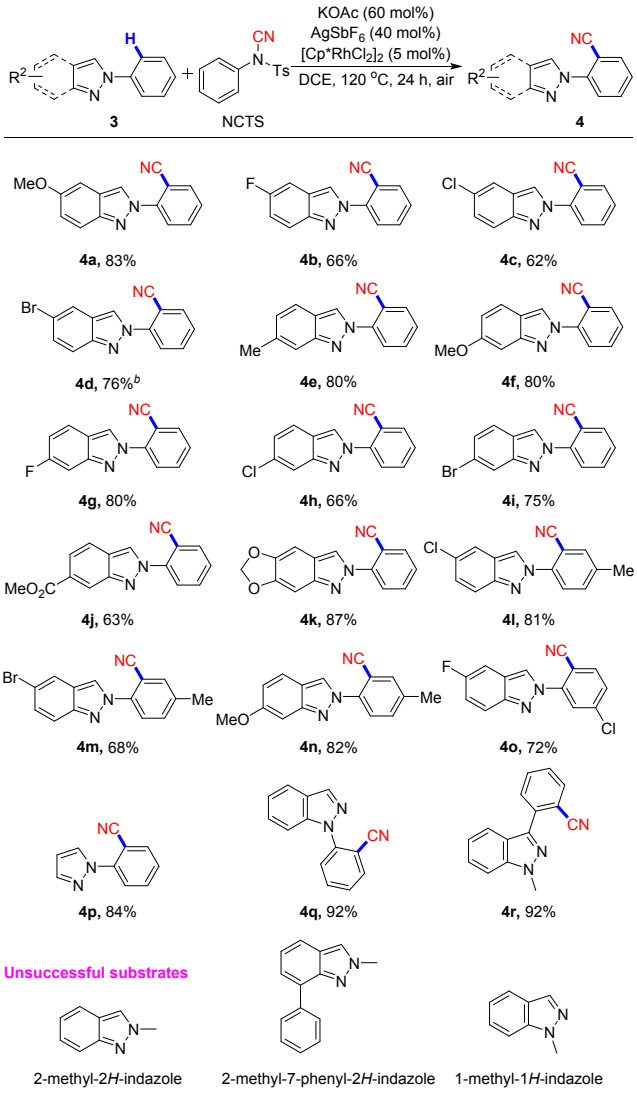
Table 2. Substrate Scope of *N*2-substituted 2*H*-indazoles[a]



[a]Reaction conditions: **1a** (0.1 mmol), NCTS (0.25 mmol), $[Cp^*RhCl_2]_2$ (5 mol%), $AgSbF_6$ (40 mol%), KOAc (60 mol%), DCE (1.0 mL), 24 h, 120 °C. Isolated yield. [b]t-BuOK (60 mol%), 1,2,3-Trichloropropane (1 mL), 130 °C.

Encouraged by the above results, the generality of the current protocol was further expanded by employing substrates bearing substitutions on the indazole ring (Table 3). In general, various functional groups, including methoxyl, halogen, and ester, at either C5 or C6 positions were all compatible to deliver the corresponding products **4a-j** in 62-83% yields irrespective of electronic effect. No dehalogenation was observed during the reaction for halo-substituted indazoles, which enabled further functionalizations. Notably, 2-phenyl-2*H*-[1,3]dioxolo[4,5-*f*]indazole bearing two oxygen atom at both C5 and C6 positions could furnish the desired product **4k** in 87% yield. With substrates bearing substituents at both indazole ring and N2-phenyl ring, products **4l-o** could also be isolated in 68-82% yields. Next, pyrazole was also utilized as the directing group, which provided product 4p in 84% yield with comparable efficiency[15a] and identical regioselectivity[29] compared with previous literatures. Finally, 1-phenyl-1*H*-indazole and 1-methyl-3-phenyl-1*H*-indazole were also proved as suitable

Table 3. Substrate Scope of 2*H*-indazoles bearing substitutions on the indazole ring[a]

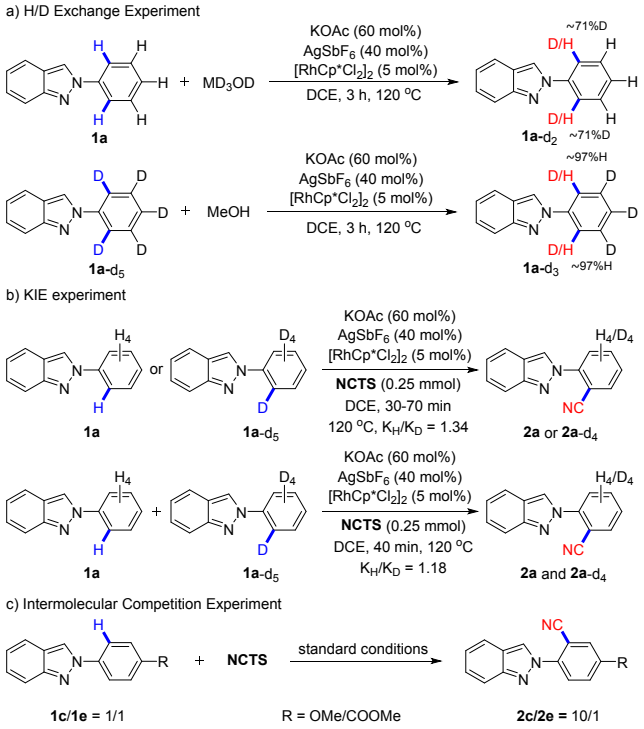


[a]Reaction conditions: **1a** (0.1 mmol), NCTS (0.25 mmol), $[Cp^*RhCl_2]_2$ (5 mol%), $AgSbF_6$ (40 mol%), KOAc (60 mol%), DCE (1.0 mL), 24 h, 120 °C. [b]*t*BuOK (60 mol%), 1,2,3-Trichloropropane (1 mL), 130 °C.

substrates to give the corresponding products **4q** and **4r** in both 92% yields. Unfortunately, for 2-methyl-2*H*-indazole, 2-methyl-7-phenyl-2*H*-indazole, and 1-methyl-1*H*-indazole, no desired cyanated products could be detected.

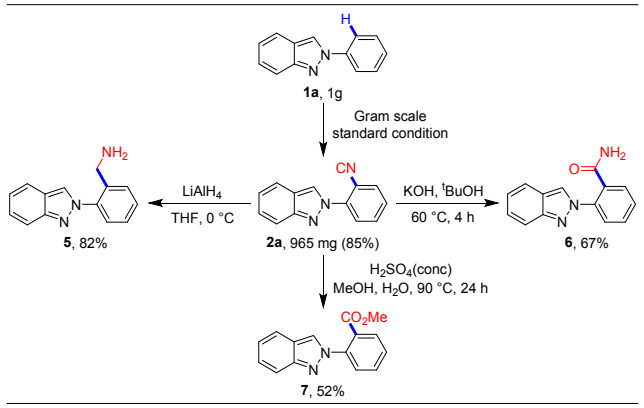
To gain insight in the cyanation mechanism, a set of control experiments were conducted (Scheme 2). First, an H/D exchangeexperiment was carried out under the optimized conditions using CD_3OD or MeOH as a co-solvent. Analysis of the ^1H NMR spectra showed that 71% of the *ortho*-C-H in **1a** was deuterated and 97% of the *ortho*-C-D in **1a**-d_5 was hydrogenated after 3 h, indicating cleavage of C-H bond is reversible (Scheme 2a). Subsequently, the kinetic isotope effect (KIE) parallel and competitive experiments of substrate **1a** or/and **1a**-d_5 with NCTS was performed (Scheme 2b). KIE values of 1.34 and 1.18 were obtained, respectively, by NMR analysis, suggesting C-H activation may not be involved in the rate-determining step. Finally, an intermolecular competition reaction between **1c** and **1e** was performed (Scheme 2c). Compared with the electron-poor group (CO_2Me), the electron-rich one (OMe) exhibit a higher reactivity.

Scheme 2. Mechanistic Studies



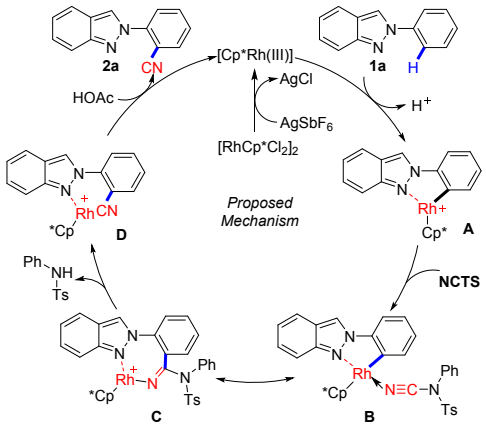
To demonstrate the synthetic utility of this Rh-catalyzed cyanation reaction, a gram-scale reaction was performed to give C2'-cyanated product **2a** in 85% yield (Scheme 3). This protocol was further highlighted by successful conversion of cyanated phenylindazole **2a** into aminomethyl **5** in 82% yield, which is very difficult to realize from indazole.[15a] During the course of these studies, we also did derivatization reactions to transform cyanated product **2a** to its corresponding amide **6** and ester **7** in 67% and 52%, respectively.[15a,17b]

Scheme 3. Gram-scale synthesis and derivatization reactions



Based on the above discussion and relevant literature, a plausible reaction mechanism was proposed (Scheme 4). First, an in situ generated active cationic Rh(III) species coordinates with 2-phenyl-2H-indazole **1a** to afford a five-membered rodacycle **A** via reversible C–H rodation. Subsequently, coordination and subsequent migratory insertion of the CN group of NCTS into the C–Rh bond affords intermediates **B** and **C**, which are generally considered to be the key intermediates in the cyanation reaction. Then, β-amine elimination from **C** provides cyanated intermediate **D**. Finally, after treatment with HOAc, the cyanated product **2a** was obtained accompanied by regeneration of reactive rhodium species to fulfill the catalytic cycle.

Scheme 4. The possible reaction mechanism



CONCLUSION

In conclusion, we have firstly developed a useful synthetic method to prepare aryl nitriles through Rh-catalyzed indazole-directed cyanation using NCTS as the cyano source. Under optimized conditions, a broad range of substrates was well tolerated to regioselectively afford ortho-cyanated phenylindazole scaffolds in good to excellent yields. The H/D exchange and KIE experiments indicate that a reversible C-H activation is not the rate-determining step. Considering the importance of the indazole pharmacophore, deprotection of the directing group is not required, which would provide an alternative way of thinking in chelation-assisted strategies.

EXPERIMENTAL SECTION

General Information All the reagents were commercially obtained and used without further purification unless otherwise noted. 2*H*-Indazoles and NCTS are known compounds and synthesized according to previous references.[14,30] 1*H*-Indazoles **2q** and **2r**,[23b,31] 2-methyl-2*H*-indazole,[32] 2-methyl-7-phenyl-2*H*-indazole,[32] and 1-methyl-1*H*-indazole[31] have also been prepared according known literatures. Melting points were measured by XT4A melting point apparatus without correction. Silica gel of 200-300 mesh was used to perform flash column chromatography. Analytical and preparative thin-layer chromatography (TLC) plates coated with commercial silica gel GF254 were used to monitor reaction and purify products. ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded at 400 MHz or 600 MHz, 101 MHz or 151 MHz, and 376 MHz respectively on a Bruker DPX instrument using TMS as an internal standard. Data are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), integration, and coupling constants (J) in hertz (Hz). HRMS were determined on a Q-Tof Micro or AB SCIEX

TripleTOF 6600 MS/MS System ESI spectrometer. The structure of product **2a** (CCDC number 1974597) was further confirmed by X-ray diffraction collected on a diffractometer with graphite-monochromated Cu K*α* radiation.

General Procedure for Cyanation. To a 35 mL oven-dried sealed tube, 2*H*-Indazole **1** or **3** (0.1 mmol), NCTS (63 mg, 0.25 mmol) and $[Cp^*RhCl_2]_2$ (3.1 mg, 5 mol%) were added under open air conditions. $AgSbF_6$ (13.7 mg, 40 mol %) and KOAc (5.9 mg, 60 mol %) were weighed and added to the tube in the glove box. And then DCE (1 mL) was added to the tube under air. The tube was sealed and placed in a preheated oil bath at 120 °C for 24 h. After the reaction was completed, the reaction mixture was cooled to room temperature and concentrated under vacuo. The crude mixture was purified by preparative thin-layer chromatography to give the desired product **2** or **4**.

2-(2H-indazol-2-yl)benzonitrile **(2a)**. Purified by TLC on silica gel with petroleum ether (PE)/acetone = 10/1 as an eluent (R_f = 0.37); faint yellow solid (19.7 mg, 90% yield); mp 136-137 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (d, J = 0.7 Hz, 1H), 7.96 (dd, J = 8.2, 0.5 Hz, 1H), 7.85 (dd, J = 7.8, 1.3 Hz, 1H), 7.80 – 7.73 (m, 3H), 7.53 (td, J = 7.7, 1.0 Hz, 1H), 7.38 - 7.34 (m, 1H), 7.17 – 7.13 (m, 1H); ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 150.3, 142.4, 134.5, 134.0, 128.4, 127.7, 126.0, 123.4, 123.1, 122.9, 120.7, 118.1, 116.6, 106.9; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{10}N_3$ 220.0869; Found 220.0870.

2-(2H-indazol-2-yl)-5-methylbenzonitrile **(2b).** Purified by TLC on silica gel with PE/ethyl acetate (EA) = 6/1 as an eluent (R_f = 0.46); white solid (16.3 mg, 70%); mp 129-129 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, J = 0.6 Hz, 1H), 7.83 (d, J = 8.3 Hz, 1H), 7.78 (dd, J = 8.9, 0.9 Hz, 1H), 7.73 (d, J = 8.5 Hz, 1H), 7.63 (s, 1H), 7.56 (dd, J = 8.3, 1.2 Hz, 1H), 7.37 – 7.33 (m, 1H), 7.16 – 7.12 (m, 1H), 2.47 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 150.1, 140.1, 139.1, 134.8, 134.6, 127.5, 125.8, 123.4, 122.9, 122.8, 120.7, 118.0, 116.7, 106.6, 20.8; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{12}N_3$ 234.1026; Found 234.1025.

2-(2H-indazol-2-yl)-5-methoxybenzonitrile **(2c)**. Purified by TLC on silica gel with PE/acetone = 14/1 as an eluent (R_f = 0.41); yellow solid (16.4 mg, 66%); mp 120-121 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (s, 1H), 7.83 – 7.80 (m, 1H), 7.78 (dd, J = 8.8, 0.9 Hz, 1H), 7.73 (d, J = 8.5 Hz, 1H), 7.37 – 7.33 (m, 1H), 7.27 (d, J = 8.5 Hz, 2H), 7.16 – 7.12 (m, 1H), 3.90 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 159.1, 150.0, 135.8, 127.5, 127.4, 123.5, 122.8, 122.7, 120.6, 120.3, 118.3, 117.9, 116.3, 107.9, 56.1; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{12}N_3O$ 250.0975; Found 250.0976.

5-(tert-Butyl)-2-(2H-indazol-2-yl)benzonitrile **(2d)**. Purified by TLC on silica gel with PE/acetone = 6/1 as an eluent (R_f = 0.52); colorless oil (22 mg, 80%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, J = 0.8 Hz, 1H), 7.88 (d, J = 8.6 Hz, 1H), 7.83 (d, J = 2.1 Hz, 1H), 7.80 – 7.79 (m, 1H), 7.78 – 7.77 (m, 1H), 7.75 – 7.72 (m, 1H), 7.37 – 7.33 (m, 1H), 7.16 – 7.12 (m, 1H), 1.39 (s, 9H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 152.3, 150.1, 139.9, 131.4, 131.3, 127.5, 125.6, 123.3, 122.9, 122.8, 120.7, 118.0, 117.0, 106.3, 35.0, 31.0; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{18}N_3$ 276.1495; Found 276.1494.

Methyl 3-cyano-4-(2H-indazol-2-yl)benzoate **(2e)**. purified by TLC on silica gel with PE/acetone = 7/1 as an eluent (R_f = 0.54); faint yellow solid (19.7 mg, 71%); mp 160-161 °C ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (d, J = 0.6 Hz, 1H), 8.52 (d, J = 1.8 Hz, 1H), 8.40 (dd, J = 8.6, 1.9 Hz, 1H), 8.13 (d, J = 8.6 Hz, 1H), 7.78 (dd, J = 8.9, 0.7 Hz, 1H), 7.73 (d, J = 8.6 Hz, 1H), 7.39 – 7.35 (m, 1H), 7.16 (dd, J = 8.2, 6.9 Hz, 1H), 4.00 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 164.3, 150.6, 145.0, 136.2, 134.9, 130.0, 128.3, 125.6, 123.6, 123.4, 123.1, 120.8, 118.1, 116.1, 106.2, 53.0; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{12}N_3O_2$ 278.0924; Found 278.0925.

5-Chloro-2-(2H-indazol-2-yl)benzonitrile **(2f)**. Purified by TLC on silica gel with PE/acetone = 9/1 as an eluent (R_f = 0.52); white solid (17 mg, 67%); mp 152-153 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (d, J = 0.8 Hz, 1H), 7.94 (d, J = 8.8 Hz, 1H), 7.81 (d, J = 2.3 Hz, 1H), 7.77 (dd, J = 8.9, 0.9 Hz, 1H), 7.75 – 7.73 (m, H), 7.72 – 7.71 (m, 1H), 7.38 – 7.34 (m, 1H), 7.17 – 7.13 (m, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 150.4, 140.9, 134.3, 133.9, 128.0, 127.1, 123.4, 123.3, 123.0, 120.7, 118.0, 115.4, 107.7; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_9ClN_3$ 254.0480; Found 254.0481.

5-Bromo-2-(2H-indazol-2-yl)benzonitrile **(2g)**. purified by TLC on silica gel with PE/acetone = 7/1 as an eluent (R_f = 0.48); faint yellow solid (19.6 mg, 66%); mp 127-128 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (d, J = 0.8 Hz, 1H), 7.97 – 7.96 (m, 1H), 7.89 – 7.88 (m, 2H), 7.77 (dd, J = 8.9, 0.9 Hz, 1H), 7.74 – 7.71 (m, 1H), 7.39 – 7.34 (m, 1H), 7.17 – 7.13 (m, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 150.4, 141.3, 137.3, 136.8, 128.0, 127.2, 123.4, 123.3, 123.0, 121.7, 120.7, 118.0, 115.3, 107.9; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_9BrN_3$ 297.9974; Found 297.9973.

2-(2H-indazol-2-yl)-5-(trifluoromethyl)benzonitrile **(2h)**. Purified by TLC on silica gel with PE/acetone = 6/1 as an eluent (R_f = 0.54); faint yellow solid (15.2 mg, 53%); mp 91-92 °C ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (d, J = 0.8 Hz, 1H), 8.21 (d, J = 8.6 Hz, 1H), 8.11 (d, J = 1.3 Hz, 1H), 8.02 (dd, J = 8.7, 1.6 Hz, 1H), 7.78 (dd, J = 8.9, 0.9 Hz, 1H), 7.75 – 7.72 (m, 1H), 7.40 – 7.36 (m, 1H), 7.19 – 7.15 (m, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 150.7, 144.6, 131.9 ($J_{C\text{-}F}$ = 3.8 Hz), 130.9 ($J_{C\text{-}F}$ = 3.5 Hz), 130.6 ($J_{C\text{-}F}$ = 34.1 Hz), 128.4, 126.3, 123.7, 123.3, 123.2, 122.6 ($J_{C\text{-}F}$ = 272.2 Hz), 120.8, 118.1, 115.6, 106.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.5; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_9F_3N_3$ 288.0743; Found 288.0745.

2-(2H-indazol-2-yl)-4-methylbenzonitrile **(2i)**. Purified by TLC on silica gel with PE/EA = 9/1 as an eluent (R_f = 0.34); faint yellow solid (22.1 mg, 95%); mp 137-138 °C . ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (d, J = 0.8 Hz, 1H), 7.80 – 7.77 (m, 2H), 7.74 – 7.71 (m, 2H), 7.38 – 7.32 (m, 2H), 7.16 – 7.12 (m, 1H), 2.51 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 150.1, 145.7, 142.2, 134.3, 129.3, 127.7, 126.6, 123.5, 123.0, 122.8, 120.7, 117.9, 116.9, 103.6, 21.9; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{12}N_3$ 234.1026; Found 234.1025.

2-(2H-indazol-2-yl)-4-methoxybenzonitrile **(2j)**. Purified by TLC on silica gel with PE/acetone = 8/1 as an eluent (R_f = 0.43); yellow solid (19.4 mg, 78%); mp 90-91 °C ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (s, 1H), 7.78 (dd, J = 8.9, 0.7 Hz, 1H), 7.73 (dd, J = 8.7, 0.7 Hz, 2H), 7.51 – 7.50 (m, 1H), 7.38 – 7.34 (m, 1H), 7.14 (dd, J = 8.5, 6.6 Hz, 1H), 7.04 – 7.01 (m, 1H), 3.95 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 163.8, 150.1, 144.2, 135.7, 127.8, 123.6, 123.1, 122.8, 120.8, 117.9, 117.1, 115.2, 111.0, 97.9, 56.1; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{12}N_3O$ 250.0975; Found 250.0974.

4-Fluoro-2-(2H-indazol-2-yl)benzonitrile **(2k)**. Purified by TLC on silica gel with PE/acetone = 8/1 as an eluent (R_f = 0.49); brown solid (13 mg, 55%); mp 107-108 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.62 (d, J = 0.8 Hz, 1H), 7.82 – 7.72 (m, 4H), 7.39 – 7.35 (m, 1H), 7.31 (td, J = 8.2, 1.2 Hz, 1H), 7.17 – 7.14 (m, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 165.5 ($J_{C\text{-}F}$ = 267.1 Hz), 150.4, 143.3, 135.2 ($J_{C\text{-}F}$ = 9.9 Hz), 128.1, 123.4 ($J_{C\text{-}F}$ = 11.7 Hz), 123.0, 121.2 ($J_{C\text{-}F}$ = 3.5 Hz), 120.7, 118.1, 115.5, 115.3, 111.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -102.9; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{14}H_9FN_3$ 238.0775; Found 238.0776.

4-Chloro-2-(2H-indazol-2-yl)benzonitrile **(2l)**. Purified by TLC on silica gel with PE/acetone = 8/1 as an eluent (R_f = 0.53); faint yellow solid (20.2 mg, 80%); mp 166-167 °C ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (d, J = 0.8 Hz, 1H), 8.07 (d, J = 2.0 Hz, 1H), 7.77 (dd, J = 8.3, 1.4 Hz, 2H), 7.73 (d, J = 8.6 Hz, 1H), 7.50 (dd, J = 8.4, 2.0 Hz, 1H), 7.39 – 7.35 (m, 1H), 7.17 – 7.13 (m, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 150.4, 143.1, 140.7, 135.4, 128.7, 128.2, 126.2, 123.5, 123.4, 123.0, 120.8, 118.0, 116.1, 104.5; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{14}H_9ClN_3$ 254.0480; Found 254.0481.

4-Bromo-2-(2H-indazol-2-yl)benzonitrile **(2m)**. Purified by TLC on silica gel with PE/acetone = 8/1 as an eluent (R_f = 0.44); yellow solid (22.6 mg, 76%); mp 178-179 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (d, J = 0.8 Hz, 1H), 8.23 (d, J = 1.6 Hz, 1H), 7.77 (dd, J = 8.9, 0.9 Hz, 1H), 7.73 (d, J = 8.6 Hz, 1H), 7.70 (d, J = 8.3 Hz, 1H), 7.66 (dd, J = 8.3, 1.7 Hz, 1H), 7.39 – 7.35 (m, 1H), 7.18 - 7.14 (m, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 150.4, 142.9, 135.3, 131.6, 129.1, 128.8, 128.2, 123.5, 123.4, 123.0, 120.8, 118.0, 116.2, 104.9; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{14}H_9BrN_3$ 297.9974; Found 297.9973.

Ethyl 4-cyano-3-(2H-indazol-2-yl)benzoate **(2n)**. Purified by TLC on silica gel with PE/EA = 8/1 as an eluent (R_f = 0.40); light green solid (18.3 mg, 63%); mp 121-122 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 8.58 (s, 1H), 8.17 (dt, J = 8.1, 1.5 Hz, 1H), 7.93 (dd, J = 8.1, 1.1 Hz, 1H), 7.82 – 7.79 (m, 1H), 7.74 (dd, J = 8.6, 1.0 Hz, 1H), 7.39 – 7.35 (m, 1H), 7.18 – 7.14 (m, 1H), 4.45 (q, J = 7.1, 2H), 1.43 (td, J = 7.1, 0.6 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 164.0, 150.4, 142.5, 135.8, 134.8, 128.9, 127.9, 126.5, 123.4, 123.3, 123.0, 120.7, 118.1, 116.0, 110.3, 62.3, 14.2; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{17}H_{14}N_3O_2$ 292.1081; Found 292.1082.

2-(2H-indazol-2-yl)-4-(trifluoromethyl)benzonitrile **(2o)**. Purified by TLC on silica gel with PE/EA = 8/1 as an eluent (R_f = 0.39); yellow solid (17.8 mg, 62%); mp 97-98 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (d, J = 0.7 Hz, 1H), 8.33 (s, 1H), 7.99 (d, J = 8.1 Hz, 1H), 7.80 – 7.76 (m, 2H), 7.74 (d, J = 8.6 Hz, 1H), 7.40 – 7.36 (m, 1H), 7.19 – 7.15 (m, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 150.6, 142.8, 136.1 ($J_{C\text{-}F}$ = 33.7 Hz), 135.4, 128.3, 124.8 ($J_{C\text{-}F}$ = 3.5Hz), 123.7, 123.3, 123.2, 123.0 ($J_{C\text{-}F}$ = 3.8 Hz), 122.5 ($J_{C\text{-}F}$ = 275 Hz), 120.8, 118.1, 115.6, 109.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.5; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{15}H_9F_3N_3$ 288.0743; Found 288.0744.

2-(2H-indazol-2-yl)-3-methoxybenzonitrile **(2p)**. Purified by TLC on silica gel with PE/acetone = 6/1 as an eluent (R_f = 0.42); yellow solid (23.4 mg, 94%); mp 90 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, J = 0.9 Hz, 1H), 7.81 (dd, J = 8.8, 0.9 Hz, 1H), 7.73 (d, J = 8.5 Hz, 1H), 7.56 – 7.52 (m, 1H), 7.42 (dd, J = 7.8, 1.2 Hz, 1H), 7.36 – 7.30 (m, 2H), 7.15 – 7.12 (m, 1H), 3.83 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 154.6, 149.7, 131.8, 130.7, 127.0, 125.9, 125.2, 122.6, 122.1, 120.5, 118.2, 116.8, 115.5, 112.7; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{15}H_{12}N_3O$ 250.0975; Found 250.0976.

2-(2H-indazol-2-yl)-3-methylbenzonitrile **(2q)**. Purified by TLC on silica gel with PE/EA = 7/1 as an eluent (R_f = 0.32); faint yellow oil (17 mg, 73%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 0.8 Hz, 1H), 7.80 (dd, J = 8.8, 0.9 Hz, 1H), 7.77 – 7.74 (m, 1H), 7.67 (dd, J = 7.7, 0.9 Hz, 1H), 7.62 (dd, J = 7.8, 0.6 Hz, 1H), 7.52 (t, J = 7.7 Hz, 1H), 7.39 – 7.35 (m, 1H), 7.19 – 7.15 (m, 1H), 2.16 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 149.9, 141.9, 137.6, 135.6, 131.1, 129.8, 127.1, 125.0, 122.8, 122.2, 120.6, 118.1, 115.5, 111.8, 17.6; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{15}H_{12}N_3$ 234.1026; Found 234.1027.

2-(5-Methoxy-2H-indazol-2-yl)benzonitrile **(4a)**. Purified by TLC on silica gel with PE/EA = 5/1 as an eluent (R_f = 0.40); white solid (20.7 mg, 83%); mp 143-144 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (d, J = 0.9 Hz, 1H), 7.95 (dd, J = 8.3, 0.8 Hz, 1H), 7.83 (dd, J = 7.8, 1.3 Hz, 1H), 7.78 – 7.74 (m, 1H), 7.68 (d, J = 9.4 Hz, 1H), 7.50 (td, J = 7.7, 1.1 Hz, 1H), 7.06 (dd, J = 9.4, 2.4 Hz, 1H), 6.90 (d, J = 2.2 Hz, 1H), 3.86 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 155.9, 147.4, 142.4, 134.5, 134.0, 128.1, 125.6, 123.4, 123.0, 122.1, 119.4, 116.8, 106.4, 96.1, 55.4; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{15}H_{12}N_3O$ 250.0975; Found 250.0976.

2-(5-Fluoro-2H-indazol-2-yl)benzonitrile **(4b)**. Purified by TLC on silica gel with PE/acetone = 6/1 as an eluent (R_f = 0.43); white solid (15.6 mg, 66%); mp 164-165 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (s, 1H), 7.94 (dd, J = 8.2, 0.7 Hz, 1H), 7.87 (dd, J = 7.8, 1.3 Hz, 1H), 7.81 - 7.76 (m, 2H), 7.56 (td, J = 7.7, 1.1 Hz, 1H), 7.31 (dd, J = 8.9, 2.3 Hz, 1H), 7.17 (td, J = 9.2, 2.4 Hz, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.9 ($J_{C\text{-}F}$ = 242.4 Hz), 147.7, 142.2, 134.6, 134.1, 128.7, 125.8, 123.5 ($J_{C\text{-}F}$ = 9.0 Hz), 122.1 ($J_{C\text{-}F}$ = 11.9 Hz), 120.3 ($J_{C\text{-}F}$ = 9.9 Hz), 119.7 ($J_{C\text{-}F}$ = 29.4 Hz), 116.4, 106.9, 102.9 ($J_{C\text{-}F}$ = 24.5 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -117.9; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{14}H_9FN_3$ 238.0775; Found 238.0774.

2-(5-Chloro-2H-indazol-2-yl)benzonitrile **(4c)**. Purified by TLC on silica gel with PE/acetone = 6/1 as an eluent (R_f = 0.33); faint yellow solid (15.7 mg, 62%); mp 131-132 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, J = 0.8 Hz, 1H), 7.94 (dd, J = 8.2, 0.8 Hz, 1H), 7.87 (dd, J = 7.8, 1.3 Hz, 1H), 7.79 (td, J = 7.9, 1.5 Hz, 1H), 7.75 – 7.72 (m, 2H), 7.57 (td, J = 7.7, 1.1 Hz, 1H), 7.29 (dd, J = 9.2, 2.0 Hz, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 148.5, 142.0, 134.6, 134.1, 129.2, 128.8, 125.9, 123.1, 123.0, 119.6, 119.3, 116.4, 107.0; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{14}H_9ClN_3$ 254.0480; Found 254.0479.

2-(5-Bromo-2H-indazol-2-yl)benzonitrile **(4d)**. Purified by TLC on silica gel with PE/acetone = 7/1 as an eluent (R_f = 0.55); faint yellow solid (22.6 mg, 76%); 151-152 °C ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, J = 0.7 Hz, 1H), 7.94 (dd, J = 8.3, 0.7 Hz, 1H), 7.91 (d, J = 1.2 Hz, 1H), 7.86 (dd, J = 7.8, 1.3 Hz, 1H), 7.79 (td, J = 7.9, 1.5 Hz, 1H), 7.68 (d, J = 9.2 Hz, 1H), 7.57 (td, J = 7.7, 1.1 Hz, 1H), 7.41 (dd, J = 9.2, 1.8 Hz, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 148.5, 142.0, 134.6, 134.1, 131.4, 128.8, 125.9, 123.9, 122.9, 122.7, 119.8, 116.7, 116.4, 107.0; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{14}H_9BrN_3$ 297.9974; Found 297.9976.

2-(6-Methyl-2H-indazol-2-yl)benzonitrile **(4e)**. Purified by TLC on silica gel with PE/acetone = 15/1 as an eluent (R_f = 0.38); white

solid (18.6 mg, 80%); mp 127-128 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, J = 0.7 Hz, 1H), 7.96 (dd, J = 8.2, 0.7 Hz, 1H), 7.83 (dd, J = 7.8, 1.3 Hz, 1H), 7.78 – 7.74 (m, 1H), 7.62 (d, J = 8.7 Hz, 1H), 7.53 – 7.49 (m, 2H), 6.99 (dd, J = 8.7, 1.1 Hz, 1H), 2.47 (d, J = 0.6 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 150.9, 142.4, 137.8, 134.5, 134.0, 128.2, 126.2, 125.8, 123.2, 121.3, 120.2, 116.7, 116.1, 106.6, 22.3; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{15}H_{12}N_3$ 234.1026; Found 234.1027.

2-(6-Methoxy-2H-indazol-2-yl)benzonitrile **(4f)**. Purified by TLC on silica gel with PE/EA = 5/1 as an eluent (R_f = 0.30); hazel solid (19.9 mg, 80%); mp 132-133 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (d, J = 0.4 Hz, 1H), 7.94 (d, J = 8.1, 0.7 Hz, 1H), 7.83 (dd, J = 7.8, 1.3 Hz, 1H), 7.75 (td, J = 8.0, 1.5 Hz, 1H), 7.58 (d, J = 9.2 Hz, 1H), 7.49 (td, J = 7.7, 1.0 Hz, 1H), 6.99 (d, J = 1.8 Hz, 1H), 6.84 (dd, J = 9.2, 2.1 Hz, 1H), 3.89 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 159.9, 151.4, 142.3, 134.6, 134.0, 127.9, 125.4, 123.3, 121.5, 118.9, 118.8, 116.8, 106.2, 94.3, 55.3; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{15}H_{12}N_3O$ 250.0975; Found 250.0976.

2-(6-Fluoro-2H-indazol-2-yl)benzonitrile **(4g)**. Purified by TLC on silica gel with PE/acetone = 7/1 as an eluent (R_f = 0.40); faint yellow solid (14.9 mg, 63%); mp 173-174 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, J = 0.6 Hz, 1H), 7.97 (dd, J = 8.2, 0.7 Hz, 1H), 7.86 (dd, J = 7.8, 1.3 Hz, 1H), 7.80 (td, J = 8.0, 1.5 Hz, 1H), 7.73 (dd, J = 9.2, 5.3 Hz, 1H), 7.56 (td, J = 7.7, 1.1 Hz, 1H), 7.38 – 7.35 (m, 1H), 6.98 (td, J = 9.1, 2.2 Hz, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 162.5 ($J_{C\text{-}F}$ = 249.2 Hz), 150.1 ($J_{C\text{-}F}$ = 13.3 Hz), 142.1, 134.5, 134.1, 128.6, 125.9, 124.0, 122.7 ($J_{C\text{-}F}$ = 10.9 Hz), 120.1, 116.5, 115.3 ($J_{C\text{-}F}$ = 28.9 Hz), 106.7, 101.0 ($J_{C\text{-}F}$ = 24.0 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -111.3; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{14}H_9FN_3$ 238.0775; Found 238.0776.

2-(6-Chloro-2H-indazol-2-yl)benzonitrile **(4h)**. Purified by TLC on silica gel with PE/acetone = 6/1 as an eluent (R_f = 0.42); white solid (16.7 mg, 66%); mp 165-166 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (d, J = 0.9 Hz, 1H), 7.95 (dd, J = 8.2, 0.8 Hz, 1H), 7.86 (dd, J = 7.8, 1.3 Hz, 1H), 7.82 – 7.77 (m, 2H), 7.68 (dd, J = 9.0, 0.6 Hz, 1H), 7.56 (td, J = 7.7, 1.1 Hz, 1H), 7.10 (dd, J = 9.0, 1.7 Hz, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 150.2, 142.0, 134.6, 134.1, 133.7, 128.8, 126.0, 124.8, 124.0, 122.0, 121.2, 117.0, 116.4, 106.8; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{14}H_9ClN_3$ 254.0480; Found 254.0478.

2-(6-Bromo-2H-indazol-2-yl)benzonitrile **(4i)**. Purified by TLC on silica gel with PE/acetone = 6/1 as an eluent (R_f = 0.38); white solid (22.3 mg, 75%); mp 148-149 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, J = 0.8 Hz, 1H), 7.98 – 7.97 (m, 1H), 7.94 (dd, J = 8.2, 0.8 Hz, 1H), 7.86 (dd, J = 7.8, 1.3 Hz, 1H), 7.81 – 7.77 (m, 1H), 7.62 (dd, J = 8.9, 0.5 Hz, 1H), 7.56 (td, J = 7.7, 1.2 Hz, 1H), 7.22 (dd, J = 9.0, 1.6 Hz, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 150.7, 142.0, 134.6, 134.2, 128.8, 127.0, 126.0, 124.0, 122.1, 121.8, 121.3, 120.4, 116.4, 106.9; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{14}H_9BrN_3$ 297.9974; Found 297.9973.

Methyl 2-(2-cyanophenyl)-2H-indazole-6-carboxylate **(4j)**. Purified by TLC on silica gel with PE/EA = 6/1 as an eluent (R_f = 0.33); white solid (17.4 mg, 63%); mp 156-157 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (d, J = 0.9 Hz, 1H), 8.60 (d, J = 1.0 Hz, 1H), 7.97 (dd, J = 8.2, 0.7 Hz, 1H), 7.88 (dd, J = 7.8, 1.3 Hz, 1H), 7.83 – 7.81 (m, 1H), 7.78 (t, J = 1.3 Hz, 2H), 7.59 (td, J = 7.7, 1.1 Hz, 1H), 3.98 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 167.2, 149.4, 142.0, 134.6, 134.2, 129.5, 129.0, 126.0, 124.5, 123.8, 122.6, 121.9, 120.8, 116.3, 107.1, 52.3; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{16}H_{12}N_3O_2$ 278.0924; Found 278.0926.

2-(2H-[1,3]dioxolo[4,5-f]indazol-2-yl)benzonitrile **(4k)**. Purified by TLC on silica gel with PE/EA = 4/1 as an eluent (R_f = 0.30); faint yellow solid (22.9 mg, 87%); mp 177-178 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.41 (s, 1H), 7.93 (d, J = 8.2 Hz, 1H), 7.81 (d, J = 7.8 Hz, 1H), 7.74 (t, J = 7.8 Hz, 1H), 7.46 (t, J = 7.6 Hz, 1H), 7.01 (s, 1H), 6.90 (s, 1H), 5.99 (s, 2H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 150.5, 148.2, 146.6, 142.3, 134.6, 134.0, 127.6, 125.1, 122.5, 119.0, 116.9, 105.7, 101.2, 94.8, 93.9; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{15}H_{10}N_3O_2$ 264.0768; Found 264.0769.

2-(5-Chloro-2H-indazol-2-yl)-5-methylbenzonitrile **(4l)**. Purified by TLC on silica gel with PE/EA = 7/1 as an eluent (R_f = 0.36); faint yellow solid (21.6 mg, 81%); mp 174-175 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, J = 0.8 Hz, 1H), 7.79 (d, J = 8.3 Hz, 1H), 7.74 – 7.71 (m, 1H), 7.71 – 7.70 (m, 1H), 7.64 (d, J = 1.0 Hz, 1H), 7.58 – 7.55 (m, 1H), 7.29 – 7.27 (m, 1H), 2.48 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 148.3, 139.8, 139.4, 134.9, 134.6, 129.0, 128.6, 125.7, 123.0, 119.6, 119.2, 116.5, 106.7, 20.8; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{15}H_{11}ClN_3$ 268.0636; Found 268.0637.

2-(5-Bromo-2H-indazol-2-yl)-5-methylbenzonitrile **(4m)**. Purified by TLC on silica gel with PE/EA = 12/1 as an eluent (R_f = 0.34); faint yellow solid (21.2 mg, 68%); mp 194-195 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, J = 0.8 Hz, 1H), 7.91 – 7.90 (m, 1H), 7.80 (d, J = 8.4 Hz, 1H), 7.67 (d, J = 9.2 Hz, 1H), 7.65 (d, J = 1.2 Hz, 1H), 7.57 (dd, J = 8.3, 1.3 Hz, 1H), 7.40 (dd, J = 9.2, 1.8 Hz, 1H), 2.48 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 148.4, 139.7, 139.5, 134.9, 134.6, 131.2, 125.7, 123.8, 122.8, 122.7, 119.7, 116.5, 116.4, 106.7, 20.8; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{15}H_{11}BrN_3$ 312.0131; Found 312.0133.

2-(6-Methoxy-2H-indazol-2-yl)-5-methylbenzonitrile **(4n)**. Purified by TLC on silica gel with PE/acetone = 8/1 as an eluent (R_f = 0.43); white solid (21.6 mg, 82%); mp 128-129 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (d, J = 0.7 Hz, 1H), 7.81 (d, J = 8.4 Hz, 1H), 7.61 (d, J = 1.2 Hz, 1H), 7.59 – 7.57 (m, 1H), 7.55 – 7.53 (m, 1H), 6.99 (d, J = 2.0 Hz, 1H), 6.83 (dd, J = 9.1, 2.1 Hz, 1H), 3.89 (s, 3H), 2.46 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 159.8, 151.2, 140.1, 138.5, 134.8, 134.6, 125.3, 123.3, 121.4, 118.7, 118.6, 116.9, 106.0, 94.3, 55.3, 20.7; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{16}H_{14}N_3O$ 264.1131; Found 264.1133.

4-Chloro-2-(5-fluoro-2H-indazol-2-yl)benzonitrile **(4o)**. Purified by TLC on silica gel with PE/acetone = 7/1 as an eluent (R_f = 0.46); faint yellow solid (19.5 mg, 72%); mp 157-158 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.60 (s, 1H), 8.03 (s, 1H), 7.79 – 7.75 (m, 2H), 7.52 (d, J = 8.4 Hz, 1H), 7.29 (d, J = 8.7 Hz, 1H), 7.18 (t, J = 9.2 Hz, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 159.1 ($J_{C\text{-}F}$ = 243.0 Hz), 147.9, 142.9, 140.7, 135.4, 128.9, 126.1, 123.4 ($J_{C\text{-}F}$ = 9.3 Hz), 122.3 ($J_{C\text{-}F}$ = 12.1 Hz), 120.4, 120.1 ($J_{C\text{-}F}$ = 20.3 Hz), 116.0, 104.6, 102.9 ($J_{C\text{-}F}$ = 24.8 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -117.1; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{14}H_8ClFN_3$ 272.0385; Found 272.0387.

2-(1*H*-Pyrazol-1-yl)benzonitrile (**4p**). Purified by TLC on silica gel with PE/EA = 12/1 as an eluent (R_f = 0.24); colorless oil (14.3 mg, 84%); mp 110-111 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.14 (d, J = 2.2 Hz, 1H), 7.81 – 7.77 (m, 3H), 7.71 (t, J = 7.9 Hz, 1H), 7.43 (t, J = 7.6 Hz, 1H), 6.55 (s, 1H); ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 142.3, 142.1, 134.5, 134.0, 129.5, 127.2, 124.3, 117.0, 108.5, 105.4;

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{10}H_8N_3$ 170.0713; Found 170.0724.

2-(1*H*-Indazol-1-yl)benzonitrile (**4q**). Purified by TLC on silica gel with PE/acetone = 6/1 as an eluent (R_f = 0.33); yellow solid (20.2 mg, 92%); mp 84-85 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.31 (s, 1H), 7.88 (d, *J* = 7.8 Hz, 1H), 7.84 (d, *J* = 8.1 Hz, 1H), 7.77 – 7.75 (m, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.52 (dd, *J* = 15.0, 7.9 Hz, 2H), 7.47 (t, *J* = 7.6 Hz, 1H), 7.28 (t, *J* = 7.5 Hz, 1H); ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 141.8, 139.5, 137.0, 134.8, 133.7, 127.8, 127.7, 126.0, 125.4, 122.3, 121.6, 116.6, 110.1, 109.5; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{10}N_3$ 220.0869; Found 220.0880.

2-(1-Methyl-1*H*-indazol-3-yl)benzonitrile (**4r**). Purified by TLC on silica gel with PE/acetone = 6/1 as an eluent (R_f = 0.23); yellow solid (18.4 mg, 92%); mp 110-111 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.84-7.80 (m, 3H), 7.69 (t, *J* = 7.6 Hz, 1H), 7.50 – 7.43 (m, 1H), 7.24 (dd, *J* = 10.0, 4.0 Hz, 1H); ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 141.2, 140.7, 136.7, 134.3, 132.7, 130.3, 128.1, 126.7, 122.0, 121.5, 120.8, 118.8, 111.8, 109.5, 35.9; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{12}N_3$ 234.1026; Found 234.1035.

General Procedure for the Synthesis of 2-phenyl-2*H*-indazole 1 and 3. To a 35 mL oven-dried sealed tube with a stir bar, 2-nitrobenzaldehyde (3.25 mmol), aniline (3.58 mmol) and i-PrOH (8.0 mL) were added in one portion. The reaction mixture was stirred in a preheated oil bath at 80 °C for 4 h. Then the mixture was cooled down to room temperature and tri-n-butylphosphine (1.98 g, 9.78 mmol) was added to the tube. After stirred at 80 °C for another 16 h, the reaction mixture was cooled down to room temperature and diluted with EtOAc (60 mL). The organic layer was washed with saturated ammonium chloride solution (30 mL × 3) and brine (30 mL × 3). After that, the organic layer was dried over $MgSO_4$ and then filtered. Filtrate was concentrated under reduced pressure. The residue was purified by silica gel chromatography (0-25% EA/PE) to afford 2*H*-indazole **1** and **3**.

Mechanistic Experiment. *Procedure for Preparation of **1a-d$_5$**.* To a 35 mL oven-dried sealed tube with a stir bar, 2-nitrobenzaldehyde **1a** (491 mg, 3.25 mmol), aniline-d_5 (351 mg, 3.58 mmol) and i-PrOH (8.0 mL) were added in one portion. The reaction mixture was stirred in a preheated oil bath at 80 °C for 4 h. Then the mixture was cooled down to room temperature and tri-n-butylphosphine (1.98 g, 9.78 mmol) was added to the tube. After stirred at 80 °C for another 16 h, the reaction mixture was cooled down to room temperature and diluted with EtOAc (60 mL). The organic layer was washed with saturated ammonium chloride solution (30 mL × 3) and brine (30 mL × 3). After that, the organic layer was dried over $MgSO_4$ and then filtered. Filtrate was concentrated under reduced pressure. The residue was purified by silica gel chromatography (0-25% EA/PE) to afford **1a-d$_5$** (542 mg, 84%).^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, *J* = 0.8 Hz, 1H), 7.79 (dd, *J* = 8.8, 0.9 Hz, 1H), 7.73 – 7.68 (m, 1H), 7.35 – 7.31 (m, 1H), 7.14 – 7.10 (m, 1H).

H/D Exchange Experiment. To a 35 mL oven-dried sealed tube, 2-phenyl-2*H*-indazole **1a** (19.4 mg, 0.1 mmol) and $[Cp^*RhCl_2]_2$ (3.1 mg, 5 mol %) were added under open air condition. $AgSbF_6$ (13.7 mg, 40 mol %) and KOAc (5.9 mg, 60 mol %) were weighed and added to the tube in the glove box. And then DCE (1 mL) and MD_3OD (72.1 mg, 2.0 mmol) were added to the tube under air. The sealed tube was capped and placed in a preheated oil bath at 120 °C for 3 h. And then the reaction mixture was immediately quenched with EtOAc, filtered through a celite pad and the filtrate was concentrated under reduced pressure. The residue was purified by preparative TLC (PE/acetone = 6/1) to recover the starting material **1a-d$_2$** (> 99%). The deuterium content of o-position was 71%. The content was determined by the ^{1}H NMR. (See the Supporting Information)

To a 35 mL oven-dried sealed tube, 2-(Phenyl-d_5)-2*H*-Indazole **1a-d$_5$** (19.9 mg, 0.1 mmol) and $[Cp^*RhCl_2]_2$ (3.1 mg, 5 mol %) were added under open air condition. $AgSbF_6$ (13.7 mg, 40 mol %) and KOAc (5.9 mg, 60 mol %) were weighed and added to the tube in the glove box. And then DCE (1 mL) and MeOH (60 mg, 2.0 mmol) were added to the tube under air. The sealed tube was capped and placed in a preheated oil bath at 120 °C for 3 h. And then the reaction mixture was immediately quenched with EtOAc and filtered through a celite pad. The filtrate was concentrated under reduced pressure. The residue was purified by preparative TLC (PE/acetone = 6/1) to recover the starting material **1a-d$_3$** (> 99%). The hydrogen content of o-position was 97% and determined by the ^{1}H NMR. (See the Supporting Information).

*Parallel KIE Experiment between **1a** and **1a-d$_5$**.* To a 35 mL oven-dried sealed tube, 2-phenyl -2*H*-Indazole **1a** (19.4 mg, 0.1 mmol) or **1a-d$_5$** (19.9 mg, 0.1 mmol) was added under the optimized conditions. The sealed tube was capped and placed in a preheated oil bath at 120 °C for 30, 40, 50, 60 or 70 minutes. Then the reaction was quenched with EtOAc separately and filtered through a celite pad. The filtrate was concentrated under reduced pressure. 1,1,2,2-Tetrachloroethane (16.8 mg, 0.1 mmol) was added to the residue as internal standard and the yield of **2a** or **2a-d$_4$** was determined by ^{1}H NMR. The calculated K_H/K_D = 0.0047/0.0035 = 1.34. (See the Supporting Information)

*Competitive KIE Experiment between **1a** and **1a-d$_5$**.* To a 35 mL oven-dried sealed tube, 2-phenyl-2*H*-Indazole **1a** (9.7 mg, 0.05 mmol) and p **1a-d$_5$** (9.9 mg, 0.05 mmol) were added under the optimized conditions. The sealed tube was capped and placed in a preheated oil bath at 120 °C for 40 minutes. Then the reaction was quenched with EtOAc immediately and filtered through a celite pad. The filtrate was concentrated under reduced pressure and the crude mixture was purified by preparative TLC (PE/acetone = 6/1) to get the desired product which was mixed by **2a** and **2a-d$_4$** in 35% yield. The ratio of **2a** and **2a-d$_4$** was determined by ^{1}H NMR. The calculated K_H/K_D = 0.541/0.459 = 1.18. (See the Supporting Information)

*Intermolecular Competition Experiment between **1c** and **1e**.* To a 35 mL oven-dried sealed tube, **1c** (22.4 mg, 0.1 mmol) and **1e** (26.6 mg, 0.1 mmol) were added under optimized conditions. The sealed tube was capped and placed in a preheated oil bath at 120 °C for 24 h. After the reaction was completed, the reaction mixture was cooled down to room temperature and filtered through a celite pad. Then the filtrate was concentrated under vacuo. 1,1,2,2-tetrachloroethane (16.8 mg, 0.1 mmol) was added to the residue as internal standard and the ratio of **2c** and **2e** was determined by ^{1}H NMR. The calculated ratio was **2c/2e** = 10 : 1. (See the Supporting Information)

Gram Scale Reaction for Synthesis of 2a. To a 150 mL oven-dried sealed bottle, 2-phenyl-2*H*-indazole **1a** (1.001g, 5.16 mmol), NCTS (3.252 g, 12.9 mmol) and $[Cp^*RhCl_2]_2$ (159.5 mg, 5 mol %) were added under open air condition. $AgSbF_6$ (709 mg, 40 mol %) and KOAc (303.8 mg, 60 mol %) were weighed and added in

the glove box. And then DCE (52 mL) was added to the bottle under air. The sealed bottle was capped and placed in a preheated oil bath at 120 °C for 24 h. After the reaction was completed, the reaction mixture was cooled down to room temperature and concentrated under vacuo. The crude mixture was purified by silica gel chromatography (0-15% PE/acetone) to give the desired product **2a** (965 mg, 85%).

Synthesis of (2-(2*H*-indazol-2-yl)phenyl)methanamine 5. To a 25 mL oven-dried Schlenk tube with a stir bar, 2-(2*H*-indazol-2-yl)benzonitrile **2a** (0.2 mmol, 43.8 mg) and 2mL THF was added under Ar. Suspensions of $LiAlH_4$ (0.6 mmol, 22.8 mg) and 0.6 mL THF was added afterwards. After stirred at 0 °C for 0.5 h, the reaction mixture was warmed to room temperature and refluxed in a preheated oil bath for 8 h. After cooling to room temperature, the reaction mixture was diluted with THF and quenched with water (200 μL) and NaOH (15%, 100 μL). Then the reaction mixture was stirred at room temperature for 1 h and dried with Na_2SO_4. After filtration and evaporation of the solvent, the crude mixture was purified by column chromatography on silica gel (dichloromethane/methanol = 10/1) to give **5**. (36.7 mg, 82%); Light green oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.24 (s, 1H), 7.76 (dd, J = 15.9, 8.6 Hz, 2H), 7.63 (d, J = 7.2 Hz, 1H), 7.49 – 7.46 (m, 3H), 7.37 – 7.34 (m, 1H), 7.17 – 7.15 (m, 1H), 4.36 (s, 2H), 3.82 (s, 2H); ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 149.5, 139.9, 135.6, 131.3, 129.6, 128.7, 127.0, 125.9, 124.4, 122.6, 122.2, 120.3, 117.8, 42.3; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{14}N_3$ 224.1182; Found 224.1185.

Synthesis of 2-(2*H*-indazol-2-yl)benzamide *6*. To a solution of **2a** (43.8 mg, 0.2 mmol) in t-BuOH (2 mL) was added solid KOH (210 mg, 3.7 mmol). After stirred in a preheated oil bath at 60 °C for 4 h, the mixture was cooled to room temperature and t-BuOH was removed under vacuo. After regular extraction with ethyl acetate, the combined organic layers were dried over Na_2SO_4 and concentrated under vacuo. The crude residue was purified by preparative TLC (PE/EA = 1/3) to generate **6** (31.6 mg, 67%); White solid; 160 – 161 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, J = 0.7 Hz, 1H), 7.91 – 7.90 (m, 1H), 7.74 – 7.72 (m, 2H), 7.61 – 7.58 (m, 2H), 7.52 – 7.50 (m, 1H), 7.39 – 7.75 (m, 1H), 7.18 – 7.14 (m, 1H), 6.35 (s, 1H), 5.61 (s, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.0, 149.7, 137.9, 132.2, 131.4, 130.2, 129.8, 127.4, 127.3, 126.1, 122.7, 122.5, 120.6, 117.5; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{14}H_{11}N_3NaO$ 260.0974; Found 260.0975.

Synthesis of methyl 2-(2*H*-indazol-2-yl)benzoate 7. To a solution of 2a (43.8 mg, 0.2 mmol) in MeOH (4 mL) was added H_2O (2 drops) and H_2SO_4 (conc., 0.6 mL). The reaction mixture was stirred in a preheated oil bath at 90 °C for 24 h. After cooling to room temperature, the reaction mixture was slowly quenched with saturated aqueous $NaHCO_3$ to pH 8 and extracted with DCM (10 mL × 3). The combined organic phases were washed with brine (15 mL), dried over anhydrous Na_2SO_4 and concentrated under vacuo. The crude residue was purified by preparative TLC (PE/EA = 6/1) to yield **7** (26 mg, 52%); Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, J = 0.8 Hz, 1H), 7.90 (dd, J = 7.7, 1.2 Hz, 1H), 7.77 – 7.71 (m, 2H), 7.64 – 7.59 (m, 2H), 7.56 – 7.52 (m, 1H), 7.34 – 7.30 (m, 1H), 7.14 – 7.10 (m, 1H), 3.61 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, CDCl3) δ 166.8, 149.7, 139.8, 132.1, 130.6, 128.8, 128.3, 126.7, 126.3, 123.8, 122., 120.4, 117.9, 52.5; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{13}N_2O_2$ 253.0972; Found 253.0973.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Experimental procedures and spectra data for **2**, **4-7** (PDF)

Singly-crystal X-ray diffraction data for compounds 2**a** (CIF)

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Notes

The authors declare no competing financial interest.

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