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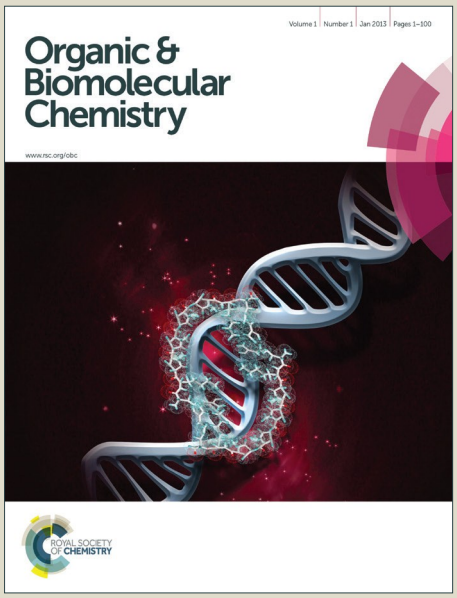

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I_2-mediated 2*H*-indazole synthesis *via* halogen-bond-assisted benzyl C-H functionalization

Xiangli Yi,[a] Lei Jiao[b] and Chanjuan Xi*[a,c]

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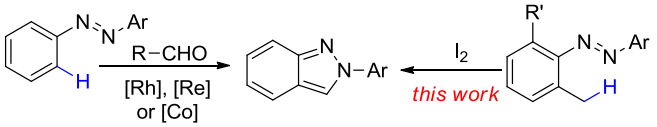
I_2-mediated benzyl C-H functionalization has been developed for synthesis of 2*H*-indazoles, which features high efficiency, simple condition and no need for metals. Mechanistic experiments and DFT calculations have revealed halogen bond assistance and a radical chain process for this reaction. Azo group and the bound iodine cooperate in hydrogen abstraction step, which circumvents the themodynamic disfavor of direct hydrogen abstraction by simple iodine radical.

Introduction

C-H functionalization is a prevalent strategy in organic synthesis because of its atom and step economy. Recently, many metal-catalyzed C-H functionalization reactions have been developed leading to efficient transformations of organic compounds.[1] On the other hand, metal-free C-H functionalization reactions are also very important[2] since they can avoid using costly metals and are more desired in drug processing without removing potentially toxic metals.

2*H*-indazole is the scaffold of many bioactive molecules and is playing an increasingly important role in pharmaceutical research.[3] Over the years, several strategies have been developed for 2*H*-indazole synthesis. Reductive cyclization of *N*-(*o*-nitrobenzylidene)aniline mediated by triethyl phosphite represents one of the first methods to synthesize 2*H*-indazoles.[4] Later, the strategies of metal-catalyzed cyclization,[5] cross coupling[6] and cycloaddition[7] diversified the synthesis of 2*H*-indazoles. More recently, metal-catalyzed C-H functionalization has been introduced to this field, converting azobenzenes (sp^2 C-H activation) to the corresponding 2*H*-indazoles (Scheme 1, left side).[8] Many of these reactions have limitations in terms of complicated procedures, difficult manipulation of reagents or poorly controlled regioselectivity, and most of them require the use of transition-metals. A few reactions of *ortho*-alkylazobenzenes with NBS[9] or base[10] to form 2*H*-indazoles have been reported, which are limited to several particular substrates. Herein, we report an efficient I_2-mediated synthesis of 2*H*-indazole from *ortho*-alkylazobenzene *via* benzyl C-H functionalization (Scheme 1, right side).



Scheme 1 2*H*-indazole synthesis *via* C-H functionalization.

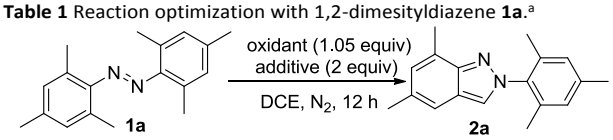
Results and discussion

Initially, 1,2-dimesityldiazene **1a** was found to react with iodine to give 2-mesityl-5,7-dimethyl-2*H*-indazole **2a** in DCE at 120 °C (71% yield, Table 1, entry 1). Then, reaction optimization was carried out by the first changing the oxidant. Iodine monocholoride gave 51% yield (entry 2), while bromine only afforded trace amount of **2a** (entry 3). Two peroxides (^{t}BuO^{t}Bu and ^{t}BuOOBz) were tried and the reaction didn't proceed (entries 4-5). The starting materials remained. Considering the generation of two equivalents of HI which may deteriorate the yield in entry 1, two equivalents of base were added. Addition of NaOAc led to an increase in yield to 93% (entry 6), and $NaHCO_3$ led to a smaller increase (entry 7). Lowering reaction temperature to 110 °C (entry 8) and shortening reaction time to 6 h (entry 9) both resulted in lower yield, 75% and 60%, respectively. To simplify the condition, the reaction was carried out under air instead of N_2, and the yield was not affected (entry 10). Therefore, the optimal condition is shown in entry 10.

[a] Key Laboratory of Bioorganic Phosphorus Chemistry & Chemical Biology (Ministry of Education), Department of Chemistry, Tsinghua University, Beijing 100084, China. E-mail: cjxi@tsinghua.edu.cn.
[b] Center of Basic Molecular Science (CBMS), Department of Chemistry, Tsinghua University, Beijing 100084, China.Address here.
[c] State Key Laboratory of Elemento-Organic Chemistry, Nankai University, Tianjin 300071, China.

† Electronic Supplementary Information (ESI) available: [Experimental procedures, full characterization including ^{1}H NMR and ^{13}C NMR data and spectra for all compounds, mechanistic experiments and computational details]. See DOI: 10.1039/x0xx00000x

Table 1 Reaction optimization with 1,2-dimesityldiazene **1a**.[a]

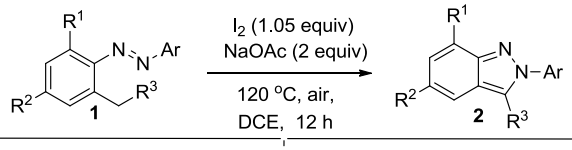


entry	T (°C)	oxidant	additive	yield[b] (%)
1	120	I_2	–	71
2	120	ICl	–	51
3	120	Br_2	–	trace
4	120	^{t}BuOO^{t}Bu	–	trace
5	120	^{t}BuOOBz	–	trace
6	120	I_2	NaOAc	93
7	120	I_2	$NaHCO_3$	85
8	110	I_2	NaOAc	75
9[c]	120	I_2	NaOAc	60
10[d]	120	I_2	NaOAc	92, 85[e]

[a] Reaction condition: 0.2 mmol of **1a**, 0.21 mmol of oxidant, 1 mL of DCE, under N_2 in sealed tube for 12 h. [b] ^{1}H-NMR yield. [c] Reaction time: 6 h. [d] Under air. [e] Isolated yield.

Based on the optimized condition, investigation on substrate scope was conducted (Table 2). Replacing the bulky mesityl with phenyl provided product 5,7-dimethyl-2-phenyl-2*H*-indazole(**2b**) in good yield (87%). Substrates with electron-donating and electron-withdrawing groups both gave excellent yields (92% for **2c** and 91% for **2d**). Altering one *ortho*-methyl in **1b** to other substituents, such as methoxyl-carbonyl, bromo, iodo and phenyl group, resulted in the corresponding products (**2f**, **2g, 2h** and **2i**) in moderate to good yields. In the case of **1g**, bromo group was partially replaced by iodo group (**2g**: **2h**= 1:0.6) in the product. When the other substituent was benzyl or $-CH_2CO_2Et$, the reaction happened completely on methylene instead of methyl (**2j**, 92% yield; **2k** 82% yield). In contrast, when the other substituent is ethyl, the reaction selectivity of methylene over methyl is about 6 times (**2l**, 73% yield; **2l'**, 12%, yield). The selectivity shown in **1j**, **1k** and **1l** suggests that the reaction is possibly a radical process. Interestingly, when mono-*ortho*-substituted azobenzenes **1m** and **1n** were employed as substrates, only trace amount of products were observed on gas chromatography mass spectrometry (GC-MS) and the starting materials remained. It indicates that di-*ortho*-substitution of

Table 2 Substrate scope of stoichiometric I_2 mediated C-H functionalization.[a]



substrates	products	yield[b]	substrates	products	yield[b]
1a	2a	92 (85)	1h	2h	90 (85)
1b	2b	87 (80)	1i	2i	59 (51)
1c	2c	92[c] (85)	1j	2j	92[e] (86)
1d	2d	91[d] (78)	1k	2k	82[e] (72)
1e	2e	85 (80)	1l	2l	73 (66)
1f	2f	43[d] (40)	1l	2l'	12 (10)
1g	2g + 2h	75[d] (70), 1:0.6	1m	2m	trace
			1n	2n	trace

[a] Reaction condition: 0.2 mmol of **1**, 0.21 mmol of I_2, 0.4 mmol of NaOAc, 1 mL of DCE, 120 °C under air in a sealed tube for 12 h. [b] ^{1}H-NMR yields(%) and isolated yields(%, in bracket) [c] Reaction time: 4 h. [d] Reaction time: 24 h. [e] Reaction time: 1 h.

the substrate is necessary for this reaction.

To understand the mechanism of this reaction, detailed investigations were conducted. First, we noticed that one salient difference between I_2 and peroxide as oxidant in this reaction is that I_2 can form halogen bond with nitrogen atom,[11] which might bind I_2 close to *ortho*-methylene and thus the reaction could be promoted. To verify this hypothesis, we first used far-infrared (FIR) spectrometer to prove the existence of halogen bond (Figure 1).[12] Compared with the background (solution of only **1c**), a new absorption peak emerged around 192 cm^{-1} for solution of **1c** and I_2. Generally, Free I_2 does not show FIR absorption, while binding of basic N (sp^2) with I_2 can polarize I-I bond to give FIR signal in the range of 200 - 180 cm^{-1}.[12b] The FIR signal at 192 cm^{-1} clearly shows the halogen bonding between azo group and iodine. Additionally, binding of I_2 with the distal N should be preferred over binding with the nearer N because the distal N is less sterically hindered and more electron-rich.

In order to see the impact of halogen bond on the substrate, ^{1}H NMR spectrum of the solution of **1b** and I_2 was recorded. We noticed that when all other peaks remained unmoved, the peak of hydrogen in *ortho*-methyl group clearly shifted to upfield (Figure 2). The result suggests that, after binding to the azo group, the iodine is situated close to the *ortho*-methyl so that an obvious impact on its' chemical shift can be observed. In the similar experiments of **1c**, **1g**, **1i**, **1m**, and **1n** (Table 3), obvious shift of peak of *ortho*-methyl could be observed in all di-*ortho*-substituted azobenzenes (≥0.01 ppm, **1c**, **1g**, and **1i**), while peak of *ortho*-methyl in **1m** and **1n** remained almost unmoved (about 0.002 ppm). This phenomenon can be rationalized by the conformation distribution analysis: It is known that rotation of C-N bond of azobenzene is flexible in solution,[13] so the two main conformations of adduct (**A** and **B**) form an equilibrium (eq. 1). When R is H, **A** (methyl stays far from bound I_2) will dominate, so the impact of bound I_2 on the ^{1}H NMR signal of *ortho*-methyl is very small. However, when R is larger, the population of B (methyl stays close to bound I_2) will increase due to steric repulsion between R and bound I_2, and thus more obvious peak shift of *ortho*-methyl can be observed.

By comparing the reactivity in Table 2 with ^{1}H NMR shift results (Table 3), we can see that obvious peak shifts promise

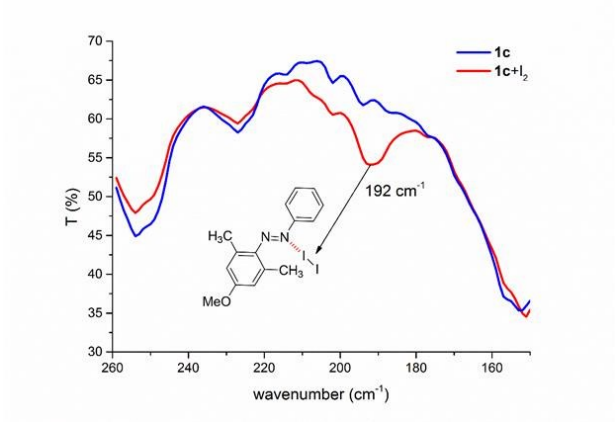


Figure 1 Far infrared spectrum of solution of **1c** and I_2 in cyclohexane.

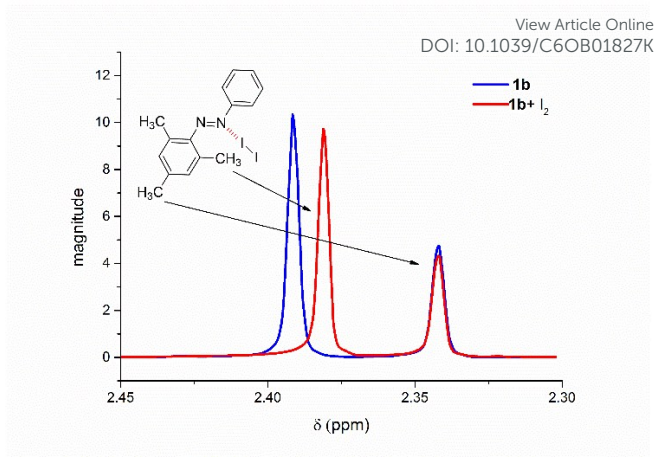
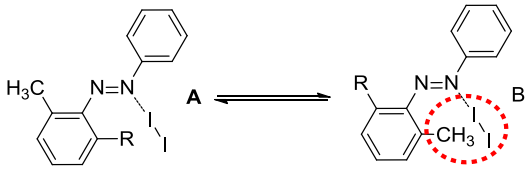


Figure 2 ^{1}H-NMR spectrum of the solution of azobenzene **1b** and I_2 in $CDCl_3$.

Table 3 ^{1}H-NMR peak shift of *ortho*-methyl and corresponding reactivity of azobenzenes.

azobenzenes	1b	1c	1g	1i	1m	1n
upfield shift of *ortho*-methyl hydrogen (ppm)	0.010	0.012	0.010	0.022	0.002	0.002
reactivity	yes	yes	yes	yes	no	no



(1)

good reactivity while unobvious peak shifts mean poor reactivity. In combination with the conformation analysis above, we can conclude that easy formation of conformation **B** where methyl stays close to iodine is crucial for this reaction.

To verify the radical assumption we inferred from the substrate selectivity, substrate 1**o** with two *ortho*-isopropyls was employed to react with iodine under electron paramagnetic resonance (EPR) monitoring. Difficulty in aromatization for 1**o** may enable us to observe the intermediate before aromatization. To our delight, EPR signal emerged after 6 minutes' heating of the reaction mixture in EPR tube, which tremendously strengthened in the following 12 minutes, suggesting the piling up of radical species (Figure 3). The obtained signal at 18 min was well simulated mainly considering the coupling of the two N (nuclear spin= 1) and one H (nuclear spin= 1/2) with the single electron (Figure 4) and thus is consistent with the assumed radical structure (**3o**, Figure 3). Notably, the EPR experiment was conducted in darkness, so the radical should be generated in thermal induced way.

Based on the above results and further DFT calculation[14] for model substrate **1e**, a plausible radical chain mechanism is proposed in Scheme 2. First, azo substrate **1** associates with I_2 to form **4**, which is exergonic by 2.9 kcal/mol. Then, the radical chain reaction starts *via* assisted homolysis of I-I bond in **4** (by iodine radical) to afford bound radical **5**, which could be

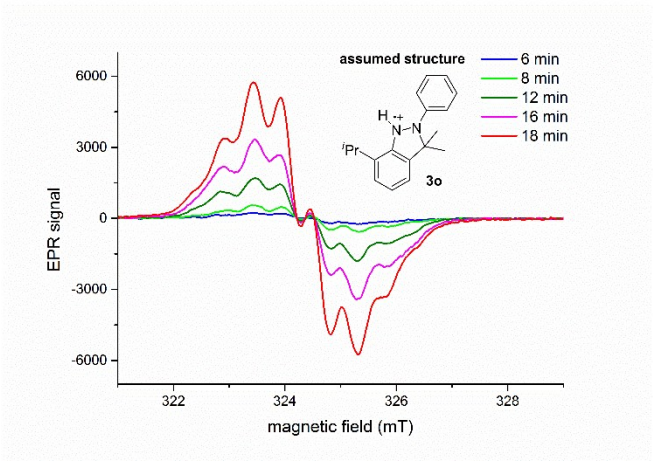


Figure 3 EPR monitoring of reaction of **1o** and I_2 in p-xylene at 120 °C.

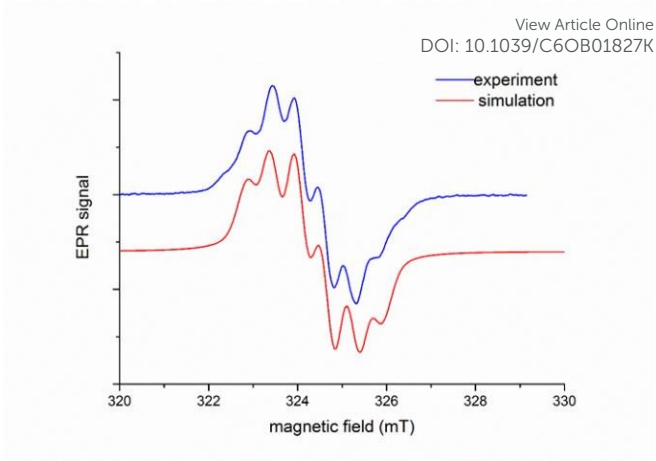
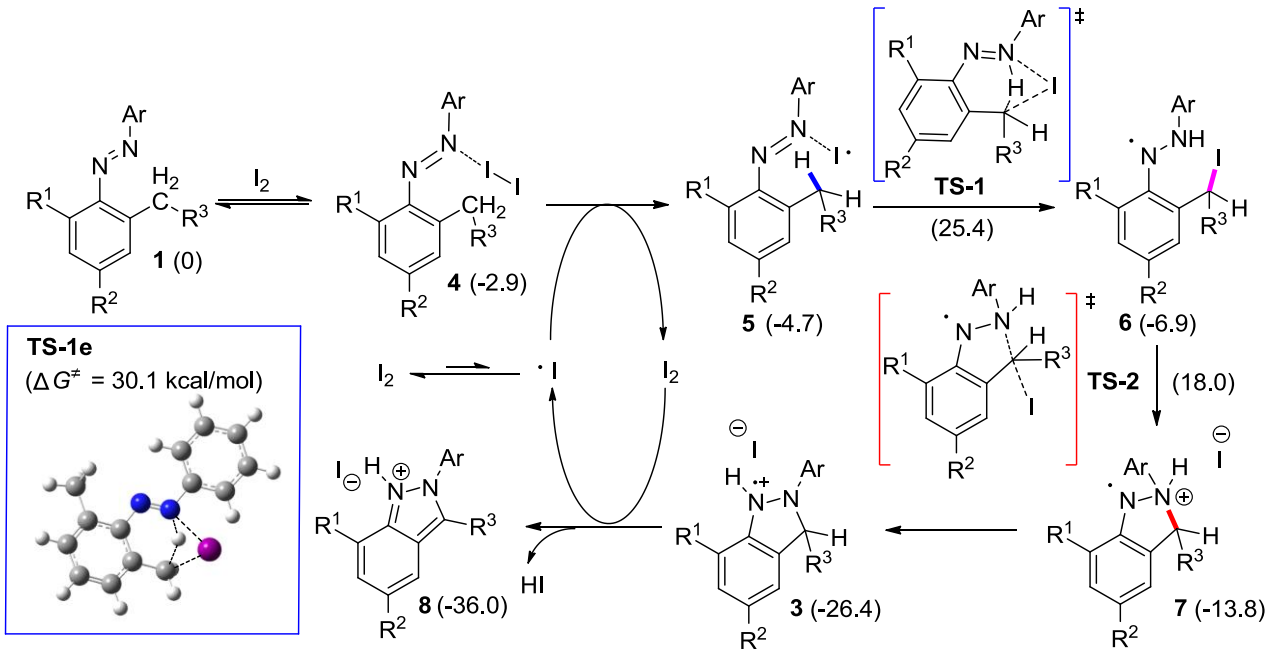


Figure 4 Simulation of EPR signal obtained in reaction of **1o**.

regarded as a complex of **1** with iodine radical. Subsequently, an iodine-assisted hydrogen transfer from the benzylic position to nitrogen *via* **TS-1** leads to intermediate **6** with an activation free energy barrier of 30.1 kcal/mol. Notably, unlike C-H hydrogen abstraction by bromine radical,[9] direct C-H hydrogen abstraction by iodine radical is very disfavoured in thermodynamics (ΔH=20-33 kcal/mol)[15] and thus is considered not feasible in this reaction. Intermediate **6** then undergoes intramolecular cyclization to afford N-centered radical species **7** *via* **TS-2** ($\Delta G_{sol}^{\neq}$ = 24.9 kcal/mol), which is later converted to a more stable intermediate **3** *via* proton transfer. Finally, abstraction of a second benzylic hydrogen by I_2 furnishes the protonated product **8** and concomitantly regenerates iodine radical. The overall activation free energy of this process is around 30 kcal/mol, which is consistent with the reaction conditions (120 °C, 12 h). A primary kinetic isotope effect (KIE) of 9.0 was observed for the deuterated substrates **1b**-d_3 (Figure S1), which is consistent with the key C-H cleavage step.

Conclusions

We have presented an efficient synthesis of 2*H*-indazoles *via* benzyl C-H functionalization without assistance of metals. Representative substrates were examined, which proved the reaction to be suitable for both electron-rich and - deficient substrates and tolerate various functional groups. Mechanistic studies show that the ease of combining I_2 close to C-H of *ortho*-alkyl is very important for this conversion. EPR and DFT studies have rationalized a radical chain mechanism. Notably, simple iodine radical has been reported to be unreactive for alkanyl C-H (including benzyl C-H) hydrogen abstraction because of thermodynamically disfavor.[15] However, bound iodine radical successfully realized benzyl C-H functionalization with the assistance of azo group in this reaction.



Scheme 2 Proposed mechanism for I_2-mediated selective benzyl C-H functionalization and DFT computational for the reaction of **1e**. The Gibbs free energies in solution (ΔG_{sol}, in kcal/mol) are given in parentheses.

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Experimental Section

General procedure for azobenzene synthesis (GP1)[16]

2.2 mmol of aniline was added into a solution of nitroso-benzene (2.0 mmol) in 20 mL acetic acid. The reaction mixture was stirred at 30 °C in darkness for 2 days. After the reaction completion, the mixture was diluted with 20 mL water and extracted 3 time with 20 mL petroleum ether (PE). The organic phase was combined, washed with $NaHCO_3$ solution, dried and evaporated. The obtained residual was eluted over silica gel column with PE-dichloromathane (DCM) to give the corresponding azobenzenes. The characterization data for azobenzenes are displayed in ESI.

General procedure for 2*H*-indazole synthesis (GP2)

A seal tube was charged with 0.2 mmol of azobenzene, 0.4 mmol of NaOAc (32.8 mg), 0.21 mmol of I_2 (54 mg), 1 mL DCE and then moved into an oil bath which was preheated to 120 °C. After 12 h, the reaction was cooled to room temperature and quenched with 1 mL of saturated $NaHCO_3$ solution and 3 drops of saturated $Na_2S_2O_3$ solution. Then, the mixture was extracted with ethyl acetate (EA) and the obtained organic phase was dried and evaporated. The residual was eluted over Silica gel column with PE-EA to give the corresponding 2*H*-indazoles.

***2-Mesityl-5,7-dimethyl-2H-indazole* (2a):** Synthesized *via* GP2; white solid (44.9 mg, 85% isolated yield); Rf: 0.42 (PE: EA=10:1); M.p. 114-116 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (s, 1H), 7.34 (s, 1H), 6.98 (s, 2H), 6.97 (s, 1H), 2.65 (s, 3H), 2.43 (s, 3H), 2.36 (s, 3H), 1.97 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.6, 139.2, 137.7, 135.5, 131.6, 128.9, 128.2, 127.9, 124.0, 122.0, 115.9, 21.9, 21.2, 17.4, 17.3; GC-MS: 264; HRMS (ESI positive mode) calcd for $C_{18}H_{20}N_2$+H^+ 265.1699, found 265.1700.

***5,7-Dimethyl-2-phenyl-2H-indazole* (2b):** Synthesized *via* GP2; white solid (35.5 mg, 80% isolated yield); Rf: 0.51 (PE: EA=10:1); M.p. 62-64 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (s, 1H), 7.91 (d, *J* = 7.5 Hz, 2H), 7.52 (t, *J* = 7.9 Hz, 2H), 7.38 (t, *J* = 7.4 Hz, 1H), 7.28 (s, 1H), 6.95 (s, 1H), 2.68 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.3, 140.9, 132.2, 129.6, 128.9, 127.8, 127.6, 123.0, 121.1, 119.8, 115.8, 21.9, 17.2; GC-MS: 222; HRMS (ESI positive mode) calcd for $C_{15}H_{14}N_2$+H^+ 223.1230, found 223.1232.

***5-Methoxy-7-methyl-2-phenyl-2H-indazole* (2c):** Synthesized *via* modified GP2 (4 h); white solid (40.4 mg, 85% isolated yield); Rf: 0.36 (PE: EA=10:1); M.p. 100-101 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.24 (s, 1H), 7.91 – 7.86 (m, 2H), 7.54 – 7.48 (m, 2H), 7.39 – 7.34 (m, 1H), 6.82 – 6.79 (m, 1H), 6.74 (d, *J* = 2.2 Hz, 1H), 3.84 (s, 3H), 2.64 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.8, 147.4, 140.9, 129.9, 129.6, 127.6, 122.6, 120.9, 120.8, 119.7, 93.8, 55.4, 17.1; GC-MS: 238; HRMS (ESI positive mode) calcd for $C_{15}H_{14}N_2O$+H^+ 239.1178, found 239.1179.

***7-Methyl-2-phenyl-2H-indazole-5-carbonitrile* (2d):** Synthesized *via* modified GP2 (24 h); white crystal (36.3 mg, 78% isolated yield); Rf: 0.15 (PE: EA=10:1); M.p. 181-183 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.51 (s, 1H), 8.01 (s, 1H), 7.91 (d, *J* = 7.7 Hz, 2H), 7.56 (t, *J* = 7.9 Hz, 2H), 7.45 (t, *J* = 7.4 Hz, 1H), 7.18 (s, 1H), 2.68 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.2, 140.1, 130.3, 129.9, 128.8, 126.1, 125.8, 122.6, 121.5, 121.4, 120.1, 106.1, 17.0; GC-MS: 233; HRMS (ESI positive mode) calcd for $C_{15}H_{11}N_3$+H^+ 234.1026, found 234.1027.

***7-Methyl-2-phenyl-2H-indazole* (2e):** Synthesized *via* GP2; colorless oil (33.3 mg, 80% isolated yield); Rf: 0.51 (PE: EA=10:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.38 (s, 1H), 7.95 – 7.90 (m, 2H), 7.58 – 7.50 (m, 3H), 7.44 – 7.37 (m, 1H), 7.12 – 7.07 (m, 1H), 7.04 (dd, *J* = 8.2, 6.7 Hz, 1H), 2.71 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.3, 140.8, 129.7, 128.2, 127.9, 125.8, 122.9, 122.7, 121.3, 120.9, 117.9, 17.3; GC-MS: 208; HRMS (ESI positive mode) calcd for $C_{14}H_{12}N_2$+H^+ 209.2659, found 209.2661.

***Methyl 5-methyl-2-phenyl-2H-indazole-7-carboxylate* (2f):** Synthesized *via* modified GP2 (24 h); white crystal (21.3 mg, 40% isolated yield); Rf: 0.51 (PE: EA=4:1); M.p. 109-111 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.41 (s, 1H), 7.99 (d, *J* = 1.6 Hz, 1H), 7.97 – 7.93 (m, 2H), 7.69 – 7.66 (m, 1H), 7.54 – 7.47 (m, 2H), 7.42 – 7.36 (m, 1H), 4.04 (s, 3H), 2.46 (d, *J* = 0.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.8, 146.0, 140.5, 134.6, 131.1, 129.6, 128.2, 124.9, 124.6, 121.2, 120.5, 119.4, 52.4, 21.5; GC-MS: 266; HRMS (ESI positive mode) calcd for $C_{16}H_{14}N_2O_2$+H^+ 267.1128, found 267.1129.

***7-Bromo-5-methyl-2-phenyl-2H-indazole* (2g) and *7-iodo-5-methyl-2-phenyl-2H-indazole* (2h):** Synthesized using **1g** *via* modified GP2 (24 h); white crystal (42.7 mg, 70% isolated yield, **2g**: **2h**= 1:0.61); Rf: 0.41(PE: EA=10:1); HRMS (ESI positive mode) calcd for $C_{14}H_{11}N_2Br$+H^+ 287.1078, found 287.1075; HRMS (ESI positive mode) calcd for $C_{14}H_{11}N_2I$+H^+ 335.0040, found 335.0039.

***7-Iodo-5-methyl-2-phenyl-2H-indazole* (2h):** Synthesized *via* GP2; white solid (56.4 mg, 85% isolated yield); M.p. 108-110 °C; Rf: 0.41 (PE: EA=10:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.41 (d, *J* = 6.7 Hz, 1H), 7.93 – 7.87 (m, 2H), 7.66 (s, 1H), 7.54 – 7.48 (m, 2H), 7.42 – 7.36 (m, 2H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.7, 140.4, 139.4, 133.4, 129.6, 128.2, 122.3, 121.2, 121.2, 119.0, 83.9, 21.4; GC-MS: 334; HRMS (ESI positive mode) calcd for $C_{14}H_{11}IN_2$+H^+ 335.0040, found 335.0039.

***5-Methyl-2,7-diphenyl-2H-indazole* (2i):** Synthesized *via* GP2; colorless oil (29.0 mg, 51% isolated yield); Rf: 0.52 (PE: EA=10:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.37 (s, 1H), 8.17 – 8.13 (m, 2H), 7.97 – 7.93 (m, 2H), 7.55 – 7.49 (m, 4H), 7.45 – 7.34 (m, 4H), 2.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.2, 140.8, 138.3, 132.3, 130.6, 129.6, 129.0, 128.5, 128.4, 127.7, 127.6, 124.3, 120.9, 119.5, 117.9, 22.0; GC-MS: 284; HRMS (ESI positive mode) calcd for $C_{20}H_{16}N_2$+H^+ 285.1386, found 285.1384.

***5,7-Dimethyl-2,3-diphenyl-2H-indazole* (2j):** Synthesized *via* modified GP2 (1 h); colorless crystal (51.5 mg, 86% isolated yield); Rf: 0.44 (PE: EA=10:1); M.p. 120-122 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 – 7.44 (m, 2H), 7.42 – 7.30 (m, 9H), 7.01 (s, 1H), 2.70 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.4, 140.5, 134.9, 132.4, 130.4, 129.8, 129.8, 129.1, 128.8, 128.2, 128.1, 127.6, 126.3, 121.9, 116.0, 22.0, 17.2; GC-MS: 298; HRMS (ESI positive mode) calcd for $C_{21}H_{18}N_2$+H^+ 299.1543, found 299.1541.

***Ethyl 5,7-dimethyl-2-phenyl-2H-indazole-3-carboxylate* (2k):** Synthesized *via* modified GP2 (1 h); colorless crystal (42.4 mg, 72% isolated yield); Rf: 0.34 (PE: EA=10:1); M.p. 122-124 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (s, 1H), 7.51 (s, 5H), 7.02 (s, 1H), 4.34 (q, *J* = 7.1 Hz, 2H), 2.65 (s, 3H), 2.48 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.9, 147.9, 141.4, 135.9, 129.3, 129.2, 128.7, 128.5, 126.6, 124.6, 124.5, 117.2,

61.0, 22.3, 17.0, 14.3; GC-MS: 294; HRMS (ESI positive mode) calcd for $C_{18}H_{18}N_2O_2+H^+$ 295.1441, found 295.1440.

***3,7-Dimethyl-2-phenyl-2H-indazole* (2l):** Synthesized *via* GP2, separated from its mixture with **2l'**; yellowish oil (29.2 mg, 66% isolated yield); Rf: 0.26 (PE: EA=10:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 – 7.52 (m, 4H), 7.50 – 7.46 (m, 2H), 7.12 – 7.08 (m, 1H), 7.01 (dd, *J* = 8.4, 6.7 Hz, 1H), 2.67 (s, 1H), 2.63 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.0, 140.2, 132.3, 129.3, 128.7, 127.7, 126.1, 125.8, 121.4, 121.3, 117.5, 17.3, 11.3; GC-MS: 222; HRMS (ESI positive mode) calcd for $C_{15}H_{14}N_2+H^+$ 223.1230, found 223.1231.

***7-Ethyl-2-phenyl-2H-indazole* (2l'):** Synthesized *via* GP2, separated from its mixture with **2l**; yellowish oil (4.4 mg, 10% isolated yield); Rf: 0.48 (PE: EA=10:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.39 (s, 1H), 7.92 (d, *J* = 7.7 Hz, 2H), 7.58 – 7.50 (m, 3H), 7.40 (t, *J* = 6.9 Hz, 1H), 7.13 – 7.03 (m, 2H), 3.14 (q, *J* = 7.5 Hz, 2H), 1.46 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.6, 140.9, 134.3, 129.7, 127.9, 123.7, 122.9, 121.3, 120.7, 117.9, 24.5, 14.0; GC-MS: 222; HRMS (ESI positive mode) calcd for $C_{15}H_{14}N_2+H^+$ 223.1230, found 223.1231.

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