RSC Advances

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Cite this: *RSC Adv.*, 2021, **11**, 14178

# Oxidative cross-dehydrogenative coupling (CDC) *via* $C_{(sp^2)}$–H bond functionalization: *tert*-butyl peroxybenzoate (TBPB)-promoted regioselective direct C-3 acylation/benzoylation of 2*H*-indazoles with aldehydes/benzyl alcohols/styrenes†

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Received 20th March 2021
Accepted 26th March 2021

DOI: 10.1039/d1ra02225c

rsc.li/rsc-advances

An efficient, cost-effective, transition-metal-free, oxidative $C_{(sp^2)}$–H/$C_{(sp^2)}$–H cross-dehydrogenative coupling *via* a $C_{(sp^2)}$–H bond functionalization protocol for the regioselective direct C-3 acylation/benzoylation of substituted 2*H*-Indazoles **1a–m** with substituted aldehydes **2a–q**/benzyl alcohols **5a–e**/styrenes **6a–e** is reported. The operationally simple protocol proceeds in the presence of *tert*-butyl peroxybenzoate (TBPB) as an oxidant in chlorobenzene (PhCl) as a solvent at 110 °C for 24 h under an inert atmosphere, which furnished a diverse variety of substituted 3-(acyl/benzoyl)-2*H*-indazoles **3a–q**/**4a–l** in up to 87% yields. The reaction involves a free-radical mechanism and proceeds *via* the addition of an *in situ* generated acyl radical (from aldehydes/benzyl alcohols/styrenes) on 2*H*-indazoles. The functional group tolerance, broad substrate scope, control/competitive experiments and gram-scale synthesis and its application to the synthesis of anti-inflammatory agent 11 and novel indazole-fused diazepine 13 further signify the versatile nature of the developed methodology.



## Introduction

During the last two decades, oxidative cross-dehydrogenative coupling, often abbreviated to "oxidative CDC reaction", between two C–H bonds has been recognized as a greener fundamental synthetic approach in C–C bond forming reactions due to its association with several advantages such as being metal-free, high yields, cost effectiveness, operational simplicity, high selectivity, step-/atom-economy, product selectivity, no pre-functionalization of starting materials, reduced waste, energy and resource competence, *etc.*[1] Indazoles are renowned bioactive heterocyclic scaffolds which are found abundantly in several pharmaceutically privileged bioactive natural products/therapeutics/drugs molecules[2] and are bestowed with a wide array of biological activities such as antimicrobial, anticancer, antitumor, HIV-protease inhibition, antiplatelet, anti-depressant, and anti-inflammatory actions.[3]

Indazole functionalization has achieved emerging demand in the fields of organic and medicinal chemistry as the functionalization of indazoles can be rendered into advantageous structural motifs for various medications.[4] Therefore, the development of a new synthetic pathway to introduce various functional groups on 2*H*-indazoles leading to an increase in the molecular abundance and the formation of new bioactive molecules, will always be of the utmost importance to medicinal chemistry and drug discovery.

In particular, acylated 2*H*-indazoles have received tremendous attention as a pharmaceutically important class of structural motifs in a large number of bioactive skeletons/therapeutic molecules. Noticeably, C3-acylated-(2*H*)-indazoles **I–V** are endowed with several biological activities, such as antiemetic and anti-inflammatory properties (Fig. 1).[5] Therefore, the development of a direct synthetic strategy *via* an oxidative cross-dehydrogenative coupling pathway for the C-3 acylation of 2*H*-indazoles is a highly desirable and challenging area of investigation. It becomes more appealing if it proceeds through a transition-metal-free approach. A few transition-metal-catalyzed (Ag, Ni) synthetic approaches *via* $C_{(sp^2)}$–H bond activation/functionalization have been reported for the direct, regioselective, C-3 acylation of (2*H*)-indazoles with either Ag-catalyzed decarboxylative cross-coupling of α-keto acids[6] or with an Ni-catalyzed reaction on substituted aldehydes[7] and with an Ag-catalyzed reaction with substituted Hantzsch esters as acyl radical sources[8] (Scheme 1). However, these strategies are associated with several drawbacks such as the use of costly metals, the use of additives/ligands, and limited substrate scope. In addition, the separate synthesis of

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† Electronic supplementary information (ESI) available: Characterization data, $^1$H NMR and $^{13}$C NMR spectra. See DOI: 10.1039/d1ra02225c

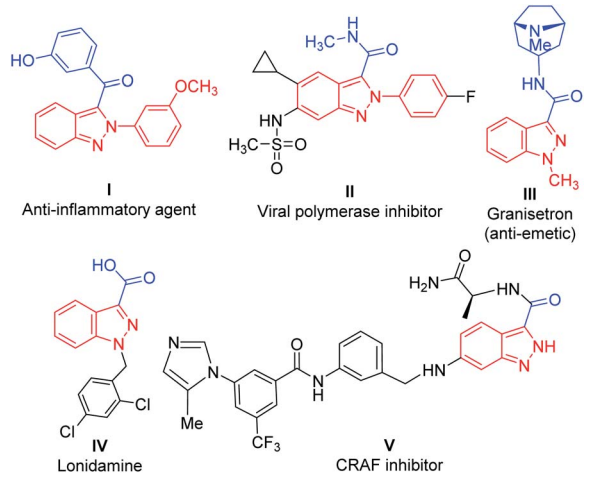
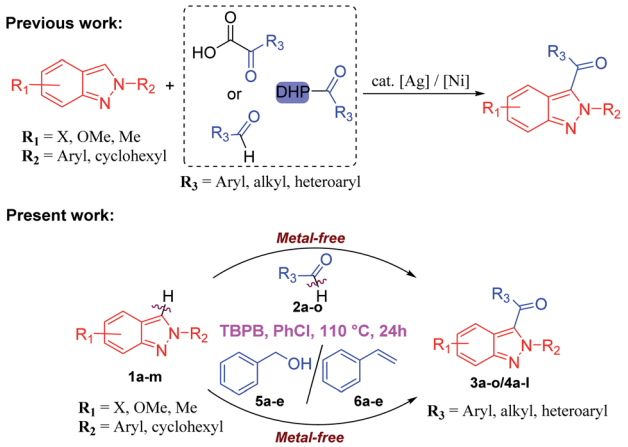



Fig. 1 Representative examples of various bioactive molecules/drugs/therapeutics with a 2*H*-indazole moiety.




Scheme 1 Previous methodologies and present work: TBPB-promoted approach to regioselective direct C-3 acylation/benzoylation of 2-aryl-2*H*-indazoles with substituted aldehydes/benzyl alcohols/styrenes.

an acylation/benzoylation source further amplifies its limitations and increases the tediousness of these methodologies. However, there has been no report of the direct C-3 acylation of 2-aryl-2*H*-indazoles with metal-free and ligand-/additive-free catalysis.

Herein, we report a cost-effective, highly efficient, *tert*-butyl peroxybenzoate (TBPB)-promoted, regioselective, direct C-3 acylation/benzoylation of 2-aryl-2*H*-indazoles **1a–m** with different aldehydes **2a–q**/benzyl alcohols **5a–e**/styrenes **6a–e** *via* $C_{(sp^2)}$–H/$C_{(sp^2)}$–H cross-dehydrogenative coupling at 110 °C for 24 h under $N_2$ atmosphere which furnished 3-(acylated/benzoylated)-2-aryl-2*H*–indazoles **3a–q**/**4a–l** in excellent (87%) yields, with a broad range of functional group tolerances and varied substrate compatibilities [Scheme 1]. Succinctly, this is the first detailed investigation of an oxidant-promoted $C_{(sp^2)}$–H/$C_{(sp^2)}$–H cross-dehydrogenative coupling method for the regioselective direct C-3 acylation/benzoylation of 2-aryl-2*H*-indazoles.

## Results and discussion

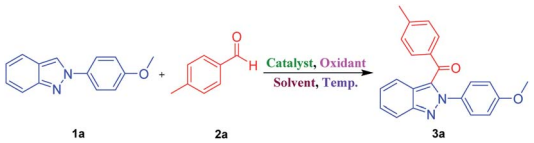
We initiated our optimization study by investigating direct $C_{(sp^2)}$–$C_{(sp^2)}$ coupling by taking 2-(4-methoxyphenyl)-2*H*-indazole **1a** and 4-methylbenzaldehyde **2a** as the starting substrate (Table 1).

It has been noted that TBHP, either alone or in combination, has been utilized in several oxidative cross-dehydrogenative coupling reactions;[9] we had chosen *tert*-butyl hydroperoxide (TBHP) as an oxidant and *N*-chlorosuccinimide (NCS) as a catalyst for the beginning of our study. Therefore, using the procedure in the literature,[9f] we carried out a reaction of **1a** with **2a** in the presence of TBHP (0.53 mmol, 4 equiv.) and NCS (30 mol%) in dichloroethane (DCE) at 110 °C for 24 h under an inert atmosphere. However, the desired product **3a** was not found at all and several spots appeared on TLC (Table 1, entry 1). Then, keeping all other reaction parameters the same, we carried out the same reaction as shown in entry no. 1 with reduced equivalents of both TBHP and NCS catalyst. Intriguingly, **3a** was obtained, albeit in low (30%) yield (Table 1, entry 2). Subsequently, we examined the screening of some other well-known reagents which had previously been utilized extensively in CDC reactions (Table 1, entries 3–7). While the reaction performed in TFA furnished **3a** in 40% yield, iodine-based catalysts were found ineffective in improving the yield of the reaction. Furthermore, keeping all the reaction conditions the same, the reaction was performed without a catalyst, which furnished **3a** in 65% yield (Table 1, entry 8). This observation instructed us to stop further use of any additives as a catalyst. However, the reaction performed with less equivalents of **2a** (1 equiv.) drastically reduced the yield of **3a** (Table 1, entry 9). It has been reported in the literature that chlorobenzene has been utilized as an effective solvent for cross-dehydrogenative coupling reactions.[10] Therefore, we conducted the same reaction in chlorobenzene instead of DCE and **3a** was obtained in 68% yield (Table 1, entry 10).

Then, we carried out the screening of several organic as well as inorganic oxidants, such as di-*tert*-butyl peroxide (DTBP), *tert*-butyl peroxybenzoate (TBPB), dicumyl peroxide (DCP), lauroyl peroxide, $H_2O_2$, cumene hydroperoxide, $K_2S_2O_8$, oxone, $(NH_4)_2S_2O_8$, (diacetoxyiodo)benzene (PIDA), and oxygen gas, while keeping all the other reaction parameters the same (Table 1, entries 11–21). It was found that while DTBP, TBPB and DCP furnished **3a** in 70%, 82% and 51% yields, respectively; the reaction performed using lauroyl peroxide gave **3a** in only 18% yield (Table 1, entries 11–14). The rest of the oxidants either did not furnish **3a** at all or afforded **3a** in only trace amounts (Table 1, entries 15–21).

Sequentially, the screening of several polar/non-polar solvents was also carried out (Table 1, entries 22–30). It should be noted that none of the solvents were found to be effective except for chlorobenzene. Afterwards, keeping all reaction parameters the same, the effect of variation in temperature and time was studied. It was observed that increasing or decreasing the temperature and time did not have a beneficial effect on the yield of the reaction (Table 1, entries

Table 1 Optimization study[a]

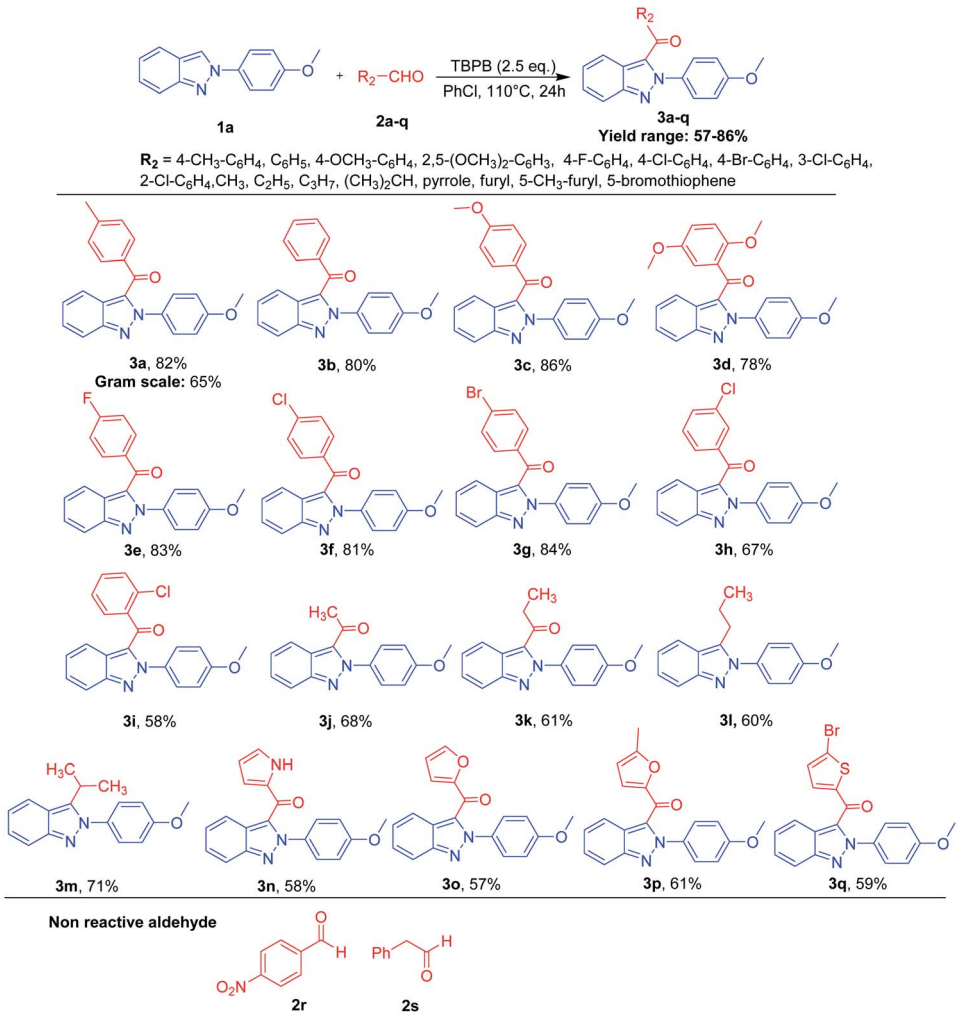



| S. no. | Oxidant (2.5 equiv.) | Catalyst (20 mol%) | Solvent | Temp. (°C) | Yield (%) |
|---|---|---|---|---|---|
| 1 | TBHP[b] | NCS | DCE | 110 | NR[c] |
| 2 | TBHP | NCS | DCE | 110 | 30 |
| 3 | TBHP | TFA | DCE | 110 | 40[d] |
| 4 | TBHP | TBAI | DCE | 110 | NR |
| 5 | TBHP | NaI | — | 110 | NR |
| 6 | TBHP | KI | DCE | 110 | NR |
| 7 | TBHP | $I_2$ | DCE | 110 | NR |
| 8 | TBHP | — | DCE | 110 | 65 |
| 9 | TBHP | — | DCE | 110 | 10[e] |
| 10 | TBHP | — | PhCl | 110 | 68 |
| 11 | DTBP | — | PhCl | 110 | 70 |
| **12** | **TBPB** | **—** | **PhCl** | **110** | **82** |
| 13 | DCP | — | PhCl | 110 | 51 |
| 14 | Lauroyl peroxide | — | PhCl | 110 | 18 |
| 15 | $H_2O_2$ | — | PhCl | 110 | NR |
| 16 | Cumene hydroperoxide | — | PhCl | 110 | Trace |
| 17 | $K_2S_2O_8$ | — | PhCl | 110 | NR |
| 18 | Oxone | — | PhCl | 110 | NR |
| 19 | $(NH_4)_2S_2O_8$ | — | PhCl | 110 | NR |
| 20 | PIDA | — | PhCl | 110 | Trace |
| 21 | $O_2$ | — | PhCl | 110 | NR |
| 22 | TBPB | — | ACN | 110 | 71 |
| 23 | TBPB | — | Toluene | 110 | 70 |
| 24 | TBPB | — | DMSO | 110 | 18 |
| 25 | TBPB | — | Dioxane | 110 | 15 |
| 26 | TBPB | — | DMF | 110 | Trace |
| 27 | TBPB | — | THF | 110 | Trace |
| 28 | TBPB | — | $H_2O$ | 110 | Trace |
| 29 | TBPB | — | AcOH | 110 | Trace |
| 30 | TBHP | — | TFA | 110 | NR |
| 31 | TBPB | — | PhCl | 80 | 72 |
| 32 | TBPB | — | PhCl | 140 | 68 |
| 33 | TBPB | — | PhCl | 110 | 71[f] |

[a] Reaction conditions: 2-(4-methoxyphenyl)-2*H*-indazole **1a** (0.13 mmol), 4-methyl benzaldehyde **2a** (0.27 mmol), oxidant (0.33 mmol), catalyst (20 mol%), $N_2$ atm, 110 °C, 24 h. [b] For details, see ref. 9*f*. [c] TBHP (0.53 mmol) and NCS (30 mol%) were used. [d] TFA (0.6 equiv.) was used. [e] **2a** (1 equiv.) was used. [f] Reaction was allowed to run for 16 h.

31–33). Thus, overall, *2 equivalents of substituted aldehydes, 2.5 equivalents of tert-butyl peroxybenzoate (TBPB) dissolved in chlorobenzene as solvent at 110 °C for 24 h under $N_2$ atmosphere* were found to be the best optimization reaction conditions for the direct C-3 acylation/benzoylation of 2-aryl-2*H*-indazoles *via* a $C_{(sp^2)}$–H/$C_{(sp^2)}$–H cross-dehydrogenative coupling methodology.

Taking 2-(4-methoxyphenyl)-2*H*-indazole **1a** as a starting substrate, several substituted aromatic/aliphatic/heteroaromatic aldehydes **2a–q** were reacted under the optimized reaction conditions, which furnished substituted 3-(acylated/benzoylated)-2-(4-methoxyphenyl)-2*H*-indazoles **3a–q** in 57–86% yield (Scheme 2). Like **3a**, **1a** was reacted with benzaldehyde **2b** under the optimized reaction conditions and furnished **3b** in 80% yield. It has been noted that aromatic aldehydes with electron-donating groups (EDGs) at the *p*-position were found to be well-tolerated and afforded the corresponding C-3 benzoylated-2*H*-indazoles **3a** and **3c** in 82% and 86% yields, respectively. However, aromatic aldehyde **2d** with two EDG (*i.e.*, $OCH_3$) groups was subjected to reaction with **1a** under the optimized conditions; **3d** was afforded in slightly lower (78%) yield compared to **3a** and **3c**. This could be due to the steric hindrance created by the $OCH_3$ group at the *o*-position to the aldehydic functionality. In the case of aromatic aldehydes containing a halo (X = F, Cl, Br) group at the *para*-position, the reaction of **1a** with **2e–g** under optimized conditions furnished **3e–g** in 81–84% yield. However, keeping all the reaction conditions the same, a decrease in the reactivity of aromatic aldehydes containing halo groups at the *meta*-/*ortho*-positions, was observed and **3h** and **3i** were obtained in 67% and 58% yields, respectively. In addition, the aromatic aldehyde containing an electron-withdrawing group (EWG) **2p** was found to



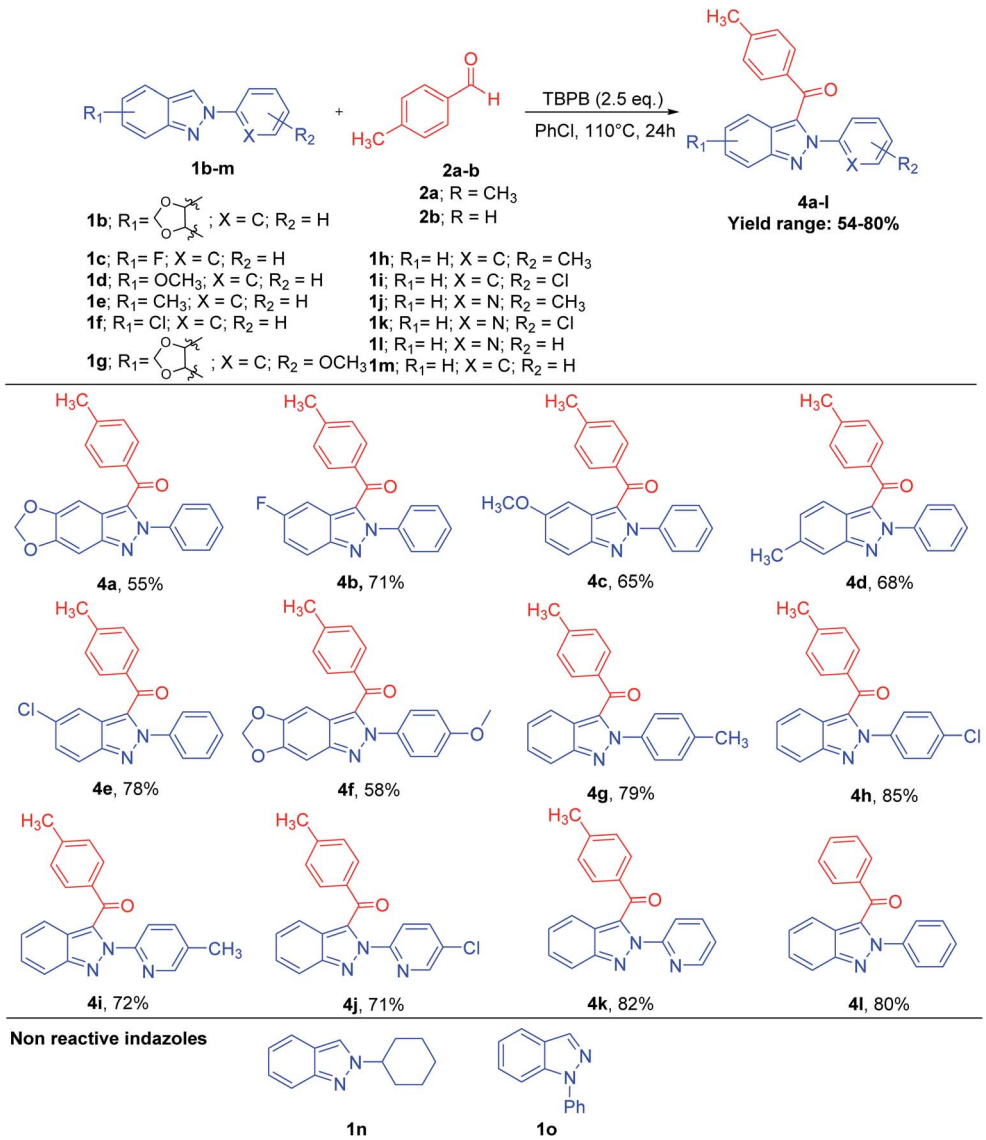

Scheme 2 Substrate scope: reaction of 2-(4-methoxyphenyl)-2*H*-indazole **1a** with various aldehydes **2a–q** for the synthesis of substituted 3-acylated 2-(4-methoxyphenyl)-2*H*-indazoles **3a–q**[a,b]. [a]Reaction conditions: 2-(4-methoxyphenyl)-2*H*-indazole **1a** (0.5 mmol), substituted aldehydes **2a–q** (1.0 mmol), oxidant (1.25 mmol), PhCl, $N_2$ atm, 110 °C, 24 h. [b]Isolated yield.

be totally reluctant to undergo the optimized reaction conditions. Similarly, phenyl acetaldehyde **2q** was also found to be unreactive. Furthermore, in order to check the versatility of the methodology, a few aliphatic aldehydes **2j–k** were reacted with **1a** under the optimized reaction conditions and afforded **3j** and **3k** in 68% and 61% yields, respectively. Comparing aromatic aldehydes with aliphatic aldehydes, the latter were found to be less reactive than the former. A different observation was noticed in the current protocol when the number of carbon atoms increased to four (unbranched and/or branched) in the aldehydes.[7] Compounds **2l–m** on reaction with **1a** under the optimized reaction conditions did not furnish C-3 acylated 2*H*-indazoles but incorporated the corresponding alkyl group of the **2l** and **2m** *via* decarbonylation and furnished **3l** and **3m** in 60% and 71% yields, respectively. We could speculate on the stability of the corresponding generated free-radicals on treatment with TBPB based on the greater +I effect of the propyl group (generated after decarbonylation of *n*-butyraldehyde) compared to the +I effect of the ethyl group (generated after decarbonylation of *n*-propionaldehyde). This could lead to the formation of unprecedented **3l** from **2l** in 60% yield. Furthermore, the instability of the acyl radical formed from **2m** on treatment with TBPB can be understood by the formation of a more stable secondary free-radical of isobutyraldehyde (generated after decarbonylation of *n*-isobutyraldehyde).[6,7] Later on, the generated alkyl free-radical attacks at the C-3 position of 2-aryl-2*H*-indazole, subsequently leading to the formation of C-3-alkylated-2-aryl-2*H*-indazoles.[6,7] Our protocol was also found to be feasible with hetero-aromatic aldehydes. Significantly, good yields were observed when pyrrole-2-carboxaldehyde **2n**, furan-2-carboxaldehyde **2o**, 5-methyl-furan-2-carboxaldehyde **2p** and 5-bromothiophene-2-carboxaldehyde **2q** were reacted under the optimized reaction conditions to furnish **3n–q**.

Overall, the reactivity order for different types of aldehydes has been depicted as:

Aromatic > aliphatic > hetero-aromatic

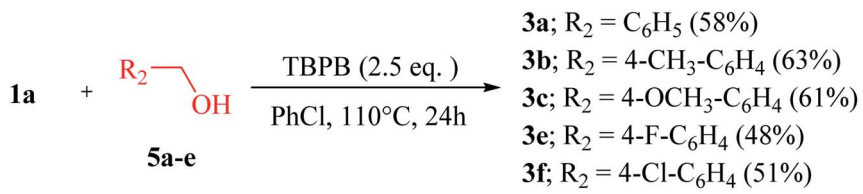
On the other hand, electron-donating groups (EDGs) containing aldehydes were found to be more favorable to the



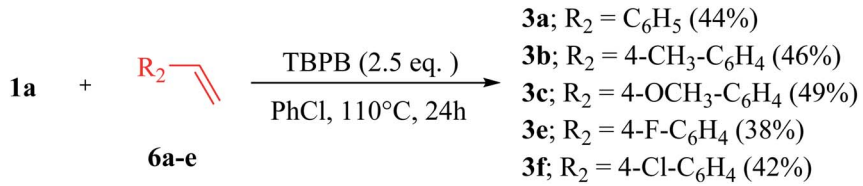

Scheme 3 Substrate scope: reaction of different substituted 2*H*-indazoles **1b–m** with benzaldehyde **2a–b** for the synthesis of **4a–l**[a,b]. [a]Reaction conditions: substituted 2*H*-indazoles **1b–m** (0.5 mmol), substituted aldehydes **2a–b** (1.0 mmol), oxidant (1.25 mmol), PhCl, $N_2$ atm, 110 °C, 24 h. [b]Isolated yield.

optimized reaction conditions compared to electron-withdrawing groups (EWGs) containing aldehydes. The synthetic utility was also demonstrated by performing a gram-scale synthesis of **3a** by the reaction of **1a** with **2a** under our optimized reaction conditions, which furnished **3a** in 65% isolated yield (Scheme 2).

Sequentially, a diverse variety of substituted 2*H*-indazoles **1b–m** were reacted with substituted benzaldehyde **2a–b** under the optimized reaction conditions, which furnished the 3-benzyolated-2*H*-indazoles **4a–l** in 54–80% yield (Scheme 3). 2*H*-Indazoles with EDGs, *i.e.*, **1b** ($R_1$ = –$OCH_2O$–), **1d** ($R_1$ = –$OCH_3$), **1e** ($R_1$ = $CH_3$) and **1g** ($R_1$ = –$OCH_2O$–), were reacted with **2a** under the optimized reaction conditions, which furnished **4a**, **4c**, **4d** and **4f** in 55%, 65%, 68% and 58% moderate yields, respectively. However, 2*H*-indazoles with a halo group ($R_1$ = F, Cl) **1c** and **1f**, when subjected to CDC reaction with **2a** under the optimized reaction conditions afforded **4b** and **4e** in 71% and 78% yields, respectively. 2*H*-Indazoles **1g–i** ($R_2$ = *p*-$OCH_3$, $CH_3$, Cl) and **1m** ($R_2$ = H) on coupling with benzaldehyde **2a** and **2b** afforded C-3 benzoylated product **4f–h** in 58–85% yields and **4l** in 80% yield, respectively. Similarly, heteroaryl 2*H*-indazoles **1j–l** were reacted with 4-methylbenzaldehyde **2a**, which furnished 3-benzyolated-(heteroaryl)-2*H*-indazoles **4i–k** in 72%, 71% and 82% yields, respectively. The substrates, 2-cyclohexyl-2*H*-indazole **1n** and 1*H*-indazole **1o** were found to be unreactive under the optimized reaction conditions. This clearly illustrates that the 2-aryl substitution in 2*H*-indazole plays a dynamic role in stabilizing the intermediate for the coupling of aldehydes. This transition-metal-free, regioselective, direct C-3 benzoylation of 2-aryl-2*H*-indazoles *via* a $C_{(sp^2)}$–H/$C_{(sp^2)}$–H cross-dehydrogenative coupling also works effectively with several substituted benzyl alcohols **5a–e** and styrenes **6a–e** on reaction



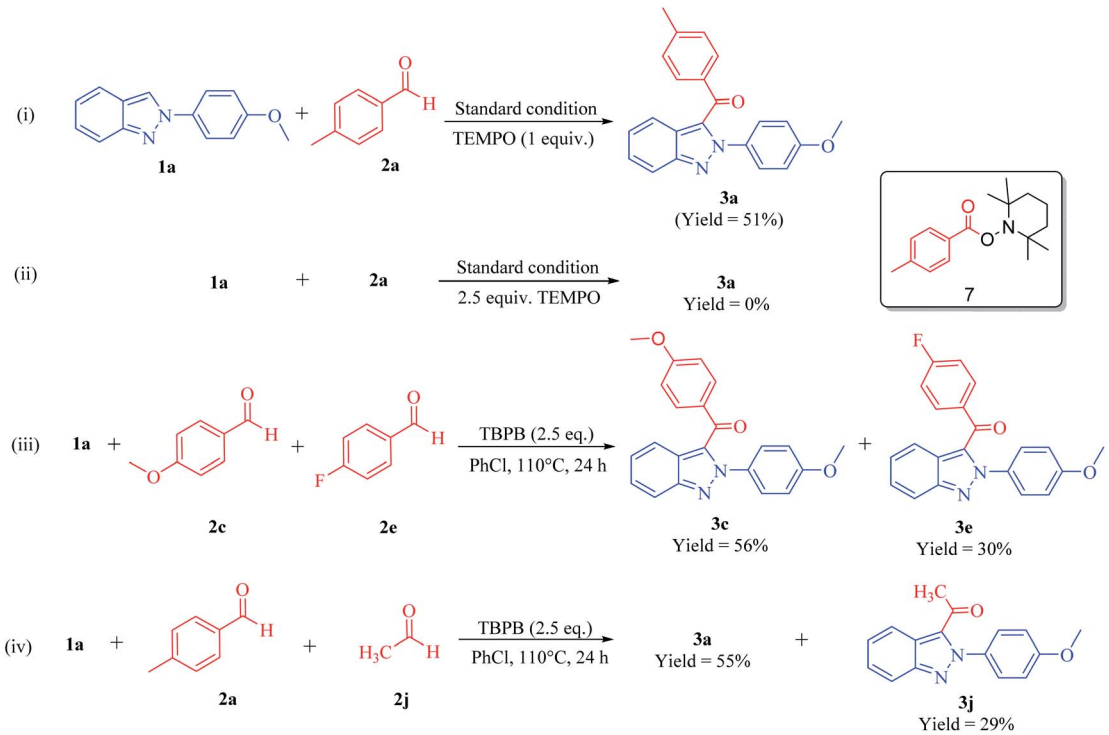

Scheme 4 Reaction of oxidative coupling of different substituted benzyl alcohol **5a–e** with 2*H*-indazole **1a**[a,b]. [a]Reaction conditions: 2-(4-methoxyphenyl)-2*H*-indazole **1a** (0.5 mmol), substituted benzyl alcohols **5a–e** (1.0 mmol), TBPB (1.25 mmol), PhCl, $N_2$ atm, 110 °C, 24 h. [b]Isolated yield.




Scheme 5 Benzoylation reaction of different substituted styrenes **6a–e** with 2*H*-indazole **1a**[a,b]. [a]Reaction conditions: 2-(4-methoxyphenyl)-2*H*-indazole **1a** (0.5 mmol), substituted styrenes **6a–e** (1.0 mmol), TBPB (1.25 mmol), PhCl, $N_2$ atm, 110 °C, 24 h. [b]Isolated yield.

with **1a**, which furnished C-3-benzoylated-2-aryl-2*H*-indazole products **3a–c** and **3e–f** in good yields (Schemes 4 and 5).

In order to understand the mechanism of this unique protocol, control experiments were conducted [Scheme 6, eqn (i)–(iv)]. It has already been exemplified in the literature that *tert*-butyl peroxybenzoate (TBPB) acts as a radical initiator.[11] Keeping all the reaction conditions the same, **1a** was reacted with **2a** under the optimized reaction conditions in the presence of TEMPO (1 equiv.), which furnished **3a** in 51% yield [Scheme 6, eqn (i)]. However, **3a** was not formed and the reaction was completely aborted when TEMPO (2.5 equiv.) was added under the standard reaction conditions. We were successful in isolating the TEMPO-trapped acyl adduct **7** in 71% yield [Scheme 6, eqn (ii)]. The isolation of adduct **7** confirmed that the synthetic pathway towards the regioselective synthesis of 3-(acyl/benzoyl)-2-aryl-2*H*-indazoles proceed *via* the free-radical pathway. This underlines the importance of the oxidant in this free-radical-catalyzed reaction. In order to interpret the




Scheme 6 Control experiments.

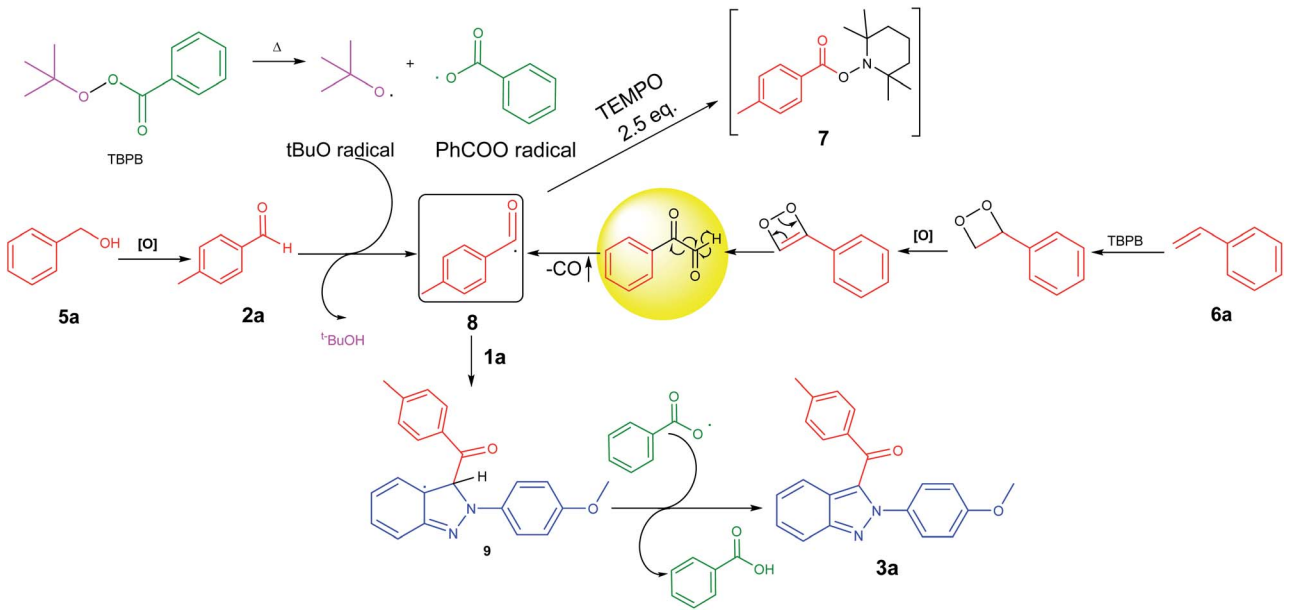
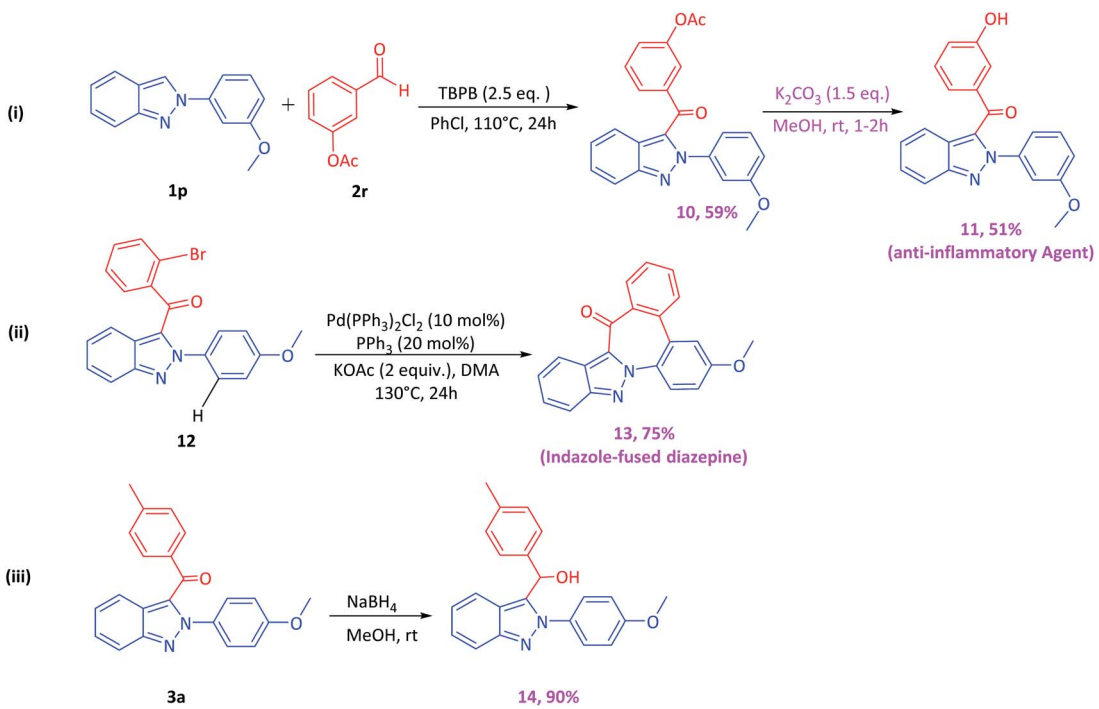



Fig. 2 Plausible mechanism.

reactivity order among EDGs and EWGs while keeping all the reaction conditions the same, a competitive experiment was executed in which substrate **1a** was reacted with an equimolar amount of **2c** and **2e**, which afforded the C-3 benzoylated products **3c** and **3e** in 56% and 30% yields, respectively [Scheme 6, eqn (iii)]. Therefore, it has been concluded that **2c** with an EDG showed higher reactivity than **2e** with an EWG. Another competitive experiment was carried out to analyse the reactivity order of this CDC reaction between aliphatic and aromatic aldehydes. Thus, substrate **1a** was reacted with an equimolar amount of **2a** and **2j** under optimized reaction conditions, which furnished 3-(4-methylbenzyolated)-2-aryl-2*H*-indazole **3a** and 3-(acetyl)-2-aryl-2*H*-indazole **3j** in 55% and 29% yields, respectively [Scheme 6, eqn (iv)]. This reaction demonstrated that the aromatic aldehydes were found to be more reactive than aliphatic aldehydes.




Scheme 7 Practical synthetic applications.

A plausible free-radical mechanism for this regioselective benzoylation method has been depicted in Fig. 2. Initially, thermal cleavage of TBPB generates a $^{t}$BuO free-radical and a carboxyl (PhCOO) free-radical. Then, the $^{t}$BuO free-radical through hydrogen radical abstraction (HRA) from 4-methylbenzaldehyde **2a** generates a benzoyl (acyl) free-radical **8** [note: the radical species **8** was trapped with TEMPO to give adduct **7**]. The free-radical **8** can also be derived from benzyl alcohol **5a** as well as styrene **6a**.[10a,b] This benzoyl free-radical species **8** was regioselectively added to the C-3 position of **1a**. Subsequently, the carboxyl free-radical abstracted the hydrogen radical from the intermediate radical species **9** to afford the desired product **3a**.

To illustrate the synthetic application of the developed CDC methodology, using our optimized reaction conditions, we synthesized the indazole-based anti-inflammatory agent **11** (Scheme 7). The substrate **1p** on reaction with *m*-acetoxybenzaldehyde **2r** under the optimized reaction conditions furnished **10**, which on deacetylation furnished anti-inflammatory agent **11** in 51% yield. It has been noted that compound **11** was earlier synthesized in 7 steps;[12] in contrast, we were successful in synthesizing **11** in 51% in two steps. Progressively, the (2-bromophenyl)(2-(4-methoxyphenyl)-2*H*-indazol-3-yl)methanone **12** was synthesized by the reaction of **1a** with *o*-bromobenzaldehyde using our optimized reaction conditions which on further subjection to Pd-catalyzed biaryl coupling leads to the formation of a novel class of heterocycles, *i.e.*, 3-methoxy-9*H*-dibenzo[4,5:6,7]azepino[1,2-*b*]indazol-9-one **13** in 75% yield, which can be utilized for medicinal chemistry applications.[13] In addition, the synthesized benzoylated product **3a** on subjection to $NaBH_4$ reduction in methanol furnished the reduced hydroxylated product, *i.e.*, (2-(4-methoxyphenyl)-2*H*-indazol-3-yl)(*p*-tolyl)methanol **14**, in 90% yield, which can be utilized further for derivatization/functionalization and other organic transformations.

## Conclusions

In summary, we have developed an efficient, cost-effective, transition-metal-free, regioselective, TBPB-promoted, oxidative $C_{(sp^2)}$–H/$C_{(sp^2)}$–H cross-dehydrogenative coupling protocol for the direct C-3 acylation/benzoylation of 2-substituted-2*H*-indazoles **3a–q**/**4a–l** *via* the reaction of various 2-substituted-2*H*-indazoles **1a–m** with different substituted aldehydes **2a–q**/benzyl alcohols **5a–e**/styrenes **6a–e** in up to 87% yields. The operationally simple, oxidant-promoted protocol exhibits a variety of functional group tolerances and wide substrate compatibilities. The reaction involves a free-radical mechanism and proceeds *via* the addition of an *in situ* generated acyl radical (from aldehydes/benzyl alcohols/styrenes) on 2*H*-indazoles. The gram-scale synthesis, and facile synthesis of anti-inflammatory agent **11**, 3-methoxy-9*H*-dibenzo[4,5:6,7]azepino[1,2-*b*]indazol-9-one **13** and hydroxylated product **14** further highlights the versatile nature of the developed methodology. We believe that our acylation/benzoylation regioselective CDC protocol will accomplish several kinds of utilization in constructing a ubiquitous class of bioactive azaheterocycles.

## Experimental

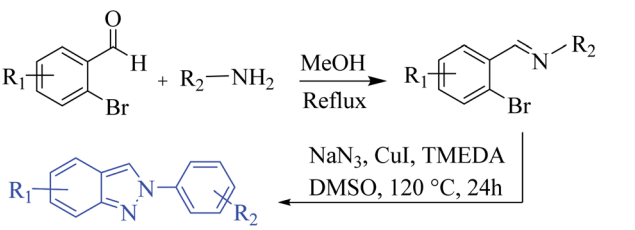
### General

Oven-dried laboratory glassware was used for carrying out all the synthetic procedures. Melting points were taken in open capillaries on Sisco melting point apparatus and are presented uncorrected. $^{1}$H NMR and $^{13}$C NMR spectra were recorded on a JEOL ECS-400 spectrometer (2-channel console with a flexible broadband RF performance), which was operating at 400 MHz for $^{1}$H and 100 MHz for $^{13}$C NMR and utilized $CDCl_3$ and DMSO-d6 as solvents for sample preparation. Tetramethylsilane ($\delta$ 0.00 ppm) and $CDCl_3$ both served as internal standards in $^{1}$H NMR ($\delta$ 7.246 ppm) and $^{13}$C ($\delta$ 77.0 ppm) NMR. Patterns of chemical shifts are reported in parts per million. Peak splitting patterns are described as singlet (s), broad singlet (brs), doublet (d), double doublet (dd), triplet (t), and multiplet (m). Coupling constants (*J*) are reported in Hertz (Hz). High-Resolution Electron Impact Mass Spectra (HR-EIMS) were obtained on Xevo G2-S Q-Tof (Waters, USA) compatible with ACQUITY UPLC® and nano ACQUITY UPLC® systems. Column chromatography was performed over normal (particle size: 60–120 mesh, 100–200 mesh) and flash (particle size: 230–400 mesh) silica gel, which was procured from Qualigens™ (India), Rankem (India), and Spectrochem (India). TLC plates coated with silica gel (Kiesel 60-$F_{254}$, Merck (India)) were used for monitoring the progress of the reactions. The visualizing agents used for TLC was UV light. A BUCHI Rotavapor R-210 was used for all drying and concentration procedures. All the analytical grade supplied solvents such as MeOH, EtOH were used without further purification. All the AR grade chemicals and reagents obtained from Sigma Aldrich (USA), Merck (India), TCI (India) and/or Spectrochem (India) *etc.* were used without further purification.

### Synthesis of starting material 2*H*-indazoles 1a–o (Scheme 8)[14]

A solution of 2-bromobenzaldehyde or substituted-2-bromobenzaldehyde (1.5 mmol) and aromatic/hetero-aromatic/aliphatic/cyclic amine (2.4 mmol) in methanol (20 mL) was refluxed for 6–7 h at 80 °C. After the completion of the reaction, the solvent was evaporated under reduced pressure to get the corresponding imine product, which was further used in the next step without prior purification.

The imine product was dissolved in anhydrous DMSO (10.0 mL) and CuI (38 mg, 0.20 mmol), $NaN_3$ (261 mg, 4.0 mmol) and TMEDA (22 mg, 0.20 mmol) were added. The reaction mixture was heated at 120 °C for 12 h. After cooling the reaction mixture,




Scheme 8 General procedure for the synthesis of 2*H*-indazole **1a–o**.

it was poured into chloroform (70.0 mL) and sequentially washed with water (3 × 30 mL) and brine (3 × 30 mL), then dried over anhyd. $Na_2SO_4$. Then, after evaporation of the solvent under reduced pressure, the crude product was further purified by column chromatography (hexane : EtOAc = 99 : 1 to 90 : 10) to produce the corresponding 2*H*-indazole **1a–m**.

### Synthetic procedure for the C-3 benzoylation of 2*H*-indazoles 3a–q/4a–l (Schemes 2 and 3)

For the C-3 benzoylation of 2*H*-indazoles **3a–q**/**4a–l**, a mixture of 2*H*-indazole **1a–m** (0.5 mmol), aromatic/hetero-aromatic/aliphatic aldehydes **2a–q** (1 mmol) and TBPB (1.25 mmol) dissolved in PhCl were taken in a sealed reaction tube under nitrogen atmosphere. Then the reaction mixture was stirred at 110 °C for 24 h. After completion of the reaction, the reaction mixture was cooled and the work-up was done with a saturated solution of $NaHCO_3$ (10 mL) and ethyl acetate (3 × 20 mL). The combined organic layers were dried over anhydrous $Na_2SO_4$, filtered, and concentrated under reduced pressure to get the crude residue which was further purified through column chromatography on silica gel (100–200 mesh) using hexane : ethyl acetate (95 : 5 ratio) as an eluent to afford the corresponding desired product.

### General procedure for the gram-scale synthesis of compound 3a

A mixture of 2-(4-methoxyphenyl)-2*H*-indazole **1a** (1.0 g, 4.46 mmol), 4-methyl benzaldehyde **2a** (1.05 mL, 8.92 mmol) and TBPB (2.12 mL, 11.15 mmol) was taken in a 50 mL round-bottom flask under nitrogen atmosphere. Then, the reaction mixture was stirred at 110 °C for 24 h. After completion of the reaction, the reaction mixture was cooled and the work-up was done with a saturated solution of $NaHCO_3$ (10 mL) and ethyl acetate (3 × 20 mL). The combined organic layers were dried over anhydrous $Na_2SO_4$, filtered, and concentrated under reduced pressure to get the crude residue which was further purified through column chromatography on silica gel (100–200 mesh) using hexane : ethyl acetate (95 : 5 ratio) as an eluent to afford compound **3a** as a yellow solid in 65% yield (0.97 g).

### Characterization of C-3 acylated/benzoylated 2*H*-indazoles

**2-(4-Methoxyphenyl)-2*H*-indazol-3-yl)(*p*-tolyl)methanone (3a).** Product **3a** was obtained by utilizing the general procedure (Scheme 2) using 2-(4-methoxyphenyl)-2*H*-indazole **1a** (112 mg, 0.5 mmol) and 4-methyl benzaldehyde **2a** (118 μL, 1 mmol) and isolated by column chromatography (hexane : EtOAc = 95 : 05) as a yellow solid in 82% yield (140 mg, 0.40 mmol); mp: 153–155 °C; $R_f$ (hexane : EtOAc = 85 : 15): 0.48; $^1$H NMR (400 MHz, chloroform-d) $\delta$ 7.86 (d, $J$ = 8.4 Hz, 1H), 7.79 (d, $J$ = 8.0 Hz, 2H), 7.49–7.44 (m, 2H), 7.38–7.33 (m, 2H), 7.27 (d, $J$ = 8.4 Hz, 2H), 7.17–7.13 (m, 1H), 6.93 (d, $J$ = 8.8 Hz, 2H), 3.82 (s, 3H), 2.44 (s, 3H); $^{13}$C NMR (100 MHz, chloroform-d) $\delta$ 185.87, 159.94, 148.41, 144.80, 135.37, 133.75, 132.41, 130.29, 129.47, 126.89, 126.70, 124.69, 123.86, 120.68, 118.44, 114.33, 55.63, 21.89; HRMS (ESI/QTOF) $m/z$: calcd for $C_{22}H_{18}N_2O_2$, 343.1441 $[M + H]^+$; found, 343.1446.

**(2-(4-Methoxyphenyl)-2*H*-indazol-3-yl)(phenyl)-methanone (3b).** Product **3b** was obtained by utilizing the general procedure (Scheme 2) using 2-(4-methoxyphenyl)-2*H*-indazole **1a** (112 mg, 0.5 mmol) and benzaldehyde **2b** (102 μL, 1 mmol) and isolated by column chromatography (hexane : EtOAc = 95 : 05) as a yellow solid in 80% yield (131 mg, 0.39 mmol); mp: 93–95 °C; $R_f$ (hexane : EtOAc = 85 : 15): 0.45; $^1$H NMR (400 MHz, chloroform-*d*) $\delta$ 7.88–7.84 (m, 3H), 7.59 (t, $J$ = 7.2 Hz, 1H), 7.47–7.43 (m, 4H), 7.38–7.32 (m, 2H), 7.17–7.13 (m, 1H), 6.91 (d, $J$ = 8.8 Hz, 2H), 3.81 (s, 3H); $^{13}$C NMR (100 MHz, chloroform-*d*) $\delta$ 186.15, 159.99, 148.46, 137.99, 133.74, 133.63, 132.20, 130.01, 128.73, 126.95, 126.78, 124.95, 124.05, 120.63, 118.51, 114.33, 55.63; HRMS (ESI/QTOF) $m/z$: calcd for $C_{21}H_{16}N_2O_2$, 329.1285 $[M + H]^+$; found, 329.1282.

**(4-Methoxyphenyl)(2-(4-methoxyphenyl)-2*H*-indazol-3-yl) methanone (3c).** Product **3c** was obtained by utilizing the general procedure (Scheme 2) using 2-(4-methoxyphenyl)-2*H*-indazole **1a** (112 mg, 0.5 mmol) and 4-methoxybenzaldehyde **2c** (121 μL, 1 mmol) and isolated by column chromatography (hexane : EtOAc = 95 : 05) as a yellow solid in 86% yield (154 mg, 0.43 mmol); mp: 123–125 °C; $R_f$ (hexane : EtOAc = 85 : 15): 0.38; $^1$H NMR (400 MHz, chloroform-*d*) $\delta$ 7.89–7.83 (m, 3H), 7.47–7.44 (m, 2H), 7.39–7.33 (m, 2H), 7.16–7.12 (m, 1H), 6.94–6.91 (m, 4H), 3.87 (s, 3H), 3.81 (s, 3H); $^{13}$C NMR (100 MHz, chloroform-*d*) $\delta$ 184.89, 164.25, 159.91, 148.39, 133.73, 132.63, 132.51, 130.67, 126.90, 126.63, 124.56, 123.71, 120.65, 118.40, 114.35, 114.07, 55.70, 55.64; HRMS (ESI/QTOF) $m/z$: calcd for $C_{22}H_{18}N_2O_3$, 359.1390 $[M + H]^+$; found, 359.1392.

**(2,5-Dimethoxyphenyl)(2-(4-methoxyphenyl)-2*H*-indazol-3-yl)methanone (3d).** Product **3d** was obtained by utilizing the general procedure (Scheme 2) using 2-(4-methoxyphenyl)-2*H*-indazole **1a** (112 mg, 0.5 mmol) and 2,5-dimethoxybenzaldehyde **2d** (166 mg, 1 mmol) and isolated by column chromatography (hexane : EtOAc = 95 : 05) as a brown oil in 78% yield (152 mg, 0.39 mmol); $R_f$ (hexane : EtOAc = 85 : 15): 0.30; $^1$H NMR (400 MHz, chloroform-*d*) $\delta$ 7.84 (d, $J$ = 8.8 Hz, 1H), 7.44 (d, $J$ = 9.2 Hz, 2H), 7.35–7.33 (m, 2H), 7.17–7.14 (m, 1H), 7.04 (d, $J$ = 3.2 Hz, 1H), 6.99–6.96 (m, 1H), 6.88 (d, $J$ = 9.2 Hz, 2H), 6.74 (d, $J$ = 9.2 Hz, 1H), 3.80 (s, 3H), 3.76 (s, 3H), 3.48 (s, 3H); $^{13}$C NMR (100 MHz, chloroform-*d*) $\delta$ 184.23, 159.38, 153.19, 151.66, 147.87, 133.21, 133.15, 128.89, 126.53, 126.34, 124.61, 123.37, 120.08, 118.91, 117.86, 113.95, 113.37, 112.36, 55.70, 55.49, 55.13. HRMS (ESI/QTOF) $m/z$: calcd for $C_{23}H_{20}N_2O_4$, 389.1496 $[M + H]^+$; found, 389.1498.

**(4-Fluorophenyl)(2-(4-methoxyphenyl)-2*H*-indazol-3-yl) methanone (3e).** Product **3e** was obtained by utilizing the general procedure (Scheme 2) using 2-(4-methoxyphenyl)-2*H*-indazole **1a** (112 mg, 0.5 mmol) and 4-flurobenzaldehyde **2e** (106 μL, 1 mmol) and isolated by column chromatography (hexane : EtOAc = 95 : 05) as a yellow solid in 83% yield (143 mg, 0.41 mmol); mp: 135–137 °C; $R_f$ (hexane : EtOAc = 85 : 15): 0.42; $^1$H NMR (400 MHz, chloroform-*d*) $\delta$ 7.92–7.87 (m, 3H), 7.46–7.44 (m, 2H), 7.40–7.36 (m, 2H), 7.22–7.18 (m, 1H), 7.14 (t, $J$ = 8.8 Hz, 2H), 6.94 (d, $J$ = 9.2 Hz, 2H), 3.83 (s, 3H); $^{13}$C NMR (100 MHz, chloroform-*d*) $\delta$ 184.52, 165.94 ($J_{C\text{-}F}$ = 254.7 Hz), 159.96, 148.37, 134.18 ($J_{C\text{-}F}$ = 2.9 Hz), 133.52, 132.60 ($J_{C\text{-}F}$ =

9.4 Hz), 131.81, 126.95, 126.65, 125.03, 123.90, 120.30, 118.52, 115.91 ($J_{C\text{-}F}$ = 22.0 Hz), 114.28, 55.57; HRMS (ESI/QTOF) *m*/*z*: calcd for $C_{21}H_{15}FN_2O_2$, 347.1191 $[M + H]^+$; found, 347.1194.

**(4-Chlorophenyl)(2-(4-methoxyphenyl)-2*H*-indazol-3-yl) methanone (3f).** Product **3f** was obtained by utilizing the general procedure (Scheme 2) using 2-(4-methoxyphenyl)-2*H*-indazole **1a** (112 mg, 0.5 mmol) and 4-chlorobenzaldehyde **2f** (141 mg, 1 mmol) and isolated by column chromatography (hexane : EtOAc = 95 : 05) as a yellow solid in 81% yield (147 mg, 0.41 mmol); mp: 142–144 °C; $R_f$ (hexane : EtOAc = 85 : 15): 0.45; $^1$H NMR (400 MHz, chloroform-*d*) $\delta$ 7.86 (d, $J$ = 8.8 Hz, 1H), 7.78 (d, $J$ = 8.8 Hz, 2H), 7.44–7.40 (m, 4H), 7.37–7.33 (m, 2H), 7.19–7.16 (m, 1H), 6.91 (d, $J$ = 8.8 Hz, 2H), 3.81 (s, 3H); $^{13}$C NMR (100 MHz, chloroform-*d*) $\delta$ 184.77, 160.07, 148.45, 140.09, 136.28, 133.57, 131.75, 131.36, 129.09, 127.05, 126.76, 125.23, 124.01, 120.38, 118.63, 114.37, 55.65; HRMS (ESI/QTOF) *m*/*z*: calcd for $C_{21}H_{15}ClN_2O_2$, 363.0895 $[M + H]^+$; found, 363.0897.

**(4-Bromophenyl)(2-(4-methoxyphenyl)-2*H*-indazol-3-yl) methanone (3g).** Product **3g** was obtained by utilizing the general procedure (Scheme 2) using 2-(4-methoxyphenyl)-2*H*-indazole **1a** (112 mg, 0.5 mmol) and 4-bromobenzaldehyde **2g** (165 mg, 1 mmol) and isolated by column chromatography (hexane : EtOAc = 95 : 05) as a yellow solid in 84% yield (170 mg, 0.42 mmol); mp: 141–143 °C; $R_f$ (hexane : EtOAc = 85 : 15): 0.48; $^1$H NMR (400 MHz, chloroform-*d*) $\delta$ 7.89–7.87 (m, 1H), 7.73 (d, $J$ = 8.4 Hz, 2H), 7.61 (d, $J$ = 8.4 Hz, 2H), 7.44 (d, $J$ = 9.2 Hz, 2H), 7.45–7.35 (m, 2H), 7.22–7.18 (m, 1H), 6.94 (d, $J$ = 8.8 Hz, 2H), 3.84 (s, 3H); $^{13}$C NMR (100 MHz, chloroform-*d*) $\delta$ 184.93, 160.08, 148.46, 136.71, 133.56, 132.07, 131.70, 131.43, 128.83, 127.05, 126.76, 125.26, 124.00, 120.38, 118.64, 114.38, 55.66; HRMS (ESI/QTOF) *m*/*z*: calcd for $C_{21}H_{15}BrN_2O_2$, 407.0390 $[M + H]^+$; found, 407.0392.

**(3-Chlorophenyl)(2-(4-methoxyphenyl)-2*H*-indazol-3-yl) methanone (3h).** Product **3h** was obtained by utilizing the general procedure (Scheme 2) using 2-(4-methoxyphenyl)-2*H*-indazole **1a** (112 mg, 0.5 mmol) and 3-chlorobenzaldehyde **2h** (141 mg, 1 mmol) and isolated by column chromatography (hexane : EtOAc = 95 : 05) as a yellow solid in 67% yield (122 mg, 0.34 mmol); mp: 155–157 °C; $R_f$ (hexane : EtOAc = 85 : 15): 0.44; $^1$H NMR (400 MHz, chloroform-*d*) $\delta$ 7.88 (d, $J$ = 8.8 Hz, 1H), 7.78 (s, 1H), 7.69 (d, $J$ = 7.6 Hz, 1H), 7.54 (d, $J$ = 8.0 Hz, 1H), 7.43–7.37 (m, 5H), 7.23–7.19 (m, 1H), 6.92 (d, $J$ = 8.8 Hz, 2H), 3.81 (s, 3H); $^{13}$C NMR (100 MHz, chloroform-*d*) $\delta$ 184.63, 160.07, 148.51, 139.52, 134.98, 133.57, 133.37, 131.66, 130.01, 129.76, 128.03, 127.11, 126.81, 125.45, 124.20, 120.37, 118.66, 114.37, 55.66; HRMS (ESI/QTOF) *m*/*z*: calcd for $C_{21}H_{15}ClN_2O_2$, 363.0895 $[M + H]^+$; found, 363.0892.

**(2-Chlorophenyl)(2-(4-methoxyphenyl)-2*H*-indazol-3-yl) methanone (3i).** Product **3i** was obtained by utilizing the general procedure (Scheme 2) using 2-(4-methoxyphenyl)-2*H*-indazole **1a** (112 mg, 0.4459 mmol) and 2-chlorobenzaldehyde **2i** (141 mg, 1 mmol) and isolated by column chromatography (hexane : EtOAc = 95 : 05) as a yellow solid in 58% yield (105 mg, 0.29 mmol); mp: 90–92 °C; $R_f$ (hexane : EtOAc = 85 : 15): 0.44; $^1$H NMR (400 MHz, chloroform-*d*) $\delta$ 7.8–7.78 (m, 1H), 7.39 (d, $J$ = 8.8 Hz, 2H), 7.36–7.24 (m, 5H), 7.14–7.09 (m, 1H), 7.06–7.04 (m, 1H), 6.84 (d, $J$ = 8.8 Hz, 2H), 3.75 (s, 3H); $^{13}$C NMR (100 MHz, chloroform-*d*) $\delta$ 183.82, 160.11, 148.53, 138.80, 133.59, 132.21, 132.16, 131.94, 130.37, 129.90, 127.20, 127.09, 126.08, 124.52, 120.20, 118.77, 114.09, 55.68; HRMS (ESI/QTOF) *m*/*z*: calcd for $C_{21}H_{15}ClN_2O_2$, 363.0895 $[M + H]^+$; found, 363.0898.

**1-(2-(4-Methoxyphenyl)-2*H*-indazol-3-yl)ethan-1-one (3j).** Product **3j** was obtained by utilizing the general procedure (Scheme 2) using 2-(4-methoxyphenyl)-2*H*-indazole **1a** (112 mg, 0.5 mmol) and acetaldehyde **2j** (57 μL, 1 mmol) and isolated by column chromatography (hexane : EtOAc = 95 : 05) as a yellow oil in 68% yield (90 mg, 0.34 mmol); $R_f$ (hexane : EtOAc = 85 : 15): 0.36; $^1$H NMR (400 MHz, chloroform-*d*) $\delta$ 7.70–7.68 (m, 1H), 7.60 (d, $J$ = 8.4 Hz, 1H), 7.45 (d, $J$ = 8.8 Hz, 2H), 7.32–7.28 (m, 1H), 7.06–7.00 (m, 3H), 3.87 (s, 3H), 2.60 (s, 3H); $^{13}$C NMR (100 MHz, chloroform-*d*) $\delta$ 188.07, 159.75, 148.49, 133.02, 132.07, 127.53, 127.06, 126.70, 120.86, 120.02, 117.52, 114.37, 55.69, 11.12; HRMS (ESI/QTOF) *m*/*z*: calcd for $C_{16}H_{14}N_2O_2$, 267.1128 $[M + H]^+$; found, 267.1131.

**1-(2-(4-Methoxyphenyl)-2*H*-indazol-3-yl)propan-1-one (3k).** Product **3k** was obtained by utilizing the general procedure (Scheme 2) using 2-(4-methoxyphenyl)-2*H*-indazole **1a** (112 mg, 0.5 mmol) and propionaldehyde **2k** (73 μL, 1 mmol) and isolated by column chromatography (hexane : EtOAc = 95 : 05) as a yellow oil in 61% yield (86 mg, 0.31 mmol); $R_f$ (hexane : EtOAc = 85 : 15): 0.31; $^1$H NMR (400 MHz, chloroform-*d*) $\delta$ 7.86–7.59 (m, 2H), 7.47–7.40 (m, 2H), 7.31–7.28 (m, 1H), 7.07–7.00 (m, 3H), 3.87 (s, 3H), 3.02 (q, $J$ = 7.6 Hz, 1H), 2.60 (s, 1H), 1.27–1.23 (m, 3H); $^{13}$C NMR (100 MHz, chloroform-*d*) $\delta$ 188.08, 159.92, 159.76, 148.55, 138.10, 133.09, 127.36, 127.06, 126.59, 120.86, 120.84, 120.15, 117.61, 114.36, 55.68, 18.91, 14.15; HRMS (ESI/QTOF) *m*/*z*: calcd for $C_{17}H_{16}N_2O_2$, 281.1285 $[M + H]^+$; found, 281.1287.

**1-(2-(4-Methoxyphenyl)-2*H*-indazol-3-yl)butan-1-one (3l).** Product **3l** was obtained by utilizing the general procedure (Scheme 2) using 2-(4-methoxyphenyl)-2*H*-indazole **1a** (112 mg, 0.5 mmol) and butyraldehyde **2l** (90 μL, 1 mmol) and isolated by column chromatography (hexane : EtOAc = 95 : 05) as a yellow oil in 60% yield (88 mg, 0.30 mmol); $R_f$ (hexane : EtOAc = 85 : 15): 0.32; $^1$H NMR (400 MHz, chloroform-*d*) $\delta$ 7.70–7.64 (m, 2H), 7.45–7.40 (m, 2H), 7.31–7.27 (m, 1H), 7.06–7.00 (m, 3H), 3.87 (s, 3H), 2.96 (t, $J$ = 7.6 Hz, 2H), 1.66 (q, $J$ = 7.6 Hz, 2H), 0.88 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, chloroform-*d*) $\delta$ 159.89, 148.49, 136.89, 133.16, 127.49, 127.06, 126.56, 120.84, 120.29, 117.58, 114.37, 114.32, 55.68, 27.36, 22.87, 14.08; HRMS (ESI/QTOF) *m*/*z*: calcd for $C_{17}H_{18}N_2O$, 267.1492 $[M + H]^+$; found, 267.1495.

**1-(2-(4-Methoxyphenyl)-2*H*-indazol-3-yl)-2-methylpropan-1-one (3m).** Product **3m** was obtained by utilizing the general procedure (Scheme 2) using 2-(4-methoxyphenyl)-2*H*-indazole **1a** (112 mg, 0.5 mmol) and isobutyraldehyde **2m** (91 μL, 1 mmol) and isolated by column chromatography (hexane : EtOAc = 95 : 05) as a yellow solid in 71% yield (104 mg, 0.35 mmol); mp: 98–100 °C; $R_f$ (hexane : EtOAc = 85 : 15): 0.34; $^1$H NMR (400 MHz, chloroform-*d*) $\delta$ 7.81 (dd, $J$ = 8.4 Hz, 0.8 Hz, 1H), 7.69 (d, $J$ = 8.8 Hz, 1H), 7.39–7.37 (m, 2H), 7.30–7.26 (m, 1H), 7.03–7.00 (m, 3H), 3.87 (s, 3H), 3.36–3.29 (m, 1H), 1.46 (d, $J$

= 7.2 Hz, 6H); $^{13}$C NMR (100 MHz, chloroform-*d*) $\delta$ 160.01, 148.77, 142.10, 133.18, 127.70, 126.28, 120.97, 120.56, 119.06, 117.86, 114.29, 55.69, 27.20, 22.51; HRMS (ESI/QTOF) *m*/*z*: calcd for $C_{17}H_{18}N_2O$, 267.1492 $[M + H]^+$; found, 267.1498.

**(2-(4-Methoxyphenyl)-2*H*-indazol-3-yl)(1*H*-pyrrol-2-yl) methanone (3n).** Product **3n** was obtained by utilizing the general procedure (Scheme 2) using 2-(4-methoxyphenyl)-2*H*-indazole **1a** (112 mg, 0.5 mmol) and 1*H*-pyrrole-2-carbaldehyde **2n** (95 mg, 1 mmol) and isolated by column chromatography (hexane : EtOAc = 95 : 05) as a brown solid in 58% yield (92 mg, 0.29 mmol); mp: 134–136 °C; $R_f$ (hexane : EtOAc = 85 : 15): 0.29; $^1$H NMR (400 MHz, chloroform-*d*) $\delta$ 10.35 (b, 1H), 7.84 (d, $J$ = 8.8 Hz, 1H), 7.74 (dd, $J$ = 8.4 Hz, 0.8 Hz, 1H), 7.51–7.49 (m, 2H), 7.38–7.34 (m, 1H), 7.21–7.17 (m, 1H), 7.03 (s, 1H), 6.96–6.94 (m, 3H), 6.33–6.31 (m, 1H), 3.83 (s, 3H); $^{13}$C NMR (100 MHz, chloroform-*d*) $\delta$ 174.34, 159.87, 148.50, 133.85, 132.45, 132.25, 127.24, 126.95, 126.66, 124.31, 123.14, 121.36, 120.80, 118.21, 114.29, 111.60, 55.65; HRMS (ESI/QTOF) *m*/*z*: calcd for $C_{19}H_{15}N_3O_2$, 318.1237 $[M + H]^+$; found, 318.1233.

**Furan-2-yl(2-(4-methoxyphenyl)-2*H*-indazol-3-yl)methanone (3o).** Product **3o** was obtained by utilizing the general procedure (Scheme 2) using 2-(4-methoxyphenyl)-2*H*-indazole **1a** (112 mg, 0.5 mmol) and furan-2-aldehyde **2o** (83 μL, 1 mmol) and isolated by column chromatography (hexane : EtOAc = 95 : 05) as a brown solid in 57% yield (91 mg, 0.28 mmol); mp: 70–72 °C; $R_f$ (hexane : EtOAc = 85 : 15): 0.29; $^1$H NMR (400 MHz, chloroform-*d*) $\delta$ 7.85 (d, $J$ = 9.6 Hz, 1H), 7.68 (d, $J$ = 8.4 Hz, 1H), 7.60 (b, 1H), 7.46 (d, $J$ = 8.8 Hz, 2H), 7.40–7.36 (m, 1H), 7.24–7.20 (m, 2H), 6.93 (d, $J$ = 8.8 Hz, 2H), 6.56–6.54 (m, 1H), 3.81 (s, 3H); $^{13}$C NMR (100 MHz, chloroform-*d*) $\delta$ 178.93, 172.80, 159.93, 152.39, 148.49, 147.78, 133.70, 127.06, 126.55, 124.94, 123.70, 121.20, 120.42, 118.45, 114.35, 112.79, 55.64; HRMS (ESI/QTOF) *m*/*z*: calcd for $C_{19}H_{14}N_2O_3$, 319.1077 $[M + H]^+$; found, 319.1073.

**(2-(4-Methoxyphenyl)-2*H*-indazol-3-yl)(5-methylfuran-2-yl) methanone (3p).** Product **3p** was obtained by utilizing the general procedure (Scheme 2) using 2-(4-methoxyphenyl)-2*H*-indazole **1a** (112 mg, 0.5 mmol) and 5-methylfuran-2-carboxaldehyde **2p** (99 μL, 1 mmol) and isolated by column chromatography (hexane : EtOAc = 95 : 05) as a brown solid in 61% yield (101 mg, 0.30 mmol); mp: 76–78 °C; $R_f$ (hexane : EtOAc = 85 : 15): 0.24; $^1$H NMR (400 MHz, chloroform-*d*) $\delta$ 7.83 (d, $J$ = 9.2 Hz, 1H), 7.72 (d, $J$ = 8.8 Hz, 1H), 7.48 (d, $J$ = 8.8 Hz, 2H), 7.39–7.35 (m, 1H), 7.24–7.19 (m, 1H), 7.12 (dd, $J$ = 3.6, 0.7 Hz, 1H), 6.93 (d, $J$ = 8.8 Hz, 2H), 6.17–6.16 (m, 1H), 3.82 (s, 3H), 2.33 (s, 3H); $^{13}$C NMR (101 MHz, chloroform-*d*) $\delta$ 172.24, 159.88, 159.60, 151.18, 148.50, 133.84, 131.85, 127.02, 126.44, 124.64, 123.63, 120.52, 118.32, 114.31, 109.71, 55.66, 14.18; HRMS (ESI/QTOF) *m*/*z*: calcd for $C_{20}H_{16}N_2O_3$, 333.1234 $[M + H]^+$; found, 333.1235.

**(5-Bromothiophen-2-yl)(2-(4-methoxyphenyl)-2*H*-indazol-3-yl)methanone (3q).** Product **3q** was obtained by utilizing the general procedure (Scheme 2) using 2-(4-methoxyphenyl)-2*H*-indazole **1a** (112 mg, 0.5 mmol) and 5-bromothiophene-2-carboxaldehyde **2q** (119 μL, 1 mmol) and isolated by column chromatography (hexane : EtOAc = 95 : 05) as a yellow solid in 59% yield (122 mg, 0.29 mmol); mp: 70–72 °C; $R_f$ (hexane : EtOAc = 85 : 15): 0.34; $^1$H NMR (400 MHz, chloroform-*d*) $\delta$ 7.78 (d, $J$ = 8.8 Hz, 1H), 7.56 (d, $J$ = 8.8 Hz, 1H), 7.39 (d, $J$ = 9.2 Hz, 2H), 7.33–7.29 (m, 2H), 7.17–7.13 (m, 1H), 7.02–7.03 (m, 1H), 6.88 (d, $J$ = 8.8 Hz, 2H), 3.76 (s, 3H); $^{13}$C NMR (101 MHz, chloroform-*d*) $\delta$ 176.80, 160.09, 148.49, 145.70, 135.74, 133.39, 131.53, 131.17, 127.12, 126.59, 125.03, 124.85, 123.46, 120.22, 118.55, 114.45, 55.67; HRMS (ESI/QTOF) *m*/*z*: calcd for $C_{19}H_{13}BrN_2O_2S$, 412.9954 $[M + H]^+$; found, 412.9957.

**(2-Phenyl-2*H*-[1,3]dioxolo[4,5-*f*]indazol-3-yl)(*p*-tolyl)methanone (4a).** Product **4a** was obtained by utilizing the general procedure (Scheme 3) using 2-phenyl-2*H*-[1,3]dioxolo[4,5-*f*] indazole **1b** (119 mg, 0.5 mmol) and 4-methylbenzaldehyde **2b** (118 μL, 1 mmol) and isolated by column chromatography (hexane : EtOAc = 95 : 05) as a yellow oil in 55% yield (91 mg, 0.26 mmol); $R_f$ (hexane : EtOAc = 85 : 15): 0.40; $^1$H NMR (400 MHz, chloroform-*d*) $\delta$ 7.75 (d, $J$ = 8.4 Hz, 2H), 7.47–7.45 (m, 2H), 7.39–7.35 (m, 4H), 7.23 (s, 1H), 7.08 (s, 1H), 6.58 (s, 1H), 5.98 (s, 2H), 2.41 (s, 3H); $^{13}$C NMR (100 MHz, chloroform-*d*) $\delta$ 185.80, 149.62, 147.86, 146.11, 144.59, 140.49, 135.13, 132.16, 130.03, 129.39, 129.00, 128.34, 125.08, 120.78, 101.40, 95.69, 94.54, 21.79; HRMS (ESI/QTOF) *m*/*z*: calcd for $C_{22}H_{16}N_2O_3$, 357.1234 $[M + H]^+$; found, 357.1239.

**(5-Fluoro-2-phenyl-2*H*-indazol-3-yl)(*p*-tolyl)methanone (4b).** Product **4b** was obtained by utilizing the general procedure (Scheme 3) using 5-fluoro-2-phenyl-2*H*-indazole **1c** (106 mg, 0.5 mmol) and 4-methylbenzaldehyde **2b** (118 μL, 1 mmol) and isolated by column chromatography (hexane : EtOAc = 95 : 05) as an off-white solid in 71% yield (101 mg, 0.31 mmol); mp: 65–67 °C; $R_f$ (hexane : EtOAc = 85 : 15): 0.51; $^1$H NMR (400 MHz, chloroform-*d*) $\delta$ 7.88–7.84 (m, 1H), 7.78 (d, $J$ = 8.4 Hz, 2H), 7.54–7.51 (m, 2H), 7.44–7.42 (m, 3H), 7.28 (d, $J$ = 7.6 Hz, 2H), 7.18 (td, $J$ = 9.2, 2.4 Hz, 1H), 6.97–6.94 (m, 1H), 2.45 (s, 3H); $^{13}$C NMR (100 MHz, chloroform-*d*) $\delta$ 185.31, 160.09 ($J_{C\text{-}F}$ = 243.3 Hz), 145.89, 144.94, 140.39, 134.92, 130.05, 129.51, 129.14, 129.02, 125.35, 123.78 ($J_{C\text{-}F}$ = 11.9 Hz), 120.77 ($J_{C\text{-}F}$ = 9.9 Hz), 118.67 ($J_{C\text{-}F}$ = 29.0 Hz), 103.63 ($J_{C\text{-}F}$ = 25.5 Hz), 97.22, 21.83.3; HRMS (ESI/QTOF) *m*/*z*: calcd for $C_{21}H_{15}FN_2O$, 331.1241 $[M + H]^+$; found, 331.1244.

**(5-Methoxy-2-phenyl-2*H*-indazol-3-yl)(*p*-tolyl)methanone (4c).** Product **4c** was obtained by utilizing the general procedure (Scheme 3) using 5-methoxy-2-phenyl-2*H*-indazole **1d** (112 mg, 0.5 mmol) and 4-methylbenzaldehyde **2b** (118 μL, 1 mmol) and isolated by column chromatography (hexane : EtOAc = 95 : 05) as a brown solid in 65% yield (111 mg, 0.32 mmol); mp: 140–142 °C; $R_f$ (hexane : EtOAc = 85 : 15): 0.48; $^1$H NMR (400 MHz, chloroform-*d*) $\delta$ 7.75–7.72 (m, 3H), 7.48–7.46 (m, 2H), 7.36–7.32 (m, 3H), 7.20 (d, $J$ = 7.2 Hz, 2H), 7.07–7.04 (m, 1H), 6.67 (s, 1H), 3.68 (s, 3H), 2.39 (s, 3H); $^{13}$C NMR (100 MHz, chloroform-*d*) $\delta$ 185.93, 157.54, 145.56, 144.41, 140.72, 135.32, 131.84, 130.07, 129.29, 129.08, 128.61, 125.39, 125.01, 122.14, 119.92, 97.13, 55.44, 21.84; HRMS (ESI/QTOF) *m*/*z*: calcd for $C_{22}H_{18}N_2O_2$, 343.1441 $[M + H]^+$; found, 343.1445.

**(6-Methyl-2-phenyl-2*H*-indazol-3-yl)(*p*-tolyl)methanone (4d).** Product **4d** was obtained by utilizing the general procedure (Scheme 3) using 6-methyl-2-phenyl-2*H*-indazole **1e** (104 mg, 0.5 mmol) and 4-methylbenzaldehyde **2b** (118 μL, 1 mmol) and isolated by column chromatography (hexane : EtOAc = 95 : 05) as a yellow solid in 68% yield (111 mg, 0.34 mmol); mp: 102–

104 °C; $R_f$ (hexane : EtOAc = 85 : 15): 0.44; $^1$H NMR (400 MHz, chloroform-*d*) $\delta$ 7.80 (d, $J$ = 8.4 Hz, 2H), 7.61 (s, 1H), 7.53–7.38 (m, 6H), 7.27–7.25 (m, 2H), 7.00 (d, $J$ = 8.8 Hz, 1H), 2.47 (s, 3H), 2.44 (s, 3H); $^{13}$C NMR (100 MHz, chloroform-*d*) $\delta$ 185.70, 149.13, 144.67, 140.56, 136.99, 135.24, 132.28, 130.18, 129.35, 129.04, 128.71, 127.75, 125.43, 122.38, 120.14, 116.69, 22.08, 21.80; HRMS (ESI/QTOF) *m*/*z*: calcd for $C_{22}H_{18}N_2O$, 327.1492 $[M + H]^+$; found, 327.1494.

**(5-Chloro-2-phenyl-2*H*-indazol-3-yl)(*p*-tolyl)methanone (4e).** Product **4e** was obtained by utilizing the general procedure (Scheme 3) using 5-chloro-2-phenyl-2*H*-indazole **1f** (114 mg, 0.5 mmol) and 4-methylbenzaldehyde **2b** (118 μL, 1 mmol) and isolated by column chromatography (hexane : EtOAc = 95 : 05) as a yellow solid in 78% yield (134 mg, 0.39 mmol); mp: 158–160 °C; $R_f$ (hexane : EtOAc = 85 : 15): 0.50; $^1$H NMR (400 MHz, chloroform-*d*) $\delta$ 7.81 (dd, $J$ = 9.2 Hz, 0.8 Hz, 1H), 7.76 (d, $J$ = 8.4 Hz, 2H), 7.52–7.50 (m, 2H), 7.42–7.37 (m, 4H), 7.32–7.26 (m, 3H), 2.26 (s, 3H); $^{13}$C NMR (100 MHz, chloroform-*d*) $\delta$ 185.29, 146.83, 145.14, 140.22, 134.78, 132.19, 130.71, 130.11, 129.55, 129.16, 129.09, 128.54, 125.33, 124.19, 120.00, 119.36, 21.85; HRMS (ESI/QTOF) *m*/*z*: calcd for $C_{21}H_{15}ClN_2O$, 347.0946 $[M + H]^+$; found, 347.0947.

**(2-(4-Methoxyphenyl)-2*H*-[1,3]dioxolo[4,5-*f*]indazol-3-yl)(*p*-tolyl)methanone (4f).** Product **4f** was obtained by utilizing the general procedure (Scheme 3) using 2-(4-methoxyphenyl)-2*H*-[1,3]dioxolo[4,5-*f*]indazole **1g** (134 mg, 0.5 mmol) and 4-methylbenzaldehyde **2b** (118 μL, 1 mmol) and isolated by column chromatography (hexane : EtOAc = 95 : 05) as a yellow oil in 58% yield (112 mg, 0.29 mmol); $R_f$ (hexane : EtOAc = 85 : 15): 0.40; $^1$H NMR (400 MHz, chloroform-*d*) $\delta$ 7.75 (d, $J$ = 8.4 Hz, 2H), 7.39 (dd, $J$ = 6.8 Hz, 2.0 Hz, 2H), 7.26 (s, 2H), 7.09 (s, 1H), 6.90 (dd, $J$ = 6.8 Hz, 2.0 Hz, 2H), 6.56 (s, 1H), 5.99 (s, 2H), 3.81 (s, 3H), 2.44 (s, 3H); $^{13}$C NMR (100 MHz, chloroform-*d*) $\delta$ 185.62, 159.25, 149.25, 147.49, 145.60, 144.32, 135.00, 133.54, 131.87, 129.82, 129.17, 126.08, 120.30, 113.95, 101.14, 95.52, 94.31, 55.31, 21.58; HRMS (ESI/QTOF) *m*/*z*: calcd for $C_{23}H_{18}N_2O_4$, 387.1340 $[M + H]^+$; found, 387.1346.

***p*-Tolyl(2-(*p*-tolyl)-2*H*-indazol-3-yl)methanone (4g).** Product **4g** was obtained by utilizing the general procedure (Scheme 3) using 2-(*p*-tolyl)-2*H*-indazole **1h** (104 mg, 0.5 mmol) and 4-methylbenzaldehyde **2b** (118 μL, 1 mmol) and isolated by column chromatography (hexane : EtOAc = 95 : 05) as a yellow solid in 79% yield (129 mg, 0.40 mmol); mp: 167–169 °C; $R_f$ (hexane : EtOAc = 85 : 15): 0.48; $^1$H NMR (400 MHz, chloroform-*d*) $\delta$ 7.87 (dd, $J$ = 8.4 Hz, 0.8 Hz, 1H), 7.81 (d, $J$ = 8.0 Hz, 2H), 7.42 (d, $J$ = 8.0 Hz, 2H), 7.35 (t, $J$ = 8.4 Hz, 2H), 7.27 (d, $J$ = 8.0 Hz, 2H), 7.22 (d, $J$ = 8.4 Hz, 2H), 7.16–7.13 (m, 1H), 2.44 (s, 3H), 2.38 (s, 3H); $^{13}$C NMR (100 MHz, chloroform-*d*) $\delta$ 185.71, 148.38, 144.72, 138.94, 138.08, 135.22, 132.33, 130.21, 129.67, 129.37, 126.81, 125.17, 124.62, 123.79, 120.59, 118.41, 21.80, 21.19; HRMS (ESI/QTOF) *m*/*z*: calcd for $C_{22}H_{18}N_2O$, 327.1492 $[M + H]^+$; found, 327.1495.

**(2-(4-Chlorophenyl)-2*H*-indazol-3-yl)(*p*-tolyl)methanone (4h).** Product **4h** was obtained by utilizing the general procedure (Scheme 3) using 2-(4-chlorophenyl)-2*H*-indazole **1i** (114 mg, 0.5 mmol) and 4-methylbenzaldehyde **2b** (118 μL, 1 mmol) and isolated by column chromatography (hexane : EtOAc = 95 : 05) as a yellow semi-solid in 85% yield (142 mg, 0.41 mmol); $R_f$ (hexane : EtOAc = 85 : 15): 0.48; $^1$H NMR (400 MHz, chloroform-*d*) $\delta$ 7.86 (dd, $J$ = 8.8 Hz, 0.8 Hz, 1H), 7.81 (d, $J$ = 8.0 Hz, 2H), 7.52–7.48 (m, 2H), 7.41 (d, $J$ = 8.8 Hz, 2H), 7.38–7.33 (m, 2H), 7.30 (d, $J$ = 8.0 Hz, 2H), 7.19–7.15 (m, 1H), 2.46 (s, 3H); $^{13}$C NMR (100 MHz, chloroform-*d*) $\delta$ 185.59, 148.70, 145.14, 139.10, 135.13, 134.90, 132.54, 130.30, 129.58, 129.35, 127.29, 126.74, 125.12, 123.97, 120.72, 118.55, 21.93; HRMS (ESI/QTOF) *m*/*z*: calcd for $C_{21}H_{15}ClN_2O$, 347.0946 $[M + H]^+$; found, 347.0942.

**(2-(5-Methylpyridin-2-yl)-2*H*-indazol-3-yl)(*p*-tolyl)methanone (4i).** Product **4i** was obtained by utilizing the general procedure (Scheme 3) using 2-(5-methylpyridin-2-yl)-2*H*-indazole **1j** (105 mg, 0.5 mmol) and 4-methylbenzaldehyde **2b** (118 μL, 1 mmol) and isolated by column chromatography (hexane : EtOAc = 95 : 05) as a yellow solid in 72% yield (118 mg, 0.36 mmol); mp: 130–132 °C; $R_f$ (hexane : EtOAc = 85 : 15): 0.34; $^1$H NMR (400 MHz, chloroform-*d*) $\delta$ 8.08 (s, 1H), 7.91 (d, $J$ = 8.0 Hz, 1H), 7.83 (d, $J$ = 8.8 Hz, 1H), 7.79 (d, $J$ = 8.0 Hz, 2H), 7.69–7.66 (m, 1H), 7.43 (d, $J$ = 8.8 Hz, 1H), 7.38–7.34 (m, 1H), 7.24 (d, $J$ = 7.6 Hz, 2H), 7.15–7.11 (m, 1H), 2.42 (s, 3H), 2.32 (s, 3H); $^{13}$C NMR (100 MHz, chloroform-*d*) $\delta$ 186.88, 149.95, 148.92, 148.30, 144.37, 139.19, 135.40, 133.35, 132.60, 129.95, 129.39, 127.60, 124.43, 123.49, 120.67, 118.40, 116.99, 21.86, 18.10; HRMS (ESI/QTOF) *m*/*z*: calcd for $C_{21}H_{17}N_3O$, 328.1445 $[M + H]^+$; found, 328.1449.

**(2-(5-Chloropyridin-2-yl)-2*H*-indazol-3-yl)(*p*-tolyl)methanone (4j).** Product **4j** was obtained by utilizing the general procedure (Scheme 3) using 2-(5-chloropyridin-2-yl)-2*H*-indazole **1k** (115 mg, 0.5 mmol) and 4-methylbenzaldehyde **2b** (118 μL, 1 mmol) and isolated by column chromatography (hexane : EtOAc = 95 : 05) as a white solid in 71% yield (124 mg, 0.35 mmol); mp: 104–106 °C; $R_f$ (hexane : EtOAc = 85 : 15): 0.38; $^1$H NMR (400 MHz, chloroform-*d*) $\delta$ 8.18–8.17 (m, 1H), 8.03–8.00 (m, 1H), 7.85–7.75 (m, 4H), 7.42–7.34 (m, 2H), 7.24 (d, $J$ = 8.8 Hz, 2H), 7.14–7.10 (m, 1H), 2.41 (s, 3H); $^{13}$C NMR (100 MHz, chloroform-*d*) $\delta$ 186.65, 150.10, 149.12, 146.77, 144.62, 138.41, 135.09, 132.81, 131.34, 129.85, 129.42, 127.98, 124.70, 123.56, 120.59, 118.33, 118.07, 21.80; HRMS (ESI/QTOF) *m*/*z*: calcd for $C_{20}H_{14}ClN_3O$, 348.0898 $[M + H]^+$; found, 348.0895.

**(2-(Pyridin-2-yl)-2*H*-indazol-3-yl)(*p*-tolyl)methanone (4k).** Product **4k** was obtained by utilizing the general procedure (Scheme 3) using 2-(pyridin-2-yl)-2*H*-indazole **1l** (98 mg, 0.5 mmol) and 4-methylbenzaldehyde **2b** (118 μL, 1 mmol) and isolated by column chromatography (hexane : EtOAc = 95 : 05) as a yellow solid in 82% yield (131 mg, 0.42 mmol); mp: 98–100 °C; $R_f$ (hexane : EtOAc = 85 : 15): 0.33; $^1$H NMR (400 MHz, chloroform-*d*) $\delta$ 8.25–8.23 (m, 1H), 8.06–8.04 (m, 1H), 7.89–7.82 (m, 2H), 7.77 (d, $J$ = 8.4 Hz, 2H), 7.46 (d, $J$ = 8.8 Hz, 1H), 7.40–7.35 (m, 1H), 7.23–7.21 (m 3H), 7.16–7.12 (m, 1H), 2.40 (s, 3H); $^{13}$C NMR (100 MHz, chloroform-*d*) $\delta$ 186.81, 151.87, 149.01, 148.04, 144.29, 138.64, 135.30, 132.73, 129.78, 129.30, 127.74, 124.47, 123.50, 123.28, 120.62, 118.35, 117.33, 21.76; HRMS (ESI/QTOF) *m*/*z*: calcd for $C_{20}H_{15}N_3O$, 31.1288 $[M + H]^+$; found, 314.1286.

**Phenyl(2-phenyl-2*H*-indazol-3-yl)methanone (4l).** Product **4l** was obtained by utilizing the general procedure (Scheme 3) using 2-phenyl-2*H*-indazole **1m** (97 mg, 0.5 mmol) and

benzaldehyde **2a** (118 μL, 1 mmol) and isolated by column chromatography (hexane : EtOAc = 95 : 05) as a yellow solid in 80% yield (119 mg, 0.40 mmol); mp: 125–127 °C; $R_f$ (hexane : EtOAc = 85 : 15): 0.42; $^1$H NMR (400 MHz, chloroform-*d*) δ 7.89–7.85 (m, 3H), 7.62–7.57 (m, 1H), 7.55–7.52 (m, 2H), 7.47–7.35 (m, 7H), 7.19–7.15 (m, 1H); $^{13}$C NMR (100 MHz, chloroform-*d*) δ 186.07, 148.66, 140.58, 137.90, 133.67, 132.35, 130.00, 129.18, 129.03, 128.74, 127.12, 125.63, 125.12, 124.16, 120.68, 118.63; HRMS (ESI/QTOF) *m*/*z*: calcd for $C_{20}H_{14}N_2O$, 299.1179 $[M + H]^+$; found, 299.1176.

### General procedure for the synthesis of 11

The starting substrate **1p** was synthesized using the reported procedure[15] and was reacted with *m*-acetoxybenzaldehyde **2r** under the optimized reaction conditions to afford **10**. In the reaction vessel, 2-(3-methoxyphenyl)-2*H*-indazole (**1p**, 112 mg, 0.5 mmol) was charged with *m*-acetoxybenzaldehyde (**2r**, 164 mg, 1 mmol) and TBPB (238 μL, 1.25 mmol) dissolved in chlorobenzene. The reaction mixture was then stirred under $N_2$ atmosphere at 110 °C for 24 h. After completion of the reaction, the reaction mixture was cooled and the work-up was done with a saturated solution of $NaHCO_3$ (10 mL) and ethyl acetate (3 × 20 mL). The combined organic layers were dried over anhydrous $Na_2SO_4$, filtered, and concentrated under reduced pressure to get the crude residue which was further purified through column chromatography on silica gel (100–200 mesh) using hexane : ethyl acetate (95 : 5 ratio) as an eluent to afford the corresponding product **10** which upon deprotection under basic conditions furnished the desire product **11** (anti-inflammatory agent).

**(3-Hydroxyphenyl)(2-(3-methoxyphenyl)-2*H*-indazol-3-yl) methanone (11).** Product **11** was obtained by utilizing the general procedure and isolated by column chromatography (hexane : EtOAc = 95 : 05) as a white solid in 51% yield (87 mg, 0.25 mmol); $R_f$ (hexane : EtOAc = 85 : 15): 0.20; $^1$H NMR (400 MHz, DMSO-$d_6$) δ 9.84 (s, 1H), 7.84 (d, $J$ = 8.8 Hz, 1H), 7.40–7.17 (m, 6H), 7.13 (t, $J$ = 2.4 Hz, 1H), 7.11–7.09 (m, 1H), 7.04–6.96 (m, 3H), 3.72 (s, 3H); $^{13}$C NMR (100 MHz, DMSO-$d_6$) δ 186.09, 160.00, 158.10, 148.30, 141.66, 139.09, 132.77, 130.49, 127.70, 125.58, 123.85, 121.48, 121.08, 120.75, 118.74, 118.22, 116.01, 115.27, 111.66, 56.02; HRMS (ESI/QTOF) *m*/*z*: calcd for $C_{21}H_{16}N_2O_3$, 345.1234 $[M + H]^+$; found, 345.1236.

### General procedure for the synthesis of 13

The starting material **12** was synthesized by utilizing our general procedure which on subjection to Pd-catalyzed direct biaryl coupling using the reported procedure[16] afforded a new class of bio-azaheterocycles, *i.e.*, 3-methoxy-9*H*-dibenzo[4,5:6,7] azepino[1,2-*b*]indazol-9-one (indazole-fused diazepine).

**3-Methoxy-9*H*-dibenzo[4,5:6,7]azepino[1,2-*b*]indazol-9-one (13).** Product **13** was obtained by utilizing the general procedure and isolated by column chromatography (hexane : DCM = 90 : 10) as a yellow solid in 75% yield (123 mg, 0.37 mmol); mp: 108–110 °C; $R_f$ (hexane : DCM = 50 : 50): 0.5; $^1$H NMR (400 MHz, chloroform-*d*) δ 8.14–8.09 (m, 2H), 8.05–8.03 (m, 1H), 7.82 (d, $J$ = 8.8 Hz, 1H), 7.77 (d, $J$ = 7.6 Hz, 1H), 7.66–7.62 (m, 1H), 7.55–7.51 (m, 1H), 7.41–7.37 (m, 1H), 7.31–7.27 (m, 1H), 7.19 (d, $J$ = 2.8 Hz, 1H), 7.09 (dd, $J$ = 9.2, 2.8 Hz, 1H), 3.89 (s, 3H); $^{13}$C NMR (100 MHz, chloroform-*d*) δ 183.27, 159.12, 148.62, 139.52, 138.11, 134.80, 132.75, 131.61, 130.70, 130.17, 129.16, 128.72, 127.93, 127.60, 125.89, 123.69, 121.09, 118.05, 116.36, 115.47, 55.84; HRMS (ESI/QTOF) *m*/*z*: calcd for $C_{21}H_{14}N_2O_2$, 327.1128 $[M + H]^+$; found, 327.1126.

### General procedure for the synthesis of 14

To a solution of **3a** (0.29 mmol; 1.0 equiv.) in methanol (10–15 mL) was added $NaBH_4$ (0.58 mmol; 2.0 equiv.) portionwise at room temperature and the reaction was stirred at the same temperature for 1 h. After completion of the reaction monitored by TLC, the solvent was evaporated under reduced pressure and the crude solid product was extracted with ethyl acetate (3 × 20 mL) and water (10 mL). The combined organic layers were dried over anhydrous $Na_2SO_4$, filtered, and concentrated under reduced pressure to get the crude residue which was further purified through column chromatography on silica gel (100–200 mesh) using hexane : ethyl acetate (80 : 20 ratio) as an eluent to afford the corresponding product **14** as a white solid in 90% yield.

**(2-(4-Methoxyphenyl)-2*H*-indazol-3-yl)(*p*-tolyl)methanol (14).** Product **14** was obtained by utilizing the general procedure and isolated by column chromatography (hexane : EtOH = 80 : 20) as a white solid in 90% yield (90 mg, 0.26 mmol); mp: 106–108 °C; $R_f$ (hexane : EtOH = 70 : 30): 0.3; $^1$H NMR (400 MHz, chloroform-*d*) δ 7.51 (d, $J$ = 9.2 Hz, 1H), 7.39 (d, $J$ = 9.2 Hz, 1H), 7.15–7.09 (m, 3H), 7.04 (d, $J$ = 8.4 Hz, 2H), 6.98 (d, $J$ = 8.0 Hz, 2H), 6.87–6.83 (m, 1H), 6.69 (d, $J$ = 8.8 Hz, 2H), 5.93 (s, 1H), 3.69 (s, 3H), 2.22 (s, 3H); $^{13}$C NMR (101 MHz, chloroform-*d*) δ 159.98, 148.56, 138.37, 137.65, 137.54, 132.49, 129.26, 127.48, 126.69, 126.47, 121.84, 121.40, 120.39, 117.40, 114.16, 68.75, 55.62, 21.25; HRMS (ESI/QTOF) *m*/*z*: calcd for $C_{22}H_{20}N_2O_2$, 345.1598 $[M + H]^+$; found, 345.1596.

### General procedure for the competition reaction

A mixture of 2-(4-methoxyphenyl)-2*H*-indazole **1a** (112 mg, 0.5 mmol), 4-methoxybenzaldehyde **2c** (61 μL, 0.5 mmol) and 4-fluorobenzaldehyde **2e** (53 μL, 0.5 mmol) and TBPB (238 μL, 1.25 mmol) was taken in a sealed reaction tube under nitrogen atmosphere. Then, the reaction mixture was stirred at 110 °C for 24 h. After completion of the reaction, the reaction mixture was cooled and the work-up was done with a saturated solution of $NaHCO_3$ (10 mL) and ethyl acetate (3 × 20 mL). The combined organic layers were dried over anhydrous $Na_2SO_4$, filtered, and concentrated under reduced pressure to get the crude residue which was further purified through column chromatography on silica gel (100–200 mesh) using hexane : ethyl acetate (95 : 5 ratio) as an eluent to afford the corresponding product **3c** in 56% (101 mg, 0.28 mmol as a yellow solid) and **3e** in 30% (52 mg, 0.15 mmol as a yellow solid) yields, respectively. Similarly, a mixture of 2-(4-methoxyphenyl)-2*H*-indazole **1a** (112 mg, 0.5 mmol), 4-methylbenzaldehyde **2a** (59 μL, 0.5 mmol) and acetaldehyde **2j** (28 μL, 0.5 mmol) and TBPB (238 μL, 1.25 mmol) was taken in a sealed reaction tube under nitrogen atmosphere. Then the reaction mixture was stirred at 110 °C for

24 h. After work-up, the crude residue was further purified through column chromatography on silica gel (100–200 mesh) using hexane : ethyl acetate (95 : 5 ratio) as an eluent to afford the corresponding product **3a** in 55% (94 mg, 0.27 mmol as a yellow solid) and **3j** in 29% (39 mg, 0.14 mmol as a yellow solid) yields, respectively.

#### Synthetic procedure for performing the control experiment

A mixture of 2-(4-methoxyphenyl)-2*H*-indazole **1a** (112 mg, 0.5 mmol), 4-methylbenzaldehyde **2a** (118 μL, 1 mmol) and TBPB (238 μL, 1.25 mmol) and TEMPO (195 mg, 1.25 mmol) was taken in a sealed reaction tube under nitrogen atmosphere. Then, the reaction mixture was stirred at 110 °C for 24 h. After completion of the reaction, the reaction mixture was cooled and the work-up was done with a saturated solution of $NaHCO_3$ (10 mL) and ethyl acetate (3 × 20 mL). The combined organic layers were dried over anhydrous $Na_2SO_4$, filtered, and concentrated under reduced pressure to get the crude residue which was further purified through column chromatography on silica gel (100–200 mesh) using hexane : ethyl acetate (95 : 5 ratio) as an eluent to afford the TEMPO trapped acyl adduct (7) as a viscous liquid. TLC observation showed that there was no formation of **3a** in the TEMPO-assisted reaction. The intermediate, *i.e.* benzoyl free radical, was trapped with TEMPO to afford the TEMPO-acyl adduct 7.

**2,2,6,6-Tetramethylpiperidin-1-yl 4-methylbenzo-ate 7.** Product 7 was obtained in 71% yield as a viscous liquid; $R_f$ (hexane : ethyl acetate = 85 : 15) 0.5; $^1$H NMR (400 MHz, chloroform-*d*) $\delta$ 7.93 (d, $J$ = 8.4 Hz, 2H), 7.21 (d, $J$ = 8.0 Hz, 2H), 2.37 (s, 3H), 1.77–1.63 (m, 3H), 1.55–1.52 (m, 2H), 1.43–1.40 (m, 1H), 1.23 (s, 6H), 1.08 (s, 6H); $^{13}$C NMR (100 MHz, chloroform-*d*) $\delta$ 166.50, 143.56, 129.66, 129.22, 128.52, 126.98, 60.40, 39.11, 32.03, 25.43, 21.72, 20.91, 17.08; HRMS (ESI/QTOF) *m*/*z*: calcd for $C_{17}H_{25}NO_2$, 276.1958 $[M + H]^+$; found, 276.1955.

## Conflicts of interest

The author declares no competing financial interest.

## Acknowledgements

S. C. acknowledges DST-NRF Indo-South Africa Joint research project [DST/INT/South Africa/P-19/2016]. R. S. acknowledges MNIT Jaipur for providing an institute fellowship. L. Y. and R. K. Y. thanks DST, New Delhi and UGC, New Delhi for providing financial assistance in the form of a senior research fellowship. Materials Research Centre (MRC), MNIT Jaipur is gratefully acknowledged for providing analytical facilities.

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