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Synthesis of (2*H*)-Indazoles from Azobenzenes Using Paraformaldehyde as a One-Carbon Synthon

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Abstract. Rhodium(III)-catalyzed hydroxymethylation followed by intramolecular annulation of azobenzenes using paraformaldehyde as a valuable C1-feedstock is described. The method is readily extended to the coupling reaction between azobenzenes and trifluoroacetaldehyde. This transformation efficiently produces a range of C3-unsubstituted and C3-trifluoromethylated (2*H*)-indazoles, which are important targets in the development of novel bioactive compounds. Excellent chemoselectivity and functional group tolerance were observed. The synthetic transformation of C3-unsubstituted (2*H*)-indazoles highlights the utility of the developed method.

Keywords: Annulation; Azobenzenes; (2*H*)-Indazoles; Paraformaldehyde; Rhodium.

Introduction

The indazole core is a ubiquitous scaffold in the field of modern drug discovery.[1] Particularly, (2*H*)-indazoles are crucial pharmacophores found in various bioactive molecules and pharmaceuticals including niraparib and pazopanib (Figure 1).[2] Therefore, much effort has been devoted to the development of methods for the synthesis of (2*H*)-indazoles.[3] Typical approaches have involved (a) the reaction of 2-chloromethylaryl zinc reagents and aryldiazonium salts,[3a] (b) Rh-catalyzed reductive *N*-cyclization of 2-nitroarylidines,[3b] and (c) Pd-catalyzed domino reactions of 2-halophenylacetylenes with hydrazines.[3c] Alternatively, Fe- or Cu-catalyzed intramolecular N–N bond formations of 2-azidoarylimines have been developed.[4] Rapid advances in C–H functionalization have led to the elegant new methods for the formation of (2*H*)-indazoles.[5] In this context, aryl and alkyl aldehydes,[5a–d] α-keto aldehydes,[5e] acrylates,[5f] sulfoxonium ylides,[5g] diazoesters,[5h] and alkynes[5i] have been coupled with azobenzenes or azoxybenzenes to afford the corresponding C3-functionalized (2*H*)-indazoles. However, to the best of our knowledge, the application of paraformaldehyde as an abundant C1-feedstock to generate C3-unsubstituted (2*H*)-indazoles is unexplored. Moreover, (2*H*)-indazoles containing a CF_3 group at the C3-position are considered as pharmacologically privileged scaffolds in drug discovery.[2c,6]

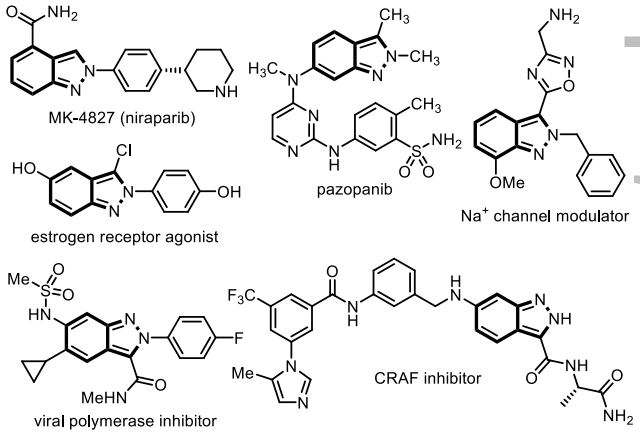
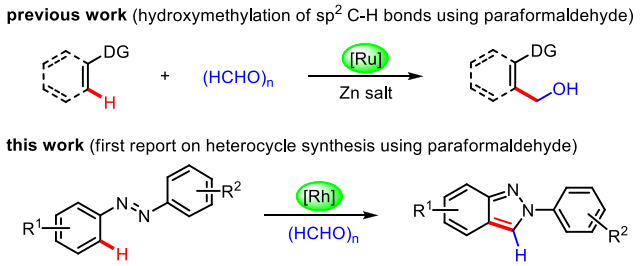


Figure 1. Selected bioactive (2*H*)-indazoles.

Paraformaldehyde has served as a valuable reagent for one-carbon homologation reactions in organic synthesis. Given the importance of hydroxymethylation in organic and medicinal chemistry, (para)formaldehyde has been exploited in the Ru(II)-catalyzed C–H functionalizations to provide hydroxymethylated arenes (Scheme 1).[7] In these reactions, a substoichiometric amount of Zn salt was essential to induce higher electrophilicity of paraformaldehyde. Using a rational design approach

based on the hydroxymethylation of C(sp^2)–H bonds, followed by intramolecular annulation, we have developed a new route to (2*H*)-indazoles. Herein, we describe the Rh(III)-catalyzed hydroxymethylation, and subsequent intramolecular annulation of azobenzenes with paraformaldehyde and trifluoroacetaldehyde, to yield a range of C3-unsubstituted and C3-trifluoromethylated (2*H*)-indazoles. It should be noted that this is the first example of C–H functionalization combined with heterocycle formation using paraformaldehyde under Rh catalysis.

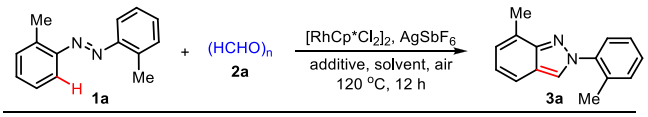


Scheme 1. Paraformaldehyde in C–H functionalization.

Results and Discussion

We began our investigation by examining the coupling of (*E*)-1,2-di-*o*-tolyldiazene (**1a**) with paraformaldehyde (**2a**) under Rh(III) catalysis, as summarized in Table 1.

Table 1. Selected optimization of reaction conditions.[a]



Entry	Additive (mol%)	Solvent	Yield[b]
1	-	DCE	trace
2	LiOAc (30)	DCE	74
3	NaOAc (30)	DCE	N.R.
4	AgOAc (30)	DCE	68
5	$Zn(OAc)_2$ (30)	DCE	61
6	LiOAc (30)	THF	14
7	LiOAc (30)	MeCN	N.R.
8	LiOAc (30)	toluene	trace
9	LiOAc (30)	TFE	53
10	LiOAc (30), AcOH (30)	DCE	71
11	LiOAc (30), Ag_2CO_3 (30)	DCE	90
12	LiOAc (30), Ag_2CO_3 (10)	DCE	75
13[c]	LiOAc (30), Ag_2CO_3 (30)	DCE	41
14[d]	LiOAc (30), Ag_2CO_3 (30)	DCE	trace
15[e]	LiOAc (30), Ag_2CO_3 (30)	DCE	N.R.
16[f]	LiOAc (30), Ag_2CO_3 (30)	DCE	23 (37)[g]
17[h]	LiOAc (30), Ag_2CO_3 (30)	DCE	67

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (1.0 mmol), $[RhCp^*Cl_2]_2$ (2.5 mol%), $AgSbF_6$ (10 mol%), additive (quantity noted), solvent (1 mL) at 120 °C for 12 h under air in sealed reaction tubes.
[b] Yield isolated by flash column chromatography.
[c] $[CoCp^*(CO)I_2]$ (5 mol%) was used as a catalyst.
[d] $[Ru(p\text{-cymene})Cl_2]_2$ (2.5 mol%) was used as a catalyst.
[e] $[IrCp^*Cl_2]_2$ (2.5 mol%) was used as a catalyst.
[f] The reaction was carried out at 60 °C.
[g] *ortho*-Hydroxymethylated azobenzene **3aa** was obtained in 37% yield.
[h] The reaction was carried out under N_2 atmosphere.

To our pleasure, **1a** was coupled with **2a** in the presence of LiOAc (30 mol%) in DCE at 120 °C to afford the C3-unsubstituted (2*H*)-indazole **3a** in 74% yield (Table 1, entry 2). However, other acetate sources including NaOAc, AgOAc, and $Zn(OAc)_2$ were unreactive or less reactive in this transformation (Table 1, entries 3−5). Subsequently, the effect of solvent was evaluated, and DCE was found to be the most effective solvent (Table 1, entries 6–9). Surprisingly, Ag_2CO_3 as a co-additive is unique in its ability to facilitate the coupling reaction to give **3a** in 90% yield (Table 1, entry 11). Lowering the amount of Ag_2CO_3 to 10 mol% decreased the yield of **3a** (Table 1, entry 12). Screening of catalysts showed that cationic Co(III), Ru(II), and Ir(III) catalysts were ineffective in this coupling reaction (Table 1, entries 13−15). The reaction could proceed at a lower temperature (60 °C) to afford (2*H*)-indazole **3a** (23%) and *ortho*-hydroxymethylated azobenzene **3aa** (37%), respectively (Table 1, entry 16). This result suggests that the product (2*H*)-indazole **3a** might be formed through intramolecular cyclization followed by the aromatization of *ortho*-hydroxymethylated azobenzene **3aa**. Finally, we performed the reaction of **1a** with **2a** using N_2 gas under otherwise identical reaction conditions to afford **3a** in 67% yield (Table 1, entry 17), suggesting that the catalytic pathway might rely on the redox-neutral Rh(III) intermediates.

With the optimal reaction conditions in hand, the substrate scope of symmetrical azobenzenes was investigated, as shown in Table 2. In cases of *ortho*- and *meta*-disubstituted azobenzenes **1b**–**1e**, high yields of (2*H*)-indazoles **3b**–**3e** were obtained. In addition, *ortho*- and *para*-disubstituted azobenzenes **1f**–**1j** afforded the corresponding products **3f**–**3j** in good to high yields. Moreover, 2,5-disubstituted azobenzenes **1k** and **1l** also coupled with **2a** to produce **3k** (58%) and **3l** (12%), respectively. However, sterically congested di-substituted azobenzene **1m** was found to be unreactive. Furthermore, *ortho*-ethyl-substituted azobenzene **1n** was successfully reacted with **2a**, providing C3-unsubstituted (2*H*)-indazole **3n** in high yield. However, *ortho*-fluoro-substituted azobenzene **1o** was found to be less reactive. Additionally, azobenzenes **1p**–**1r** with *meta*- or *para*-substituents were less reactive to afford **3p**–**3r** in lower yields. These results suggest that the formation of (2*H*)-

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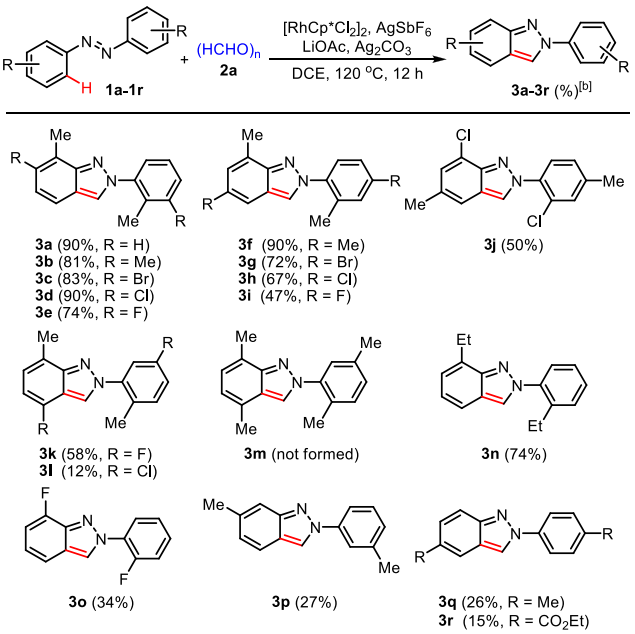
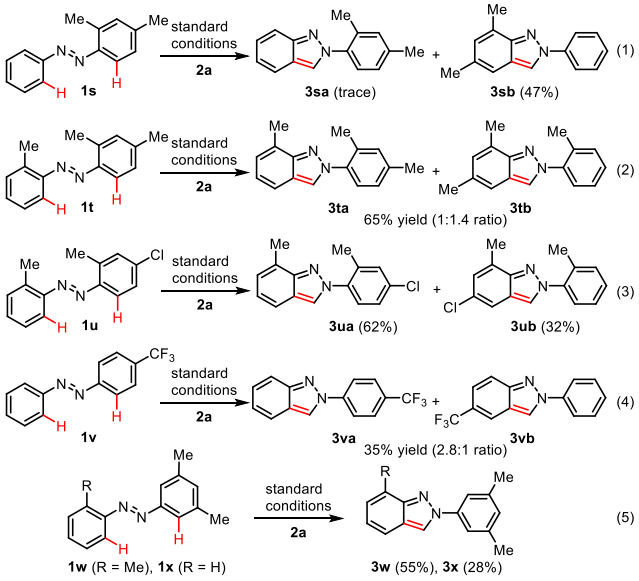
indazoles might be significantly affected by the steric influence of *ortho*-substituents during the intramolecular cyclization step.

Table 2. Scope of symmetrical azobenzenes.[a]



[a] Reaction conditions: **1a**–**1r** (0.2 mmol), **2a** (1.0 mmol), $[RhCp^*Cl_2]_2$ (2.5 mol%), $AgSbF_6$ (10 mol%), LiOAc (30 mol%), Ag_2CO_3 (30 mol%), DCE (1 mL) at 120 °C for 12 h under air in sealed reaction tubes.
[b] Yield isolated by flash column chromatography.

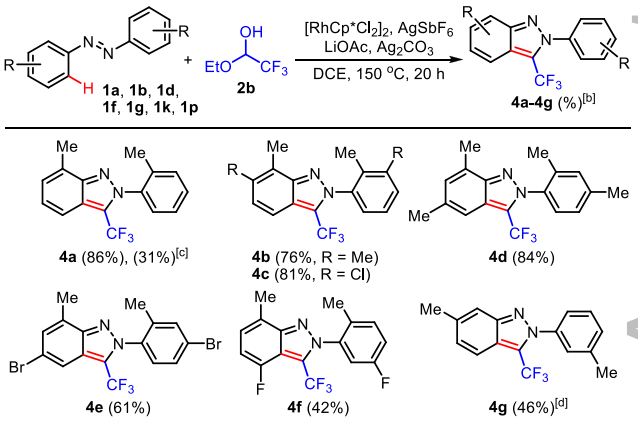


Scheme 2. Scope of unsymmetrical azobenzenes.

The substrate scope of unsymmetrical azobenzenes was investigated under the standard reaction conditions, as shown in Scheme 2. In case of the unsymmetrical azobenzene **1s**, the reaction predominantly occurred at the C–H bonds on the *ortho*-substituted aromatic ring to produce the corresponding (2*H*)-indazole **3sb** as the major product (Scheme 2, eq 1). Subsequently, the electronic effect of the aromatic ring was evaluated by using unsymmetrical azobenzenes **1t**–**1v**. Indazole products generated from electron-rich aromatic rings were formed as major products (Scheme 2, eqs 2–4). These results might be explained by the rapid formation of rhodacycle intermediates in the C–H bond cleavage step. Next, we investigated the influence of sterically congested azobenzenes on reaction outcomes. Single products **3w** and **3x** were detected in 55% and 28% yields, respectively (Scheme 2, eq 5). It is important to note that the steric environment of azobenzene is also crucial in controlling the regioselectivity of this transformation.

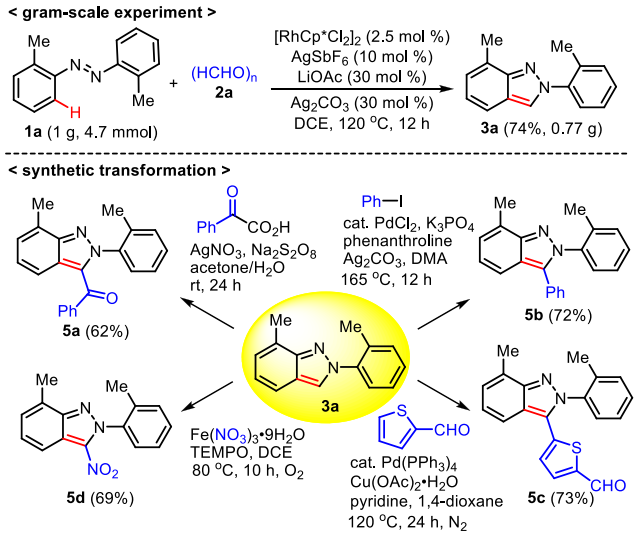
The trifluoromethyl (-CF_3) group is a key structural motif found in a range of pharmaceuticals and agrochemicals. In general, the CF_3 functionality on (hetero)aromatic rings allows significant changes to their chemical, physical and biological properties including drug efficacy, metabolic stability and bioavailability.[8] Despite this importance, to the best of our knowledge, the installation of a CF_3 group into the (2*H*)-indazole framework relies on the use of C3-halogenated (2*H*)-indazoles[2c] or on multi-step synthesis.[6] Inspired by the direct formation of (2*H*)-indazoles containing a CF_3 group, we first performed the reaction of azobenzene **1a** and $CF_3CHO{\cdot}H_2O$ to afford the corresponding adduct **4a** in 31% yield, as shown in Table 3. The replacement of $CF_3CHO{\cdot}H_2O$ with trifluoroacetaldehyde ethyl hemiacetal (**2b**), as a synthetic precursor to CF_3CHO, resulted in the significantly increased formation of **4a** (86%). To extend the scope of this transformation, the optimized reaction conditions were applied to a range of azobenzenes, and moderate to high yields of C3-CF_3 substituted (2*H*)-indazoles **4b**–**4g** were observed.

Table 3. Synthesis of C3-CF_3-substituted (2*H*)-indazoles.[a]



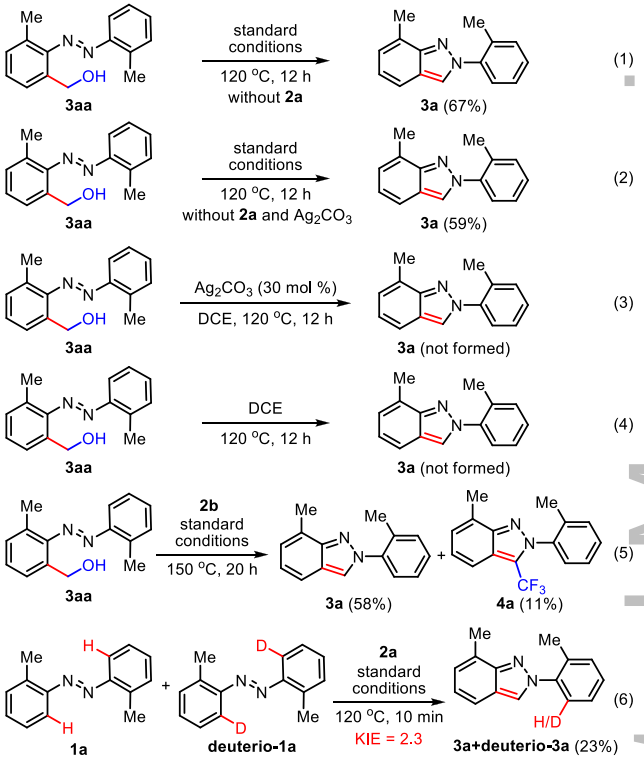
[a] Reaction conditions: **1a**, **1b**, **1d**, **1f**, **1g**, **1k** and **1p** (0.2 mmol), **2b** (1.0 mmol), $[RhCp^*Cl_2]_2$ (2.5 mol%), $AgSbF_6$ (10 mol%), LiOAc (30 mol%), Ag_2CO_3 (30 mol%), DCE (1 mL) at 150 °C for 20 h under air in sealed reaction tubes.
[b] Yield isolated by flash column chromatography.
[c] $CF_3CHO{\cdot}H_2O$ (1.0 mmol) was used instead of **2b**.
[d] After the reaction was carried out at 150 °C for 20 h, the resulting mixture was further stirred at 180 °C for 6 h.

To highlight the synthetic utility of C3-unsubstituted (2*H*)-indazoles, gram-scale experiment and various transformations including acylation, arylation, and nitration were performed,[9] as shown in Scheme 3. This reaction was successfully scaled up to 1 g of **1a** to provide **3a** in 74% yield. Next, the Ag-catalyzed decarboxylative acylation of **3a** with phenylglyoxylic acid in the presence of $Na_2S_2O_8$ afforded C3-acylated (2*H*)-indazole **5a** in 62% yield.[9a] Additionally, the Mizoroki–Heck and dehydrogenative cross-coupling reactions were performed on **3a**, and C3-arylated products **5b** and **5c** were obtained in 72% and 73% yields, respectively. Moreover, we performed a C–H nitration reaction on **3a** with $Fe(NO_3)_3{\cdot}9H_2O$ to deliver the corresponding (2*H*)-indazole **5d** in 69% yield.[9b]



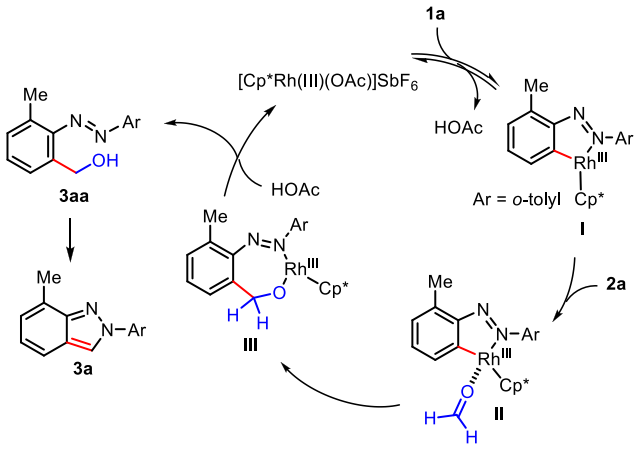
Scheme 3. Gram-scale experiment and synthetic transformations.

To gain mechanistic insight into this process, some control experiments were performed, as shown in Scheme 4. The reaction of **3aa** in the absence of **2a** under the standard reaction conditions afforded **3a** in 67% yield, indicating that (2*H*)-indazoles might be generated by the intramolecular annulation of *ortho*-hydroxymethylated azobenzene intermediates (Scheme 4, eq 1). Next, we further performed the reaction of **3aa** under the standard reaction conditions in the absence of **2a** and Ag_2CO_3 to furnish (2*H*)-indazole **3a** in 59% yield (Scheme 4, eq 2), indicating that a cationic Rh(III) catalyst can play a role as a Lewis acid to promote the intramolecular cyclization and aromatization. Although the exact effect of Ag_2CO_3 is still unclear in this process, Ag(I) might play a role as a terminal oxidant for subsequent aromatization after intramolecular cyclization of compound **3aa**. In addition, the use of only Ag_2CO_3 in DCE solvent afforded no formation of **3a** (Scheme 4, eq 3). This result suggests that the formation of (2*H*)-indazole **3a** through intramolecular cyclization of benzylic aldehyde intermediate formed by Fétizon oxidation is completely excluded. Moreover, the reaction of **3aa** in DCE solvent was unsuccessful for the formation of **3a** (Scheme 4, eq 4). Additionally, the reversibility was studied by using **3aa** and **2b** under the standard reaction conditions at 150 °C for 20 h, producing C3-unsubstituted (2*H*)-indazole **3a** (58%) and C3-CF_3-substituted (2*H*)-indazole **4a** (11%), respectively (Scheme 4, eq 5). This result suggests that the Rh(III)-catalyzed hydroxymethylation reaction might be reversible. Moreover, a kinetic isotope effect (KIE) experiment resulted in a KIE value of 2.3 (Scheme 4, eq 6), suggesting that C–H bond cleavage might be involved in the rate-determining step.



Scheme 4. Mechanistic investigations.

Based on the mechanistic investigations and existing literature[5b,5e,10] on the Rh(III)-catalyzed carbonyl addition to sp^2 C–H bonds, a plausible reaction mechanism for the formation of C3-unsubstituted (2*H*)-indazoles is outlined in Scheme 5. Coordination of **1a** to a cationic Rh(III) catalyst followed by C−H bond activation affords rhodacycle intermediate **I**. Subsequent coordination and migratory insertion of paraformaldehyde (**2a**) produces a seven-membered rhodacycle species **III**, which undergoes protonation to produce *ortho*-hydroxymethylated azobenzene **3aa** and a regenerated Rh(III) catalyst. Finally, cyclization and subsequent aromatization affords our target product **3a**.



Scheme 5. Proposed reaction mechanism.

Conclusion

In conclusion, we described the rhodium(III)-catalyzed hydroxymethylation followed by intramolecular annulation of azobenzenes with paraformaldehyde. This protocol was readily extended to the formation of C3-CF_3-substituted (2*H*)-indazoles using trifluoroacetaldehyde as a coupling partner. A wide range of suitable substrates, high levels of site selectivity, and good functional group tolerance were observed. Importantly, the synthesized C3-unsubstituted and C3-trifluoromethylated (2*H*)-indazoles as well as the synthetic transformation of C3-unsubstituted (2*H*)-indazoles can be utilized for further development of novel bioactive compounds.

Experimental Section

General procedure for the formation of C3-unsubstituted (2*H*)-indazoles 3a–3x: To an oven-dried sealed tube charged with 1,2-di-*o*-tolyldiazene (**1a**) (42.1 mg, 0.2 mmol, 100 mol%), $[RhCp^*Cl_2]_2$ (3.1 mg, 0.005 mmol, 2.5 mol%), LiOAc (3.9 mg, 0.06 mmol, 30 mol%), Ag_2CO_3 (16.5 mg, 0.06 mmol, 30 mol%) and paraformaldehyde (**2a**) (30.0 mg, 1.0 mmol, 500 mol%) was added $AgSbF_6$ (6.9 mg, 0.02 mmol, 10 mol%) and DCE (1 mL) under air at room temperature. The reaction mixture was allowed to stir at 120 °C for 12 h, and cooled to room temperature. The reaction mixture was diluted with EtOAc (3 mL) and concentrated in vacuo. The residue was purified by flash column chromatography (*n*-hexanes/EtOAc = 40:1) to afford 40.0 mg of **3a** in 90% yield.

7-Methyl-2-(*o*-tolyl)-2*H*-indazole (3a): 40.0 mg (90%); yellow sticky solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.58 (d, *J* = 8.0 Hz, 1H), 7.44 (d, *J* = 7.6 Hz, 1H), 7.41–7.31 (m, 3H), 7.11–7.04 (m, 2H), 2.67 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.6, 140.4, 134.1, 131.2, 129.1, 128.0, 126.7, 126.5, 125.3, 124.5, 122.4, 121.7, 117.6, 17.8, 17.2; IR (KBr) υ 3119, 3025, 2923, 2853, 1623, 1584, 1531, 1501, 1469, 433,1378,1348, 1245, 1186, 1120, 1051, 1037, 958, 866, 796, 752 cm^{-1}; HRMS (orbitrap, ESI) calcd for $C_{15}H_{15}N_2$ $[M+H]^+$ 223.1235, found 223.1230.

(3-Methyl-2-(*o*-tolyldiazenyl)phenyl)methanol (3aa): 17.8 mg (37%); orange solid; mp = 67.3–69.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 8.0 Hz, 1H), 7.43–7.28 (m, 6H), 4.47 (s, 2H), 2.72 (s, 3H), 2.62 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 151.2, 150.3, 137.3, 137.2, 131.8, 131.6, 131.3, 131.2, 130.1, 128.6, 126.7, 116.3, 63.4, 19.1, 18.2; IR (KBr) υ 3423, 3057, 2956, 2922, 1590, 1479, 1458, 1434, 1376, 1298, 1242, 1170, 1129, 1058, 1005, 962, 943, 884, 766 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{15}H_{16}N_2O$ $[M]^+$ 240.1263, found 240.1260.

2-(2,3-Dimethylphenyl)-6,7-dimethyl-2*H*-indazole (3b): 40.6 mg (81%); light yellow solid; mp = 88.1–89.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.48 (d, *J* = 8.8 Hz, 1H), 7.29–7.26 (m, 2H), 7.21 (t, *J* = 7.6 Hz, 1H), 6.93 (d, *J* = 8.4 Hz, 1H), 2.61 (s, 3H), 2.42 (s, 3H), 2.37 (s, 3H), 2.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.2, 140.6, 138.3, 133.2, 132.1, 130.5, 126.1, 125.7, 124.6, 124.5, 124.3, 120.3, 116.7, 20.3, 19.2, 14.2, 13.2; IR (KBr) υ 3121, 3042, 2919, 2858, 2731, 1625, 1582, 1523, 1485, 1448, 1377, 1351, 1265, 1210, 1190, 1111, 1097, 1081, 1025, 960, 802, 785, 734 cm^{-1}; HRMS (orbitrap, ESI) calcd for $C_{17}H_{19}N_2$ $[M+H]^+$ 251.1548, found 251.1543.

6-Bromo-2-(3-bromo-2-methylphenyl)-7-methyl-2*H*-indazole (3c): 63.1 mg (83%); light yellow solid; mp = 129.3–130.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (s, 1H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.43 (d, *J* = 9.2 Hz, 1H), 7.37 (d, *J* = 7.6 Hz, 1H), 7.27 (d, *J* = 8.8 Hz, 1H), 7.20 (t, *J* = 8.0 Hz, 1H), 2.71 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.1, 141.0, 134.9, 133.6, 127.6, 127.3, 127.2, 126.3, 126.0, 125.3, 121.5, 120.5, 118.6, 18.3, 16.9; IR (KBr) υ 3130, 3078, 2919, 2853, 2777, 1929, 1872, 1737, 1687, 1614, 1569, 1512, 1476, 1443, 1372, 1349, 1267, 1212, 1172, 1126, 1051, 992, 959, 876, 802, 781, 747 cm^{-1}; HRMS (orbitrap, ESI) calcd for $C_{15}H_{13}Br_2N_2$ $[M+H]^+$ 378.9445, found 378.9440.

6-Chloro-2-(3-chloro-2-methylphenyl)-7-methyl-2*H*-indazole (3d): 52.4 mg (90%); orange solid; mp = 110.0–111.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (s, 1H), 7.53–7.48 (m, 2H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.27 (t, *J* = 7.8 Hz, 1H), 7.11 (d, *J* = 8.8 Hz, 1H), 2.69 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.1, 141.2, 135.8, 133.2, 130.7, 130.2, 126.9, 125.4, 125.3, 125.2, 124.7, 120.1, 118.4, 15.3, 13.9; IR (KBr) υ 3122, 3079, 2922, 2854, 1728, 1618, 1571, 1517, 1480, 1448, 1375, 1350, 1297, 1268, 1172, 1134, 1059, 1010, 961, 884, 803, 785 cm^{-1}; HRMS (orbitrap, ESI) calcd for $C_{15}H_{13}Cl_2N_2$ $[M+H]^+$ 291.0456, found 291.0450.

6-Fluoro-2-(3-fluoro-2-methylphenyl)-7-methyl-2*H*-indazole (3e): 38.2 mg (74%); orange solid; mp = 75.8–77.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.52 (dd, *J* = 9.0, 5.0 Hz, 1H), 7.33–7.24 (m, 2H), 7.18 (t, *J* = 8.4 Hz, 1H), 6.94 (t, *J* = 9.4 Hz, 1H), 2.54 (d, *J* = 2.0 Hz, 3H), 2.15 (d, *J* = 2.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4 (d, J_{C-F} = 244.9 Hz), 158.5 (d, J_{C-F} = 239.5

Hz), 150.1 (d, $J_{C–F}$ = 10.5 Hz), 141.5 (d, $J_{C–F}$ = 6.6 Hz), 127.0 (d, $J_{C–F}$ = 9.6 Hz), 125.0 (d, $J_{C–F}$ = 1.0 Hz), 122.3 (d, $J_{C–F}$ = 19.3 Hz), 122.2 (d, $J_{C–F}$ = 3.3 Hz), 118.8 (d, $J_{C–F}$ = 11.7 Hz), 118.7 (d, $J_{C–F}$ = 10.6 Hz), 115.9 (d, $J_{C–F}$ = 23.0 Hz), 114.4 (d, $J_{C–F}$ = 29.3 Hz), 110.8 (d, $J_{C–F}$ = 19.8 Hz), 10.0 (d, $J_{C–F}$ = 4.5 Hz), 8.8 (d, $J_{C–F}$ = 3.8 Hz); ^{19}F NMR (470 MHz, $CDCl_3$) δ -114.0, -120.8; IR (KBr) υ 3126, 3058, 2925, 2856, 2742, 1634, 1584, 1494, 1475, 1394, 1378, 1362, 1311, 1245, 1205, 1159, 1108, 1090, 1064, 1023, 962, 906, 854, 790, 780 cm^{-1}; HRMS (orbitrap, ESI) calcd for $C_{15}H_{13}F_2N_2$ $[M+H]^+$ 259.1047, found 259.1041.

2-(2,4-Dimethylphenyl)-5,7-dimethyl-2*H*-indazole (3f): 45.1 mg (90%); light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.31–7.29 (m, 2H), 7.15 (s, 1H), 7.11 (d, *J* = 8.0 Hz, 1H), 6.95 (s, 1H), 2.63 (s, 3H), 2.41 (s, 3H), 2.39 (s, 3H), 2.18 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.4, 138.9, 138.1, 133.8, 131.7, 131.6, 128.2, 127.5, 127.0, 126.4, 123.7, 121.9, 115.6, 21.7, 21.1, 17.7, 17.1; IR (KBr) υ 3120 3014, 2916, 2857, 2731, 1558, 1535, 1509, 1447, 1392, 1377, 1332, 1250, 1202, 1131, 1040, 964, 840, 815, 746 cm^{-1}; HRMS (orbitrap, ESI) calcd for $C_{17}H_{19}N_2$ $[M+H]^+$ 251.1548, found 251.1543.

5-Bromo-2-(4-bromo-2-methylphenyl)-7-methyl-2*H*-indazole (3g): 54.7 mg (72%); dark yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.71 (s, 1H), 7.52 (s, 1H), 7.46 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.18 (s, 1H), 2.62 (s, 3H), 2.21 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.3, 139.1, 136.1, 134.1, 130.2, 129.7, 129.0, 127.9, 123.9, 123.1, 122.7, 119.6, 115.9, 17.7, 16.8; IR (KBr) υ 3117, 3085, 2921, 2852, 2757, 1725, 1614, 1552, 1515, 1489, 1433, 1370, 1317, 1285, 1239, 1180, 1126, 1088, 1069, 1041, 999, 956, 879, 845, 816, 765 cm^{-1}; HRMS (orbitrap, ESI) calcd for $C_{15}H_{13}Br_2N_2$ $[M+H]^+$ 378.9445, found 378.3440.

5-Chloro-2-(4-chloro-2-methylphenyl)-7-methyl-2*H*-indazole (3h): 39.0 mg (67%); light yellow solid; mp = 104.0–104.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.54 (s, 1H), 7.38–7.36 (m, 2H), 7.34 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.08 (s, 1H), 2.63 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.0, 138.5, 135.9, 135.1, 131.2, 129.9, 128.1, 127.8, 127.0, 126.8, 124.3, 121.9, 116.2, 17.8, 17.0; IR (KBr) υ 3121, 2923, 2853, 1618, 1519, 1494, 1442, 1372, 1319, 1239, 1183, 1126, 1099, 1075, 1043, 984, 958, 894, 846, 819, 786 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{15}H_{12}Cl_2N_2$ $[M]^+$ 290.0378, found 290.0379.

5-Fluoro-2-(4-fluoro-2-methylphenyl)-7-methyl-2*H*-indazole (3i): 24.3 mg (47%); yellow solid; mp = 107.1–108.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.39 (dd, *J* = 8.6, 5.4 Hz, 1H), 7.12 (dd, *J* = 9.0, 2.2 Hz, 1H), 7.08–6.99 (m, 2H), 6.92 (d, *J* = 10.0 Hz, 1H), 2.65 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5 (d, $J_{C–F}$ = 247.3 Hz), 158.6 (d, $J_{C–F}$ = 238.5 Hz), 147.1, 136.9 (d, $J_{C–F}$ = 8.7 Hz), 136.4 (d, $J_{C–F}$ = 2.7 Hz), 130.7 (d, $J_{C–F}$ = 9.7 Hz), 128.3 (d, $J_{C–F}$ = 9.4 Hz), 124.8 (d, $J_{C–F}$ = 8.5 Hz), 120.7 (d, $J_{C–F}$ = 12.4 Hz), 117.7 (d, $J_{C–F}$ = 22.5 Hz), 117.0 (d, $J_{C–F}$ = 28.5 Hz), 113.4 (d, $J_{C–F}$ = 22.7 Hz), 99.7 (d, $J_{C–F}$ = 24.1 Hz), 17.8, 17.1 (d, $J_{C–F}$ = 1.0 Hz); ^{19}F NMR (470 MHz, $CDCl_3$) δ -112.5, -119.8; IR (KBr) υ 3059, 2927, 2855, 1630, 1590, 1538, 1507, 1449, 1384, 13634, 1270, 1223, 1189, 1132, 1046, 993, 959, 865, 830 cm^{-1}; HRMS (orbitrap, ESI) calcd for $C_{15}H_{13}F_2N_2$ $[M+H]^+$ 259.1047, found 259.1041.

7-Chloro-2-(2-chloro-4-methylphenyl)-5-methyl-2*H*-indazole (3j): 29.1 mg (50%); light yellow solid; mp = 115.7–117.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) 8.21 (s, 1H), 7.58 (d, *J* = 8.4 Hz, 1H), 7.37 (s, 1H), 7.36 (s, 1H), 7.22 (s, 1H), 7.21 (d, *J* = 8.4 Hz, 1H), 2.41 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.8, 140.7, 135.9, 132.3, 130.7, 128.7, 128.5, 128.3 (two carbons overlap), 125.5, 123.2, 122.5, 117.4, 21.5, 20.9; IR (KBr) υ 3141, 3035, 2969, 2917, 2857, 2731, 1908, 1728, 1633, 1530, 1501, 1453, 1407, 1375, 1330, 1264, 1222, 1262, 1136, 1079, 1032, 1016, 981, 957, 890, 846, 814, 739 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{15}H_{12}Cl_2N_2$ $[M]^+$ 290.0378, found 290.0384.

4-Fluoro-2-(5-fluoro-2-methylphenyl)-7-methyl-2*H*-indazole (3k): 30.0 mg (58%); light yellow solid; mp = 84.6–85.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.33 (dd, *J* = 8.4, 6.0 Hz, 1H), 7.22 (dd, *J* = 8.6, 2.6 Hz, 1H), 7.13 (td, *J* = 8.4, 2.8 Hz, 1H), 6.99 (ddd, *J* = 7.4, 5.0, 1.0 Hz, 1H), 6.66 (dd, *J* = 10.4, 7.2 Hz, 1H), 2.60 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8 (d, $J_{C–F}$ = 245.1 Hz), 153.9 (d, $J_{C–F}$ = 250.0 Hz), 151.3 (d, $J_{C–F}$ = 5.3 Hz), 140.5 (d, $J_{C–F}$ = 9.6 Hz), 132.4 (d, $J_{C–F}$ = 8.2 Hz), 129.5 (d, $J_{C–F}$ = 3.6 Hz), 125.1 (d, $J_{C–F}$ = 6.5 Hz), 123.8 (d, $J_{C–F}$ = 4.7 Hz), 121.9 (d, $J_{C–F}$ = 4.2 Hz), 116.3 (d, $J_{C–F}$ = 20.5 Hz), 114.1 (d, $J_{C–F}$ = 24.0 Hz), 113.6 (d, $J_{C–F}$ = 20.3 Hz), 104.9 (d, $J_{C–F}$ = 17.2 Hz), 17.3, 16.6; ^{19}F NMR (470 MHz, $CDCl_3$) δ -115.8, -121.8; IR (KBr) υ 3131, 3073, 3040, 2970, 2926, 2855, 2746, 1645, 1612, 1570, 1544, 1508, 1476, 1394, 1348, 1243, 1166, 1118, 1045, 976, 882, 865, 811, 785, 742 cm^{-1}; HRMS (orbitrap, ESI) calcd for $C_{15}H_{13}F_2N_2$ $[M+H]^+$ 259.1047, found 259.1041.

4-Chloro-2-(5-chloro-2-methylphenyl)-7-methyl-2*H*-indazole (3l): 7.0 mg (12%); orange oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.48 (d, *J* = 2.0 Hz, 1H), 7.38 (dd, *J* = 8.2, 2.2 Hz, 1H), 7.31 (d, *J* = 8.4 Hz, 1H), 7.05–7.00 (m, 2H), 2.61 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.0, 140.7, 132.5, 132.4, 131.9, 129.4, 126.9, 126.8, 125.9, 124.2, 122.5, 121.9, 121.7, 17.5, 16.7; IR (KBr) υ 3127, 3072, 3029, 2924, 2737, 1824, 1732, 1625, 1601, 1573, 1533, 1496, 1445, 1397, 1382, 1339, 1232, 1186, 1132, 1094, 1046, 998, 975,0945, 875, 813, 786 cm^{-1}; HRMS (orbitrap, ESI) calcd for $C_{15}H_{13}Cl_2N_2$ $[M+H]^+$ 291.0456, found 291.0450.

7-Ethyl-2-(2-ethylphenyl)-2*H*-indazole (3n): 37.1 mg (74%); yellow sticky oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.58 (d, *J* = 8.0 Hz, 1H), 7.46–7.39 (m, 3H), 7.35–7.30 (m, 1H), 7.14–7.07 (m, 2H), 3.11 (q, *J* = 7.6 Hz, 2H), 2.55 (q, *J* = 7.6 Hz, 2H), 1.42 (t, *J* = 7.6 Hz, 3H), 1.11 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.8, 140.4, 140.0, 134.1, 129.6, 129.4, 126.9, 126.4, 124.6, 123.2, 122.4, 121.8, 117.6, 24.5, 24.3, 15.0, 14.0; IR (KBr) υ 3118, 3063, 3033, 2965, 2931, 2872, 2731, 1621, 1582, 1531, 1498, 1456, 1389, 1648, 1261, 1184, 1124, 1050, 959, 945, 862, 805, 750 cm^{-1}; HRMS (orbitrap, ESI) calcd for $C_{17}H_{19}N_2$ $[M+H]^+$ 251.1548, found 251.1534.

7-Fluoro-2-(2-fluorophenyl)-2*H*-indazole (3o): 15.7 mg (34%); yellow solid; mp = 71.3–71.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (t, *J* = 2.6 Hz, 1H), 8.14 (td, *J* = 8.0, 2.0 Hz, 1H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.44–7.38 (m, 1H), 7.36–7.28 (m, 2H), 7.05–6.95 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.1 (d, J_{C-F} = 249.3 Hz), 153.0 (d, J_{C-F} = 254.8 Hz), 140.6 (d, J_{C-F} = 15.8 Hz), 129.5 (d, J_{C-F} = 7.9 Hz), 128.4 (d, J_{C-F} = 9.1 Hz), 126.1, 125.6 (d, J_{C-F} = 5.2 Hz), 125.3 (dd, J_{C-F} = 10.3, 2.5 Hz), 125.1 (d, J_{C-F} = 3.7 Hz), 122.3 (d, J_{C-F} = 5.6 Hz), 116.9 (d, J_{C-F} = 20.3 Hz), 116.5 (d, J_{C-F} = 5.0 Hz), 109.7 (d, J_{C-F} = 16.0 Hz); ^{19}F NMR (470 MHz, $CDCl_3$) δ -124.7, -128.8; IR (KBr) υ 3144, 3052, 2925, 2853, 2776, 1613, 1597, 1555, 1505, 1474, 1385, 1359, 1323, 1275, 1240, 1228, 1198, 1165, 1110, 1076, 1047, 957, 878, 817, 800, 755 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{13}H_8F_2N_2$ $[M]^+$ 230.0656, found 230.0659.

6-Methyl-2-(*m*-tolyl)-2*H*-indazole (3p): 12.0 mg (27%); yellow solid; mp = 88.1–89.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, *J* = 0.8 Hz, 1H), 7.74 (s, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.59 (d, *J* = 8.8 Hz, 1H), 7.53 (s, 1H), 7.38 (t, *J* = 7.8 Hz, 1H), 7.19 (d, *J* = 7.6 Hz, 1H), 6.95 (dd, *J* = 8.4, 1.2 Hz, 1H), 2.47 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.3, 140.5, 139.7, 136.6, 129.2, 128.4, 125.4, 121.6, 121.1, 120.2, 119.8, 117.8, 116.1, 22.2, 21.4; IR (KBr) υ 3126, 3044, 2917, 2857, 2732, 1725, 1639, 1611, 1591, 1509, 1446, 1383, 1353, 1289, 1224, 1156, 1140, 1055, 1007, 968, 861, 802, 783 cm^{-1}; HRMS (orbitrap, ESI) calcd for $C_{15}H_{15}N_2$ $[M+H]^+$ 223.1235, found 223.1230.

5-Methyl-2-(*p*-tolyl)-2*H*-indazole (3q): 11.7 mg (26%); yellow solid; mp = 107.2–109.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (s, 1H), 7.76 (d, *J* = 8.4 Hz, 1H), 7.68 (d, *J* = 9.2 Hz, 1H), 7.43 (s, 1H), 7.30 (d, *J* = 8.0 Hz, 1H), 7.15 (d, *J* = 8.8 Hz, 1H), 2.43 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.6, 138.3, 137.6, 131.6, 130.0, 129.6, 123.0, 120.6, 119.3, 118.3, 117.5, 21.8, 21.0; IR (KBr) υ 3131, 3034, 2917, 2856, 2732, 1733, 1608, 1530, 1512, 1447, 1402, 1373, 1325, 1309, 1252, 1216, 1206, 1140, 1117, 1047, 1007, 957, 833, 800, 776 cm^{-1}; HRMS (orbitrap, ESI) calcd for $C_{15}H_{15}N_2$ $[M+H]^+$ 223.1235, found 223.1230.

Ethyl 2-(4-(ethoxycarbonyl)phenyl)-2*H*-indazole-5-carboxylate (3r): 10.1 mg (15%); yellow solid; mp = 166.5–166.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (s, 1H), 8.55 (s, 1H), 8.22 (d, *J* = 8.0 Hz, 2H), 8.02 (d, *J* = 8.0 Hz, 2H), 7.95 (d, *J* = 9.2 Hz, 1H), 7.78 (d, *J* = 9.2 Hz, 1H), 4.45–4.40 (m, 4H), 1.43 (t, *J* = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 165.6, 151.1, 143.1, 131.2, 130.2, 127.1, 125.3, 125.1, 122.8, 122.3, 120.4, 117.9, 61.4, 61.0, 14.4, 14.3; IR (KBr) υ 3128, 3038, 2910, 2847, 2730, 1739, 1601, 1524, 1511, 1456, 1412, 1362, 1320, 1298, 1242, 1210, 1201, 1147, 1118, 1049, 1011, 958, 843, 802, 710 cm^{-1}; HRMS (orbitrap, ESI) calcd for $C_{19}H_{18}N_2O_4$ $[M]^+$ 338.1267, found 338.1266.

5,7-Dimethyl-2-phenyl-2*H*-indazole (3sb): 20.9 mg (47%); yellow sticky solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (s, 1H), 7.90 (d, *J* = 7.6 Hz, 2H), 7.51 (t, *J* = 8.0 Hz, 2H), 7.38 (t, *J* = 7.4 Hz, 1H), 7.27 (s, 1H), 6.93 (s, 1H), 2.66 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.2, 140.8, 132.0, 129.4, 128.7, 127.6, 127.5, 122.9, 120.9, 119.6, 115.7, 21.8, 17.0; IR (KBr) υ 3127, 3041, 2968, 2938, 2914, 2858, 2731, 1633, 1598, 1536, 1500, 1462, 1390, 1338, 1257, 1206, 1072, 1049, 958, 906, 842, 756 cm^{-1}; HRMS (orbitrap, ESI) calcd for $C_{15}H_{15}N_2$ $[M+H]^+$ 222.1235, found 222.1230.

2-(2,4-Dimethylphenyl)-7-methyl-2*H*-indazole (3ta) and 5,7-dimethyl-2-(*o*-tolyl)-2*H*-indazole (3tb): 30.7 mg (65%); yellow sticky solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.96 (s, 1.35H), 7.57 (d, *J* = 8.4 Hz, 1H), 7.43 (d, *J* = 7.6 Hz, 1.35H), 7.40–7.30 (m, 1H, 5.4H), 7.17 (s, 1H), 7.14–7.03 (m, 3H), 6.97 (s, 1.35H), 2.68 (s, 3H), 2.65 (s, 4.05H), 2.42 (s, 4.05H), 2.41 (s, 3H), 2.24 (s, 4.05H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.5, 148.5, 140.5, 139.0, 138.0, 134.1, 133.7, 131.8, 131.7, 131.1, 128.9, 128.3, 127.9, 127.5, 127.1, 126.6, 126.5, 126.4, 125.2, 124.5, 123.6, 122.2, 121.9, 121.6, 117.6, 115.6, 21.7, 21.1, 17.8, 17.7, 17.2, 17.1; IR (KBr) υ 3121, 3022, 2916, 2857, 2730, 1623, 1584, 1532, 1502, 1459, 1377, 1332, 1248, 1191, 1155, 1120, 1037, 960, 841, 794 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{16}H_{16}N_2$ $[M]^+$ 236.1313, found 236.1312.

2-(4-Chloro-2-methylphenyl)-7-methyl-2*H*-indazole (3ua): 31.8 mg (62%); yellow sticky solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.39–7.36 (m, 2H), 7.51 (dd, *J* = 8.2, 2.2 Hz, 1H), 7.12–7.04 (m, 2H), 2.67 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.6, 138.8, 136.0, 134.8, 131.1, 127.9, 127.8, 126.7, 125.6, 124.6, 122.6, 121.7, 117.6, 17.8, 17.2; IR (KBr) υ 3120, 3046, 2923, 2852, 2729, 1623, 1561, 1532, 1495, 1438, 1375, 1350, 1245, 1185, 1125, 1099, 1041, 956, 873, 857, 818, 794 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{15}H_{13}ClN_2$ $[M]^+$ 256.0767, found 256.0764.

5-Chloro-7-methyl-2-(*o*-tolyl)-2*H*-indazole (3ub): 16.4 mg (32%); yellow sticky solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.55 (s, 1H), 7.43–7.33 (m, 4H), 7.07 (s, 1H), 2.64 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.9, 140.0, 134.0, 131.3, 130.0, 129.4, 127.8, 126.7 (two carbons overlap), 126.6, 124.2, 121.9, 116.2, 17.8, 17.0; IR (KBr) υ 3117, 3055, 2922, 2853, 1725, 1584, 1519, 1498, 1464, 1379, 1322, 1239, 1186, 1121, 1074, 984, 959, 894, 847, 814, 761 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{15}H_{13}ClN_2$ $[M]^+$ 256.0767, found 256.0764.

2-(4-(Trifluoromethyl)phenyl)-2*H*-indazole (3va) and 2-phenyl-5-(trifluoromethyl)-2*H*-indazole (3vb): 18.4 mg (35%); yellow sticky solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 8.48 (s, 2.75H), 8.08–8.06 (m, 1H), 8.07 (d, *J* = 8.4 Hz, 5.5H), 7.92–7.88 (m, 2.75H), 7.81–7.79 (m, 3H), 7.80 (d, *J* = 8.4 Hz, 5.5H), 7.72 (d, *J* = 8.0 Hz, 2.75H), 7.58–7.54 (m, 2H), 7.50–7.44 (m, 2H), 7.37–7.33 (m, 2.75H), 7.14 (dd, *J* = 8.2, 3.0 Hz, 2.75H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.0, 142.8, 140.1, 129.8 (q, J_{C-F} = 33.1 Hz), 129.7, 128.6, 127.6, 126.9 (q, J_{C-F} = 3.7 Hz), 126.3 (q, J_{C-F} = 4.9 Hz), 124.6 (q, J_{C-F} = 31.5 Hz), 124.5 (q, J_{C-F} = 258.8 Hz), 123.7 (q, J_{C-F} = 270.1 Hz), 123.1, 122.9, 122.7

(q, $J_{C–F}$ = 3.0 Hz), 122.3, 121.3, 121.2, 120.8, 120.5, 120.4, 119.3 (q, $J_{C–F}$ = 4.9 Hz), 119.0, 118.0; ^{19}F NMR (470 MHz, $CDCl_3$) δ -62.4, -62.8; IR (KBr) υ 3132, 3065, 2923, 2855, 1730, 1614, 1526, 1502, 1431, 1384, 1325, 1206, 1165, 1107, 1070, 1048, 953, 895, 840, 820, 780 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{14}H_9F_3N_2$ $[M]^+$ 262.0718, found 262.0719.

2-(3,5-Dimethylphenyl)-7-methyl-2*H*-indazole (3w): 26.0 mg (55%); yellow sticky solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (s, 1H), 7.55–7.53 (m, 3H), 7.08 (d, *J* = 6.8 Hz, 1H), 7.04–7.00 (m, 2H), 2.70 (s, 3H), 2.42 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.4, 140.3, 139.5, 129.6, 126.8, 122.5, 122.3, 120.6, 120.3, 118.8, 117.8, 21.3; IR (KBr) υ 3128, 3019, 2916, 2855, 2732, 1904, 1758, 1612, 1595, 1531, 1482, 1373, 1292, 1248, 1177, 1159, 1076, 1036, 1001, 970, 880, 842, 791 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{16}H_{16}N_2$ $[M]^+$ 236.1313, found 236.1310.

2-(3,5-Dimethylphenyl)-2*H*-indazole (3x): 12.5 mg (28%); yellow sticky solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (s, 1H), 7.80 (d, *J* = 8.8 Hz, 1H), 7.70 (d, *J* = 8.4 Hz, 1H), 7.52 (s, 2H), 7.32 (dd, *J* = 8.6, 6.6 Hz, 1H), 7.11 (dd, *J* = 8.4, 6.8 Hz, 1H), 7.04 (s, 1H), 2.42 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.0, 140.6, 139.3, 129.4, 128.0, 125.5, 122.5, 122.4, 120.8, 119.0, 117.7, 21.3, 17.1; IR (KBr) υ 3127, 3061, 3020, 2918, 2856, 1725, 1628, 1612, 1598, 1518, 1482, 1388, 1350, 1294, 1229, 1177, 1078, 1039, 967, 912, 844, 754 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{15}H_{14}N_2$ $[M]^+$ 222.1157, found 222.1156.

General procedure for the formation of C3-CF_3-substituted (2*H*)-indazoles 4a–4g: To an oven-dried sealed tube charged with 1,2-di-*o*-tolyldiazene (**1a**) (42.1 mg, 0.2 mmol, 100 mol%), $[RhCp^*Cl_2]_2$ (3.1 mg, 0.005 mmol, 2.5 mol%), LiOAc (3.9 mg, 0.06 mmol, 30 mol%), Ag_2CO_3 (16.5 mg, 0.06 mmol, 30 mol%) and trifluoroacetaldehyde ethyl hemiacetal (**2b**) (181.1 mg, 1.0 mmol, 500 mol%) was added $AgSbF_6$ (6.9 mg, 0.02 mmol, 10 mol%) and DCE (1 mL) under air at room temperature. The reaction mixture was allowed to stir at 150 °C for 20 h, and cooled to room temperature. The reaction mixture was diluted with EtOAc (3 mL) and concentrated in vacuo. The residue was purified by flash column chromatography (*n*-hexanes/EtOAc = 30:1) to afford 49.9 mg of **4a** in 86% yield.

7-Methyl-2-(*o*-tolyl)-3-(trifluoromethyl)-2*H*-indazole (4a): 49.9 mg (86%); yellow sticky solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.4 Hz, 1H), 7.48–7.44 (m, 1H), 7.38–7.32 (m, 3H), 7.24–7.17 (m, 2H), 2.67 (s, 3H), 2.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.5, 138.4, 135.9, 130.8, 130.4, 128.7, 127.4, 126.2, 126.0, 125.2, 124.4 (q, $J_{C–F}$ = 38.8 Hz), 120.8 (q, $J_{C–F}$ = 267.2 Hz), 120.6 (q, $J_{C–F}$ = 1.0 Hz), 116.7 (q, $J_{C–F}$ =1.3 Hz), 17.0, 16.8; ^{19}F NMR (470 MHz, $CDCl_3$) δ -56.7; IR (KBr) υ 3042, 2924, 1585, 1536, 1503, 1469, 1452, 1372, 1277, 1238, 1178, 1166, 1123, 1079, 1053, 989, 870, 785 cm^{-1}; HRMS (orbitrap, ESI) calcd for $C_{16}H_{13}F_3N_2Na$ $[M+Na]^+$ 313.0929, found 313.0923.

2-(2,3-Dimethylphenyl)-6,7-dimethyl-3-(trifluoromethyl)-2*H*-indazole (4b): 48.4 mg (76%); orange solid; mp = 92.0–93.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.8 Hz, 1H), 7.56 (dd, *J* = 6.2, 2.6 Hz, 1H), 7.25–7.20 (m, 2H), 7.13 (d, *J* = 8.8 Hz, 1H), 2.58 (s, 3H), 2.42 (s, 3H), 2.36 (s, 3H), 1.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.1, 138.5, 138.2, 134.6, 133.2, 131.6, 129.0, 125.6, 125.1, 125.0, 124.3 (q, $J_{C–F}$ = 38.8 Hz), 120.8 (q, $J_{C–F}$ = 267.4 Hz), 119.3, 115.8, 20.1, 19.2, 13.8, 13.1; ^{19}F NMR (470 MHz, $CDCl_3$) δ -56.8; IR (KBr) υ 3043, 2923, 2864, 2735, 1585, 1531, 1485, 1456, 1385, 1315, 1268, 1242, 1213, 1184, 1163, 1119, 1099, 1055, 990, 902, 785 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{18}H_{17}F_3N_2$ $[M]^+$ 318.1344, found 318.1349.

6-Chloro-2-(3-chloro-2-methylphenyl)-7-methyl-3-(trifluoromethyl)-2*H*-indazole (4c): 58.2 mg (81%); yellow solid; mp = 103.1–103.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60–7.58 (m, 2H), 7.33–7.26 (m, 3H), 2.68 (s, 3H), 1.98 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.0, 139.1, 135.6, 134.9, 131.7, 131.5, 127.6, 126.7, 126.1, 126.0, 125.2 (q, $J_{C–F}$ = 39.1 Hz), 120.3 (q, $J_{C–F}$ = 267.6 Hz), 119.1, 117.4 (q, $J_{C–F}$ = 1.2 Hz), 14.8, 13.8; ^{19}F NMR (470 MHz, $CDCl_3$) δ -56.8; IR (KBr) υ 3076, 2927, 2738, 1932, 1806, 1742, 1575, 1522, 1484, 1448, 1380, 1308, 1264, 1240, 1168, 1125, 1105, 1074, 1019, 983, 896, 788 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{16}H_{11}Cl_2F_3N_2$ $[M]^+$ 358.0251, found 358.0253.

2-(2,4-Dimethylphenyl)-5,7-dimethyl-3-(trifluoromethyl)-2*H*-indazole (4d): 53.5 mg (84%); yellow sticky solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (s, 1H), 7.24 (d, *J* = 8.0 Hz, 1H), 7.16 (s, 1H), 7.12 (d, *J* = 8.0 Hz, 1H), 7.02 (s, 1H), 2.62 (s, 3H), 2.45 (s, 3H), 2.41 (s, 3H), 1.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.4, 140.3, 136.0, 135.5, 134.9, 131.4, 128.9, 128.2, 127.2, 126.8, 123.4 (q, $J_{C–F}$ = 38.6 Hz), 120.9 (q, $J_{C–F}$ = 267.3 Hz), 121.0, 114.7 (q, $J_{C–F}$ =1.3 Hz), 21.9, 21.2, 16.9, 16.7; ^{19}F NMR (470 MHz, $CDCl_3$) δ -56.7; IR (KBr) υ 3019, 2974, 2922, 2862, 2737, 1632, 1561, 1538, 1508, 1452, 1379, 1354, 1281, 1256, 1232, 1184, 1143, 1116, 1079, 989, 954, 849, 818, 768 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{18}H_{17}F_3N_2$ $[M]^+$ 318.1344, found 318.1347.

5-Bromo-2-(4-bromo-2-methylphenyl)-7-methyl-3-(trifluoromethyl)-2*H*-indazole (4e): 54.7 mg (61%); yellow solid; mp = 104.2–105.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.55 (d, *J* = 1.2 Hz, 1H), 7.49 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.28 (s, 1H), 7.22 (d, *J* = 8.4 Hz, 1H), 2.62 (s, 3H), 1.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.2, 138.0, 137.1, 133.9, 130.9, 130.0, 129.6, 128.8, 124.7, 124.0 (q, $J_{C–F}$ = 39.3 Hz), 121.5, 120.3 (q, $J_{C–F}$ = 267.5 Hz), 119.3, 118.8 (q, $J_{C–F}$ =1.4 Hz), 16.7, 16.6; ^{19}F NMR (470 MHz, $CDCl_3$) δ -56.8; IR (KBr) υ 3086, 2982, 2922, 1620, 1558, 1522, 1492, 1449, 1349, 1271, 1237, 1168, 1124, 1074, 982, 887, 846, 819, 788 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{16}H_{11}Br_2F_3N_2$ $[M]^+$ 445.9241, found 445.9234.

4-Fluoro-2-(5-fluoro-2-methylphenyl)-7-methyl-3-(trifluoromethyl)-2*H*-indazole (4f): 27.4 mg (42%); yellow sticky solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33

(dd, *J* = 8.4, 5.6 Hz, 1H), 7.21 (td, *J* = 8.4, 2.4 Hz, 1H), 7.13–7.07 (m, 2H), 6.87 (dd, *J* = 10.4, 7.6 Hz, 1H), 2.60 (s, 3H), 1.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.4 (d, J_{C-F} = 245.8 Hz), 152.2 (d, J_{C-F} = 253.2 Hz), 150.2 (d, J_{C-F} = 4.6 Hz), 139.1 (d, J_{C-F} = 9.5 Hz), 131.9 (d, J_{C-F} = 8.4 Hz), 131.4 (d, J_{C-F} = 3.7 Hz), 126.0 (d, J_{C-F} = 6.3 Hz), 124.5 (d, J_{C-F} = 5.3 Hz), 123.6 (qd, J_{C-F} = 41.4, 4.2 Hz), 119.7 (q, J_{C-F} = 268.5 Hz), 117.7 (d, J_{C-F} = 20.7 Hz), 114.8 (d, J_{C-F} = 23.9 Hz), 111.7 (d, J_{C-F} = 19.1 Hz), 108.5 (d, J_{C-F} = 18.9 Hz), 16.4, 16.1; ^{19}F NMR (470 MHz, $CDCl_3$) δ -55.3, -115.9, -119.3; IR (KBr) υ 3078, 3038, 2931, 1644, 1611, 1574, 1548, 1505, 1472, 1435, 1388, 1257, 1177, 1125, 1073, 1045, 1009, 898, 869, 817, 749 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{16}H_{11}F_5N_2$ $[M]^+$ 326.0842, found 326.0843.

6-Methyl-2-(*m*-tolyl)-3-(trifluoromethyl)-2*H*-indazole (4g): 26.7 mg (46%); yellow sticky solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.8 Hz, 1H), 7.55 (s, 1H), 7.43–7.33 (m, 4H), 7.13 (d, *J* = 8.8 Hz, 1H), 2.49 (s, 3H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.7, 139.5, 139.2, 137.2, 130.6, 128.7, 127.9, 126.6, 123.4 (q, J_{C-F} = 39.3 Hz), 123.0 (q, J_{C-F} = 0.9 Hz), 120.9 (q, J_{C-F} = 267.2 Hz), 119.9, 118.8 (q, J_{C-F} = 1.3 Hz), 116.4, 22.1, 21.2; ^{19}F NMR (470 MHz, $CDCl_3$) δ -55.0; IR (KBr) υ 3043, 2922, 2858, 2737, 1611,1556, 1496, 1477, 1440, 1375, 1315, 1283, 1220, 1169, 1143, 1103, 1016, 943, 911, 787 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{16}H_{13}F_3N_2$ $[M]^+$ 290.1031, found 290.1031.

Gram scale experiment: To an oven-dried sealed tube charged with 1,2-di-*o*-tolyldiazene (**1a**) (1 g, 4.7 mmol, 100 mol%), $[RhCp^*Cl_2]_2$ (74.2 mg, 0.12 mmol, 2.5 mol%), LiOAc (93.03 mg, 1.41 mmol, 30 mol%), Ag_2CO_3 (388.8 mg, 1.41 mmol, 30 mol%) and paraformaldehyde (**2a**) (705.0 mg, 23.5 mmol, 500 mol%) was added $AgSbF_6$ (161.5 mg, 0.47 mmol, 10 mol%) and DCE (10 mL) under air at room temperature. The reaction mixture was allowed to stir at 120 °C for 12 h, and cooled to room temperature. The reaction mixture was diluted with EtOAc (25 mL) and concentrated in vacuo. The residue was purified by flash column chromatography (*n*-hexanes/EtOAc = 40:1) to afford 0.77 g of **3a** in 74% yield.

Experimental procedure and characterization data for the formation of 5a: To an oven-dried sealed tube charged with **3a** (44.4 mg, 0.2 mmol, 100 mol%), phenylglyoxylic acid (150.1 mg, 1 mmol, 500 mol%), $Na_2S_2O_8$ (142.8 mg, 0.6 mmol, 300 mol%) and $AgNO_3$ (6.9 mg, 0.04 mmol, 20 mol%) was added acetone (0.5 mL) and H_2O (0.5 mL) under air at room temperature. The reaction mixture was allowed to stir at room temperature for 24 h. The reaction mixture was quenched with saturated aqueous Na_2CO_3 solution and extracted with ethyl acetate (50 mL). The combined organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by flash column chromatography (*n*-hexanes/EtOAc = 50:1) to afford 40.5 mg of **5a** in 62% yield.

(7-Methyl-2-(*o*-tolyl)-2*H*-indazol-3-yl)(phenyl)methanone (5a): 40.5 mg (62%); yellow solid; mp = 113.7–114.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86–7.84 (m, 2H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.49–7.45 (m, 2H), 7.39–7.26 (m, 4H), 7.16–7.06 (m, 3H), 2.72 (s, 3H), 2.12 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.3, 148.6, 140.1, 137.9, 134.8, 133.4, 133.2, 130.8, 129.8, 129.5, 128.9, 128.5, 127.2, 126.4, 125.8, 125.2, 122.8, 118.1, 17.6, 17.1; IR (KBr) υ 3053, 2922, 2853, 1737, 1649, 1597, 1518, 1497, 1449, 1420, 1375, 1356, 1275, 1246, 1177, 1078, 908, 847, 754 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{22}H_{18}N_2O$ $[M]^+$ 326.1419, found 326.1417.

Experimental procedure and characterization data for the formation of 5b: To an oven-dried sealed tube charged with **3a** (44.4 mg, 0.2 mmol, 100 mol%), iodobenzene (81.6 mg, 0.4 mmol, 200 mol%), $PdCl_2$ (3.5 mg, 0.02 mmol, 10 mol%), 1,10-phenanthroline (3.6 mg, 0.02 mmol, 10 mol%), Ag_2CO_3 (82.7 mg, 0.3 mmol, 150 mol%) and K_3PO_4 (84.9 mg, 0.4 mmol, 200 mol%) was added DMAc (0.8 mL). The reaction mixture was allowed to stir at 165 °C for 12 h, and cooled to room temperature. The reaction mixture was diluted with EtOAc (3 mL) and concentrated in vacuo. The residue was purified by flash column chromatography (*n*-hexanes/EtOAc = 35:1) to afford 43.0 mg of **5b** in 72% yield.

7-Methyl-3-phenyl-2-(*o*-tolyl)-2*H*-indazole (5b): 43.0 mg (72%); dark yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.0 Hz, 1H), 7.38–7.24 (m, 9H), 7.16 (d, *J* = 6.8 Hz, 1H), 7.16 (dd, *J* = 8.2, 7.0 Hz, 1H), 2.71 (s, 3H), 1.95 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.1, 139.5, 136.8, 135.2, 130.9, 129.8, 129.2, 129.0, 128.5, 128.2, 128.0, 127.9, 126.5, 125.7, 122.6, 120.3, 118.0, 17.5, 17.2; IR (KBr) υ 3058, 2917, 2847, 1599, 1504, 1464, 1445, 1377, 1358, 1273, 1243, 1190, 1159, 1101, 1028, 969, 869, 787, 763 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{21}H_{18}N_2$ $[M]^+$ 298.1470, found 298.1468.

Experimental procedure and characterization data for the formation of 5c: To an oven-dried sealed tube charged with **3a** (44.4 mg, 0.2 mmol, 100 mol%), thiophene-2-carbaldehyde (67.3 mg, 0.6 mmol, 300 mol%), $Pd(PPh_3)_4$ (11.6 mg, 0.01 mmol, 5 mol%), $Cu(OAc)_2{\cdot}H_2O$ (50.0 mg, 0.3 mmol, 150 mol%) and pyridine (15.8 mg, 0.2 mmol, 100 mol%) was added 1,4-dioxane (0.5 mL) under N_2 gas at room temperature. The reaction mixture was allowed to stir at 120 °C for 24 h, and cooled to room temperature. The reaction mixture was quenched with saturated aqueous NH_4Cl solution and extracted with EtOAc (30 mL). The organic layer was washed with H_2O and brine, dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by flash column chromatography (*n*-hexanes/EtOAc = 40:1) to afford 48.5 mg of **5c** in 73% yield.

5-(7-Methyl-2-(*o*-tolyl)-2*H*-indazol-3-yl)thiophene-2-carbaldehyde (5c): 48.5 mg (73%); dark yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.84 (s, 1H), 7.84 (d, *J* = 7.2 Hz, 1H), 7.62 (d, *J* = 4.0 Hz, 1H), 7.49 (td, *J* = 6.8, 3.0 Hz, 1H), 7.40–7.36 (m, 3H), 7.24–7.18 (m, 2H), 7.01 (d, *J* = 4.0 Hz, 1H), 2.69 (s, 3H), 1.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.6, 149.2, 143.1, 140.2, 138.9, 136.3, 135.9, 131.4, 130.6, 129.5, 128.7, 128.0, 127.2, 126.6, 126.2, 124.4, 120.7, 117.6, 17.2, 17.1; IR (KBr) υ 3053,

2922, 2854, 2730, 1666, 1497, 1473, 1398, 1359, 1320, 1225, 1212, 1175, 1100, 1064, 934, 868, 807, 753 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{20}H_{16}N_2OS$ $[M]^+$ 332.0983, found 332.0981.

Experimental procedure and characterization data for the formation of 5d: To an oven-dried sealed tube charged with **3a** (44.4 mg, 0.2 mmol, 100 mol%), TEMPO (31.3 mg, 0.2 mmol, 100 mol%) and $Fe(NO_3)_3{\cdot}9H_2O$ (242.4 mg, 0.6 mmol, 300 mol%) was added DCE (2 mL) under O_2 gas at room temperature. The reaction mixture was allowed to stir at 80 °C for 10 h, and cooled to room temperature. The reaction mixture was quenched with saturated aqueous NH_4Cl solution and extracted with EtOAc (50 mL). The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by flash column chromatography (*n*-hexanes/EtOAc = 50:1) to afford 36.9 mg of **5d** in 69% yield.

7-Methyl-3-nitro-2-(*o*-tolyl)-2*H*-indazole (5d): 36.9 mg (69%); yellow solid; mp = 87.3–89.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.4 Hz, 1H), 7.50–7.43 (m, 2H), 7.41–7.37 (m, 2H), 7.31 (d, *J* = 8.0 Hz, 1H), 7.28 (d, *J* = 6.8 Hz, 1H), 2.69 (s, 3H), 2.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.7, 139.2, 134.7, 131.0, 130.2, 129.9, 129.3, 127.5, 126.8, 126.5, 117.8, 117.4, 17.1, 16.4; IR (KBr) υ 3046, 2923, 2854, 1691, 1598, 1504, 1461, 1395, 1321, 1297, 1239, 1150, 1130, 1107, 1041, 970, 872, 808, 787 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{15}H_{13}N_3O_2$ $[M]^+$ 267.1008, found 267.1007.

Kinetic isotope effect (KIE) experiment: A mixture of **1a** (42.1 mg, 0.1 mmol, 50 mol%), **deuterio-1a** (42.5 mg, 0.1 mmol, 50 mol%), $[Cp^*RhCl_2]_2$ (3.1 mg, 0.005 mmol, 2.5 mol%), LiOAc (3.9 mg, 0.06 mmol, 30 mol%), Ag_2CO_3 (16.5 mg, 0.06 mmol, 30 mol%) and $AgSbF_6$ (6.9 mg, 0.02 mmol, 10 mol%) were added paraformaldehyde (**2a**) (30.0 mg, 1.0 mmol, 500 mol%) and DCE (1 mL) under air at room temperature. The reaction mixture was allowed to stir at 120 °C for 10 min, and cooled to room temperature. The reaction mixture was diluted with EtOAc (3 mL) and concentrated in vacuo. The residue was purified by flash column chromatography (*n*-hexanes/EtOAc = 40:1) to afford 10.1 mg of **3a**+**deuterio-3a** in 23% yield. The kinetic isotope effect (k_H/k_D) value was determined to be 2.3 by ^{1}H NMR analysis.

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References

[1] a) J. Elguero In *Comprehensive Heterocyclic Chemistry*, *Vol. 5* (Eds.: A. R. Katrizky, C. W. Rees), Pergamon: New York, **1984**, pp. 167–303; b) H. Cerecetto, A. Gerpe, M. González, V. J. Arán, C. O. de Ocáriz, *Mini-Rev. Med. Chem.* **2005**, *5*, 869; c) J. Magano, M. Waldo, D. Greene, E. Nord, *Org. Process Res. Dev*. **2008**, *12*, 877; d) M. J. Haddadin, W. E. Conrad, M. J. Kurth, *Mini-Rev. Med. Chem.* **2012**, *12*, 1293.

[2] a) C. K. Chung, P. G. Bulger, B. Kosjek, K. M. Belyk, N. Rivera, M. E. Scott, G. R. Humphrey, J. Limanto, D. C. Bachert, K. M. Emerson, *Org. Process Res. Dev.* **2014**, *18*, 215; b) Y. Jia, J. Zhang, J. Feng, F. Xu, H. Pan, W. Xu, *Chem. Biol. Drug Des.* **2014**, *83*, 306; c) M. D. Angelis, F. Stossi, K. A. Carlson, B. S. Katzenellenbogen; J. A. Katzenellenbogen, *J. Med. Chem.* **2005**, *48*, 1132; d) L. A. Clutterbuck, C. G. Posada, C. Visintin, D. R. Riddal, B. Lancaster, P. J. Gane, J. Garthwaite, D. L. Selwood, *J. Med. Chem.* **2009**, *52*, 2694; e) R. Halim, M. Harding, R. Hufton, C. J. Morton, S. Jahangiri, B. R. Pool, T. P. Jeynes, A. G. Draffan, M. J. Lilly, B. Frey, WO 2012051659 A1, 2011; f) W. Aman, J. Lee, M. Kim, S. Yang, H. Jung, J.-M. Hah, *Bioorg. Med. Chem. Lett.* **2016**, *26*, 1188.

[3] a) B. Haag, Z. Peng, P. Knochel, *Org. Lett.* **2009**, *11*, 4270; b) K. Okuro, J. Gurnham, H. Alper, *Tetrahedron Lett.* **2012**, *53*, 620; c) N. Halland, M. Nazaré, O. R'kyek, J. Alonso, M. Urmann, A. Lindenschmidt, *Angew. Chem., Int. Ed.* **2009**, *48*, 6879.

[4] a) B. J. Stokes, C. V. Vogel, L. K. Urnezis, M. Pan, T. G. Driver, *Org. Lett.* **2010**, *12*, 2884; b) J. Hu, Y. Huang, Y. Yang, Y. Rao, *Chem. Commun.* **2011**, *47*, 10133.

[5] a) H. Li, P. Li, L. Wang, *Org. Lett.* **2013**, *15*, 620; b) Y. Lian, R. G. Bergman, L. D. Lavis, J. A. Ellman, *J. Am. Chem. Soc.* **2013**, *135*, 7122; c) J. R. Hummel, J. A. Ellman, *J. Am. Chem. Soc.* **2015**, *137*, 490; d) X. Geng, C. Wang, *Org. Lett.* **2015**, *17*, 2434; e) T. Jeong, S. H. Han, S. Han, S. Sharma, J. Park, J. S. Lee, J. H. Kwak, Y. H. Jung, I. S. Kim, *Org. Lett.* **2016**, *18*, 232; f) S. Cai, S. Lin, X. Yi, C. Xi, *J. Org. Chem.* **2017**, *82*, 512; g) H. Oh, S. Han, A. K. Pandey, S. H. Han, N. K. Mishra, S. Kim, R. Chun, H. S. Kim, J. Park, I. S. Kim, *J. Org. Chem.* **2018**, *83*, 4070; h) Z. Long, Z. Wang, D. Zhou, D. Wan, J. You, *Org. Lett.* **2017**, *19*, 2777; i) Z. Long, Y. Yang, J. You, *Org. Lett.* **2017**, *19*, 2781.

[6] T. N. Ngo, S. A. Ejaz, T. Q. Hung, T. T. Dang, J. Iqbal, J. Lecka, J. Sévigny, P. Langer, *Org. Biomol. Chem.* **2015**, *13*, 8277.

[7] a) G.-F. Zhang, Y. Li, X.-Q. Xie, C.-R. Ding, *Org. Lett.* **2017**, *19*, 1216; b) Y. Wu, B. Zhou, *ACS Catal.* **2017**, *7*, 2213; c) S. H. Lee, T. Jeong, K. Kim, N. Y. Kwon, A. K. Pandey, H. S. Kim, J.-M. Ku, N. K. Mishra, I. S. Kim, *J. Org. Chem.* **2019**, DOI: 10.1021/acs.joc.8b02873.

[8] a) K. Müller, C. Faeh, F. Diederich, *Science* **2007**, *317*, 1881; b) S. Purser, P. R. Moore, S. Swallow, V. Gouverneur, *Chem. Soc. Rev.* **2008**, *37*, 320; c) T. Furuya, A. S. Kamlet, T. Ritter, *Nature* **2011**, *473*, 470; d) D. A. Nagib, D. W. C. MacMillan, *Nature* **2011**, *480*, 224; e) Y. Ji, T. Brueckl, R. D. Baxter, Y. Fujiwara, I. B. Seiple, S. Su, D. G. Blackmond, P. S. Baran, *Proc. Natl. Acad. Sci. U. S. A.* **2011**, *108*, 14411.

10.1002/adsc.201801547

[9] a) G. Bogonda, H. Y. Kim, K. Oh, *Org. Lett.* **2018**, *20*, 2711; b) A. Murugan, K. R. Gorantla, B. S. Mallik, D. S. Sharada, *Org. Biomol. Chem.* **2018**, *16*, 5113.

[10] a) J. Park, E. Park, A. Kim, Y. Lee, K.-W. Chi, J. H. Kwak, Y. H. Jung, I. S. Kim, *Org. Lett.* **2011**, *13*, 4390; b) S. Sharma, E. Park, J. Park, I. S. Kim, *Org. Lett.* **2012**, *14*, 906.

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FULL PAPER

Synthesis of (2*H*)-Indazoles from Azobenzenes Using Paraformaldehyde as One Carbon Synthon

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