JOC The Journal of Organic Chemistry

Albright COLLEGE

Subscriber access provided by ALBRIGHT COLLEGE

Article

Regioselective C3-H trifluoromethylation of 2H-indazole under transition-metal-free photoredox catalysis

Arumugavel Murugan, Venkata Nagarjuna Babu, Ashok Polu, Nagaraj Sabarinathan, Manickam Bakthadoss, and Duddu S. Sharada

J. Org. Chem., **Just Accepted Manuscript** • Publication Date (Web): 22 May 2019

Just Accepted

is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

Regioselective C3-H trifluoromethylation of 2*H*-indazole under transition-metal-free photoredox catalysis

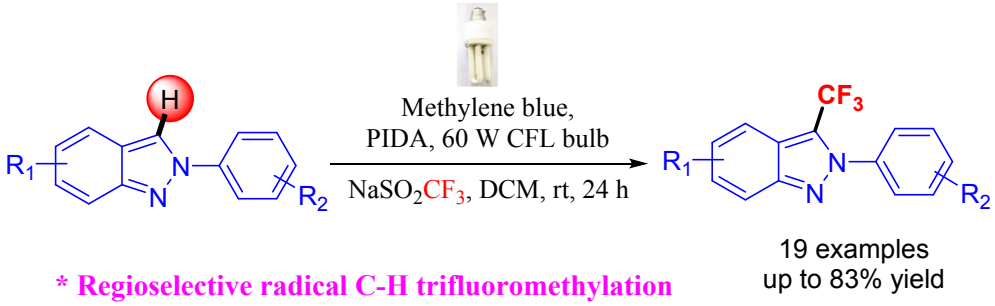
Arumugavel Murugan,† Venkata Nagarjuna Babu,† Ashok Polu,† Nagaraj Sabarinathan,† Manickam Bakthadoss*‡ and Duddu S. Sharada*†

†Catalysis & Chemical Biology Laboratory, Department of Chemistry, Indian Institute of Technology Hyderabad, Kandi – 502285, Sangareddy, Telangana, INDIA, Phone: +91 8106644794; Fax: (040) 2301 6032.

E-mail: sharada@iith.ac.in *Web:* http://drsharadagroup.wixsite.com/sharada

‡Department of Chemistry, Pondicherry University, Pondicherry 605 014, INDIA

Phone: (0413) 2654 830; E-mail: bhakthadoss@yahoo.com



*** Regioselective radical C-H trifluoromethylation**
*** Chelation-free and metal-free C-H functionalization**
*** Inexpensive and benchtop-stable CF_3 radical source**
*** Scale-up synthesis**

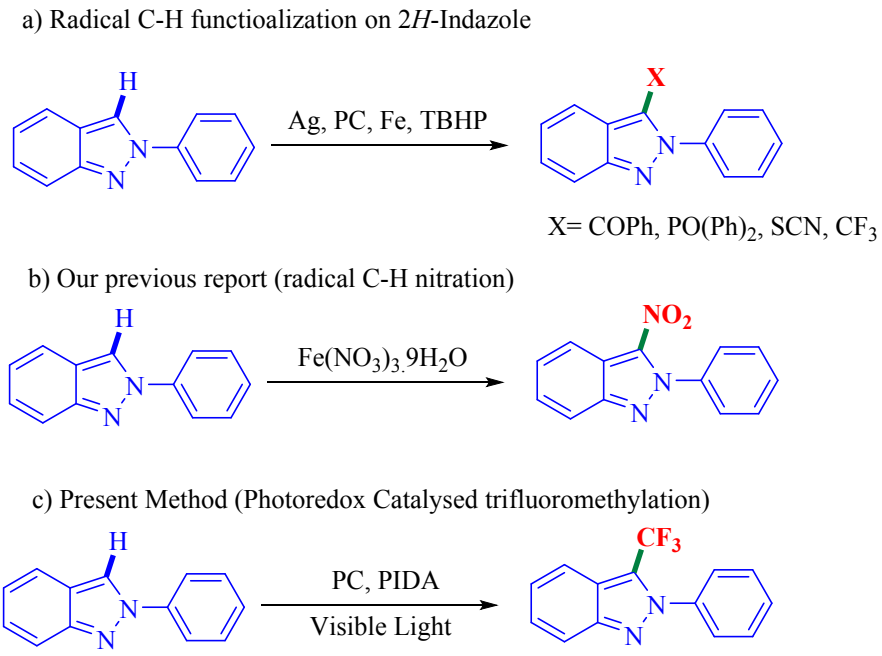
Abstract: The trifluoromethylation-substituted heteroarenes are biologically active compounds and useful building blocks. In this sequence, we have developed a visible-light-promoted regioselective C3-H trifluoromethylation of 2*H*-indazole under metal-free conditions which proceed *via* a radical mechanism. The combination of photocatalysis and hypervalent iodine reagent provides a practical approach to a library of trifluoromethylated indazoles in 35-83% yields.

Introduction

Halo-organic compounds are typically considered as sites of high electron density because of their high electronegativity. In general, the halogen atoms can form attractive interaction due to electron donor sites (*i.e.* nucleophiles).[1] Among them, the C-F bond finds important application in the field of synthetic and medicinal chemistry, Which is owed to the similar size and increased electronegativity of fluorine over hyderogen.[2] In this context, the trifluoromethyl group represents important structural motif in agrochemicals, pharmaceuticals, and drug candidates. The CF_3 moieties can enhance in metabolic

stability, increase lipophilicity, bioavailability, and hydrolytic stability. Further, the trifluoromethyl-containing organic compounds are commonly applied in material such as liquid crystals.[3]

Over the past decade, due to the importance of trifluoromethylation process, several methods have been developed, using various radical, nucleophilic, and electrophilic trifluoromethylating agents such as CF_3I,[4] CF_3SO_2Cl,[5] CF_3COOH,[6] Ruppert-Prakash reagent ($TMSCF_3$),[7] Tognis' reagent,[8] Umemotos' reagent[9] and Baran reagent $(CF_3SO_2)_2Zn$[10] and Langlois' (CF_3SO_2Na)[11]. Among these, Langlois' reagent is benchtop-stable, inexpensive, easy to handle and convenient reagent for trifluoromethylation.[12] Despite these developments, the approach for radical trifluoromethylation of arenes and heteroarenes have achieved over the past years.[13]



Scheme 1: Regioselective C3-H functionalization of 2*H*-indazole

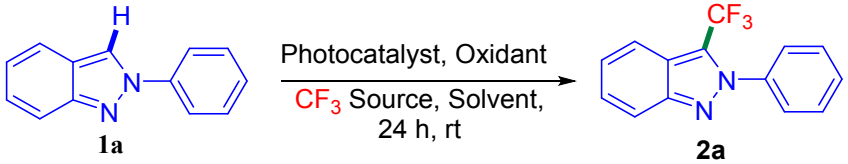
In recent years, the visible light induced photoredox catalytic activation of organic molecules has been established as a powerful strategy in modern organic synthesis which provide attractive features, like mild, environmentally benign, excellent functional group tolerance, and high reactivity.[14] The photoredox strategy can involve *via* single-electron-transfer (SET) process upon irradiation with visible light using metal complexes and organic dyes as photocatalyst.[15] Moreover, the usage of organic dyes

is inexpensive and easy to handle as photoredox catalysts, and hence this would be an excellent substitute to inorganic transition-metal photocatalyst.

Nitrogen-containing heterocycle compounds have gained significant importance in natural products and they exhibit a wide range of biological activities.[16] Among them, indazoles are broadly known for their bioactivities[17] such as antitumor,[18] antimicrobial,[19] anti-inflammatory,[20] anti-HIV,[21] anti-platelet[22] and anti-contraceptive.[23] Considering the immense importance of derivatives of 2*H*-indazoles, extensive efforts have been devoted for the synthesis and functionalization of 2*H*-indazole.[24] Recently, Oh *et.al* have reported the silver-catalyzed direct acyl radical addition to 2*H*-indazole[25a] and Hajra *et al.* have also realized the construction of carbon-phosphorus (C-P)[25b] and carbon-sulfur (C-S)[25c] bond formations on 2*H*-indazole (Scheme 1a). Very recently, Hajra *et.al* have described a new approach for the direct C3-trifluoromethylation of 2*H*-indazole mediated by peroxides (Scheme 1a).[25d] The C3-H functionalization of 2*H*-indazoles has few disadvantages such as usage of transition-metal catalyst, peroxides and high temperature. Encouraged by the significant advances in the recent radical C-H functionalization,[26] our group initiated the research program on the C-H functionalization of indazoles.[27] Herein, we report a novel metal-free visible-light-promoted organic dye catalyzed regioselective C3-trifluoromethylation of 2*H*-indazole. An initial version of this work was deposited in ChemRxiv on 5th March-2019.[28]

Results and Discussion

Table 1. Optimization of Reaction Conditions for the Synthesis of 2a[a]



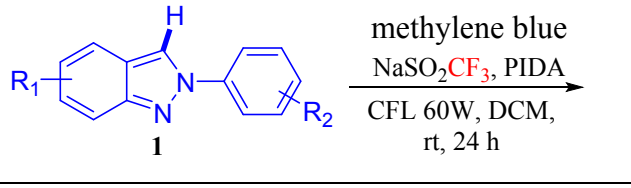
entry	catalyst	oxidants	CF_3 Source	Solvent	yield (%)[b]
1	rose bengal	PIDA	$NaSO_2CF_3$	DCM	60

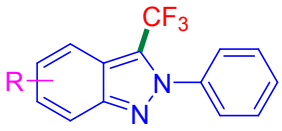
2	rose bengal	$K_2S_2O_8$	$NaSO_2CF_3$	DCM	n.d
3	rose bengal	TBHP	$NaSO_2CF_3$	DCM	n.d
4	rose bengal	IBA-OAc	$NaSO_2CF_3$	DCM	Trace
5	rose bengal	PhIO	$NaSO_2CF_3$	DCM	Trace
6	rose bengal	-	$NaSO_2CF_3$	DCM	n.d
7	-	PIDA	$NaSO_2CF_3$	DCM	Trace
8	$Ru(bpy)_3Cl_2$	PIDA	$NaSO_2CF_3$	DCM	Trace
9	$Ir(ppy)_3$	PIDA	$NaSO_2CF_3$	DCM	Trace
10	eosin-Y	PIDA	$NaSO_2CF_3$	DCM	50
11	rhodamine B	PIDA	$NaSO_2CF_3$	DCM	Trace
12	**methylene blue**	**PIDA**	$NaSO_2CF_3$	**DCM**	**75**
13	azure-B	PIDA	$NaSO_2CF_3$	DCM	55
14	riboflavin	PIDA	$NaSO_2CF_3$	DCM	Trace
15	methylene blue	PIDA	$NaSO_2CF_3$	CH_3CN	30
16	methylene blue	PIDA	$NaSO_2CF_3$	DCE	50
17	methylene blue	PIDA	$NaSO_2CF_3$	Acetone	Trace
18	methylene blue	PIDA	$NaSO_2CF_3$	DMSO	n.d
19	methylene blue	PIDA	$NaSO_2CF_3$	Toluene	n.d
20	methylene blue	PIDA	$NaSO_2CF_3$	MeOH	n.d
21	methylene blue	PIDA	$NaSO_2CF_3$	EtOH	n.d
22	methylene blue	PIDA	$NaSO_2CF_3$	Dioxane	n.d
23	methylene blue	PIDA	$NaSO_2CF_3$	DMF	n.d
24	methylene blue	PIDA	$TMSCF_3$	DCM	n.d
25	methylene blue	PIDA	ICH_2CF_3	DCM	n.d
26	methylene blue	PIDA	CF_3SO_2Cl	DCM	n.d

[a]Reaction conditions:**1a** (1 mmol), methylene blue (1 mol%), PIDA (2 mmol), $NaSO_2CF_3$ (2 mmol), DCM (1 mL), 60 W CFL blub, rt, 24 h. [b]Isolated yield of chromatographically pure products. n.d = not detected.

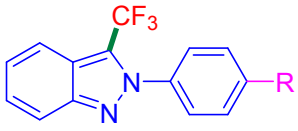
In the initial experiments, we have chosen 2-phenyl-2*H*-indazole as the model substrate, Langlois' reagent as radical CF_3 source and phenyliodine(III) diacetate (PIDA) as an oxidant with 2 mol% rose bengal as a photocatalyst in MeCN and irradiated with 60 W Compact Fluorescent Bulb (CFL) at room temperature for 24 h. Delightfully, we observed C3-trifluoromethylated product **2a** with 60% yield (Table 1, entry 1). Then, the effect of other oxidants such as $K_2S_2O_8$, TBHP, IBA-OAc, and PhIO was examined (table 1, entry 2-5). Unfortunately, our attempts went in vain. To improve the reaction efficiency in terms of yield, we have tested the various photocatalysts. Among all, methylene blue (Table 1, entry 12) was found to be effective photocatalyst and provided the desired product **2a** with 75% yield. Among the solvents screened (table 1, entry 15-23), DCM was found to be the most efficient solvent for this strategy. To improve the yield, a variety of CF_3 sources were examined, but without much success (table 1, entry 24-26).

Table 2. Substrate scope for the C3-trifluoromethylation of 2*H*-indazole [a,b]

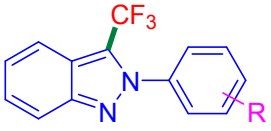




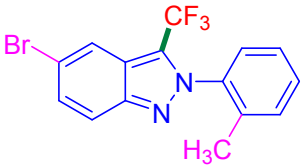
R = H	**2a**	75%
R = 6-Cl	**2b**	35%
R = 6-Br	**2c**	37%
R = 5-Br	**2d**	43%



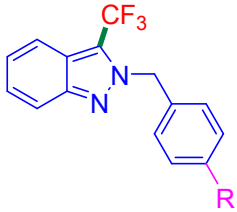
R = F	**2e**	45%
R = Cl	**2f**	53%
R = Br	**2g**	62%
R = I	**2h**	68%



R = *o*-CH_3	**2i**	45%
R = *o*-OMe	**2j**	42%
R = *m*-CH_3	**2k**	64%
R = *m*-OMe	**2l**	70%
R = *p*-CH_3	**2m**	83%
R = *p*-OMe	**2n**	83%
R = *m*-$(CO)CH_3$	**2o**	40%
R = *o*, *m*, *p*-OCH_3	**2p**	80%



2q (42%)



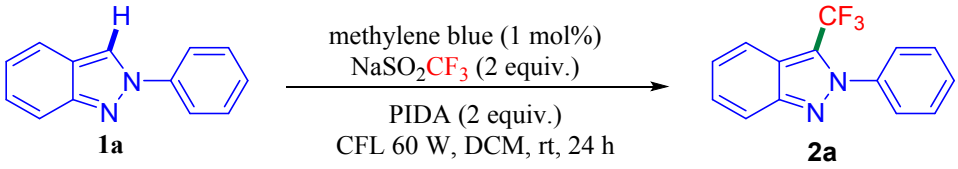
R = H	**2r**	55%
R = CH_3	**2s**	45%

[a]Reaction Conditions: **1a** (1 mmol), methylene blue (1 mol%), PIDA (2 mmol), $NaSO_2CF_3$ (2 mmol), DCM (1 mL), 60 W CFL blub, rt, 24 h. [b]Isolated yield of chromatographically pure products.

With the established optimized reaction conditions (table 1, entry 12), we have examined the scope of this protocol with various substitutions on 2*H*-indazoles (table 2). Initially, we checked the halogen substitution on 2*H*-indazole (**2b-h**). The presence of halogen at C5 and C6-positions of 2*H*-indazoles (**2b-d**) gave poor yields. The halogen substituent at *para* position of the amine partner of 2*H*-indazoles (**2e-h**) gave 45% to 68% yields. Likewise, the amine partner of 2*H*-indazoles bearing electron-donating groups (-Me, -OMe) resulted in the products with very good yields (**2i-n** & **2p**). This might be due to the increased electron density at C3-position of 2*H*-indazole. This observation was similar to our earlier report.[27a]

However, the electron donating groups (-Me, -OMe) at *ortho* position (**2i**, **2j**) gave moderate yields; this is due to the steric hindrance of the *ortho* substitution. We observed poor yield, while the electron-withdrawing group substituted on 2*H*-indazole (**2o**), because the electron density might be reduced at C3-position on 2*H*-indazole. In the case of benzylamine partner, the C3-H trifluoromethylated indazoles (**2r, 2s**) were obtained in low yield.

Scheme 2. Gram-scale synthesis of 2-phenyl-3-(trifluoromethyl)-2*H*-indazole **2a**

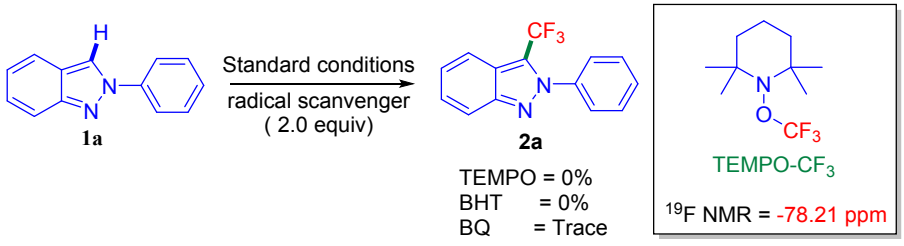


1 g, 5.15mmol

0.932 g, 69 %

Due to the presence of 2*H*-indazole skeleton in various biologically relevant compounds, we have also evaluated the scalability of our protocol. Consequently, when we performed the reaction on 1g scale, it produced the C3-trifluoromethylation of 2*H*-indazole **2a** with 69% yield (Scheme 2).

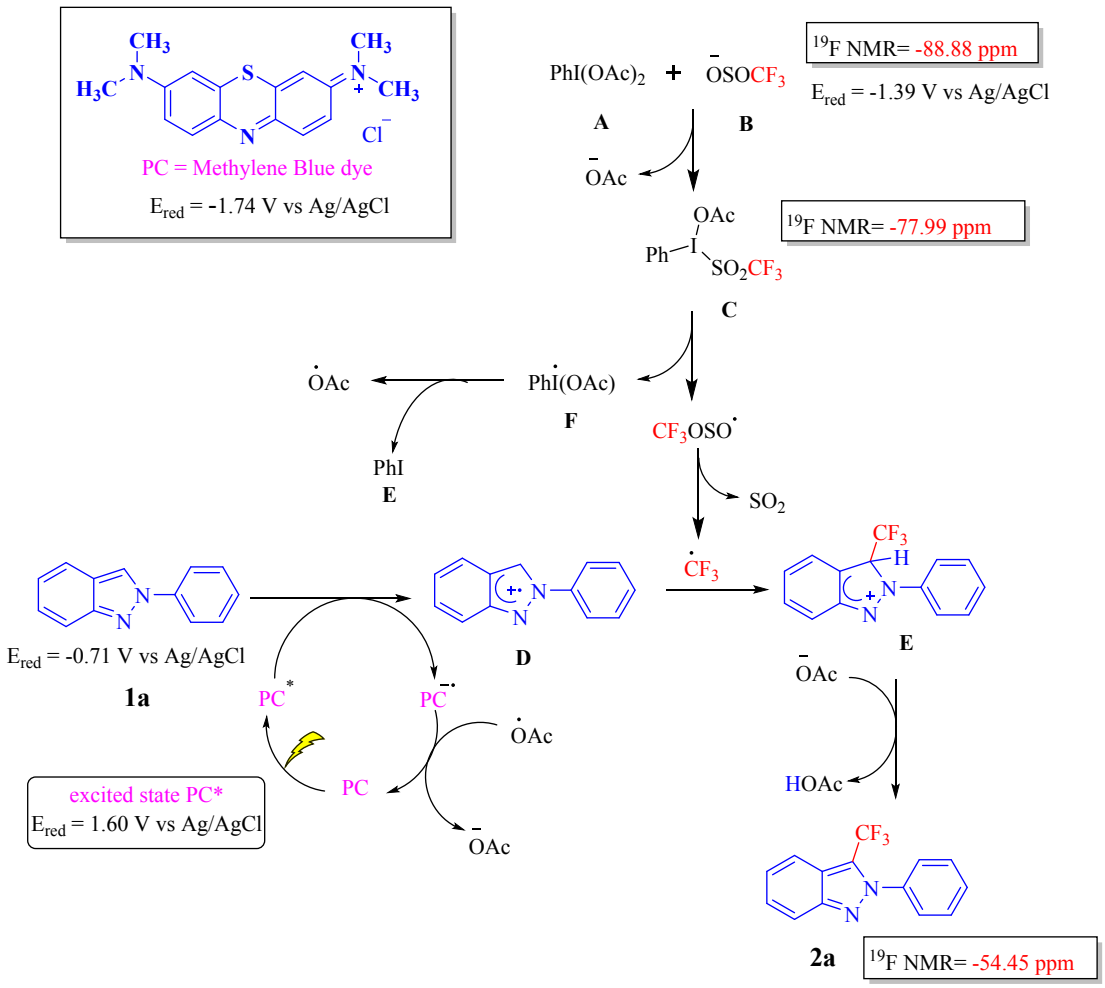
Scheme 3. Control Experiments



To investigate the reaction mechanism, we performed few control experiments as shown in scheme 3. We observed that 2-phenyl-2*H*-indazole **1a** failed to produce the corresponding trifluoromethylation product **2a** in the presence of radical scavengers such as TEMPO, BHT and BQ. Also, we observed the intermediate **C** and TEMPO-CF_3 adduct in ^{19}F NMR. These results indicate that the reaction mechanism proceeded through the radical pathway as depicted in scheme 4. Moreover, we have performed NMR experiments to confirm intermediates, however we did not observe the peaks corresponding to any hypervalent iodine complexes other than iodobenzene peaks in NMR spectra. In addition, we measured the redox potentials for the 2*H*-indazole **1a** (E_{red} = −0.71 V vs Ag/AgCl), Langlois' reagent (E_{red} = −1.39 V vs Ag/AgCl), photocatalyst (**PC**) (E_{red} = −1.74 V vs Ag/AgCl), using cyclic voltammetry (see SI) and reduction potential for excited state photocatalyst (**PC***) (E_{red} = 1.60 V vs Ag/AgCl).[29] The reduction potentials of 2*H*-indazole and excited state photocatalyst (**PC***) clearly signifies that 2*H*-indazole **1a** has the potential to transfer a single electron to excited state photocatalyst (**PC***), thus supporting the proposed mechanism.

Based on the control experiment results and the previous literature reports,[27] a plausible reaction mechanism of the present trifluoromethylation of 2-phenyl-2*H*-indazole is depicted in scheme 4. Initially, the CF_3 radical species would be generated by the reaction of $NaSO_2CF_3$ (**B**) with PIDA (**A**) via intermediate **C**. Meanwhile, the photocatalyst (**PC**) converted to its excited state **PC*** upon the absorption of photons from visible light. The **PC*** produce the indazole radical cation **D** from the oxidation of indazole along with the generation of photocatalytic radical anion $\mathbf{PC}^{\bullet-}$ through single-electron-transfer (SET) process. After that, the photocatalyst radical anion ($\mathbf{PC}^{\bullet-}$) is oxidized to **PC** by reducing acetate radical to acetate anion. Then the generated CF_3 radical would attack intermediate **D** to form intermediate **E** which on deprotonation would result in trifluoromethylation product **2a**.

Scheme 4. Plausible reaction mechanism



Conclusions

We have successfully demonstrated a novel photoredox catalyzed regioselective C3-H trifluoromethylation of 2*H*-indazoles. This protocol offers the transition metal-free photoredox catalyzed C3-H trifluoromethylation of 2*H*-indazole. This method utilizes an inexpensive and benchtop-stable Langlois' reagent under mild reaction conditions. Further the developed protocol for regioselective trifluoromethylation of 2*H*-indazole would be great significance in pharmaceutical chemistry and material sciences.

Experimental Section

General Considerations

IR spectra were recorded on an FTIR spectrophotometer. ^{1}H NMR spectra were recorded on 400 MHz spectrometers at 295 K in $CDCl_3$; chemical shifts (δ ppm) and coupling constants (Hz) are reported in standard fashion concerning either internal standard tetramethylsilane (TMS) (δ_H = 0.00 ppm) or $CHCl_3$ (δ_H = 7.25 ppm). ^{13}C NMR spectra were recorded on 100 MHz spectrometers at RT in $CDCl_3$; chemical shifts (δ ppm) are reported relative to $CHCl_3$ [δ_C = 77.00 ppm (central line of the triplet)]. In the 1HNMR, the following abbreviations were used throughout: s = singlet, d = doublet, t = triplet, q = quartet, qui = quintet, m = multiplet and br s. = broad singlet. The assignment of signals was confirmed by ^{1}H, ^{13}C and DEPT spectra. High-resolution mass spectra (HR-MS) were recorded using a Q-TOF multimode source. Melting points were determined on an electrothermal melting point apparatus and are uncorrected. All dry solvents were used, toluene was dried over sodium metal and DMSO, CH_3CN and DMF were dried over calcium hydride and which are commercially available.

All small scale dry reactions were carried out using a standard syringe-septum technique. Reactions were monitored by TLC on silica gel using a combination of petroleum ether and ethyl acetate as eluents. Reactions were generally run under argon, nitrogen and oxygen atmosphere wherever necessary. Solvents were distilled before use; petroleum ether with a boiling range of 40 to 60 ˚C was used. Acme's silica gel (60–120 mesh) was used for column chromatography (approximately 20g per one gram of crude material). All 2-azidobenzaldehydes (**A-B and C**) except **D** have been synthesized by using literature known procedures. [30,27c]

General procedure (GP-I) for the synthesis of 2-phenyl-2*H*-indazole:[27f]

Azidobenzaldehyde **1** (1 mmol), aniline **2** (1 mmol) were taken in a 10 mL oven dried schlenck tube and it was closed with stopcock with argon balloon and placed in an external heating oil bath at 120 ˚C for 1-3 hrs (oil bath temperature). After completion of the starting material, the mixture was cooled to room temperature and was purified on a silica gel column chromatography (hexane/ethylacetate 90:10) which furnished the respective products **1a-s.**

General procedure (GP-II) for the synthesis of 2-phenyl-3-(trifluoromethyl)-2*H*-indazole:

In an oven-dried reaction vessel equipped charged with 2-phenyl-2*H*-indazole (1 mmol), PIDA (2 mmol), sodium triflate (2 mmol) were added and followed by addition of DCM (1 mL). The resulting reaction mixture was irradiated using a 60 W CFL bulb. The progress of the reaction was monitored by TLC until the reaction was completed. The reaction mixture was quenched by addition of aq. NH_4Cl solution and extracted with ethyl acetate (3 × 10 mL). The organic layer was dried (Na_2SO_4) and concentrated in a vacuum. Purification of the residue on a silica gel column chromatography using petroleum ether/ethyl acetate as (petroleum ether/ethylacetate 97:3 to 95:5) eluent furnished the product trifluoromethylated indazoles **2a-s**.

Characterization Data of the Products

2-phenyl-3-(trifluoromethyl)-2*H*-indazole (2a) Dark yellow Solid (50 mg, 75%), mp 40-42 ℃; IR (MIR-ATR, 4000–600 cm^{-1}): υmax = 3736, 3673, 3613, 3565, 3032, 2968, 2381, 1734, 1700, 1650, 1556, 1540, 1521, 1508, 1458, 1420, 1218, 1120, 940, 757, 667, 631; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 7.79 - 7.87 (m, 2H), 7.52 - 7.63 (m, 5H), 7.39 - 7.45 (m, 1H), 7.28 - 7.34 (m, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): 148.2, 139.6, 130.0, 29.1, 127.3, 126.1, 125.1, 123.5 (q, $J_{C\text{-}F}$ = 40.0 Hz), 121.3 (q, $J_{C\text{-}F}$ = 269.0 Hz), 119.4, 118.4; ^{19}F NMR ($CDCl_3$, 376 MHz): −54.5; HR-MS (ESI-TOF) m/z: $[M+H]^+$ calcd for $[C_{14}H_{10}F_3N_2]^+$ = 263.0791; found: 263.0794.

6-chloro-2-phenyl-3-(trifluoromethyl)-2*H*-indazole (2b): Dark orange Solid (29 mg, 35%), mp 44-46 ℃; IR (MIR-ATR, 4000–600 cm^{-1}): *υ*max = 3673, 3613, 3565, 3525, 3068, 2926, 2854, 2355, 1695, 1634, 1596, 1549, 1502, 1470, 1439, 1314, 1290, 1222, 1178, 1126, 1104, 999, 768, 691, 621, 544; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 7.73 (d, 1H, *J* = 8.8 Hz), 7.56 - 7.41 (m, 5H), 7.34 (s, 1H), 6.95 - 6.87 (m, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ = 148.4, 139.6, 139.3, 135.5, 129.8 (q, $J_{C\text{-}F}$ = 36.0 Hz), 127.7, 126.0, 121.4 (q, $J_{C\text{-}F}$ = 252.0 Hz), 119.4, 119.3, 105.7; ^{19}F NMR ($CDCl_3$, 376 MHz): −54.7; HR-MS (ESI-TOF) m/z: $[M+H]^+$ calcd for $[C_{14}H_9ClF_3N_2]^+$ = 297.0401; found: 297.0408.

6-bromo-2-phenyl-3-(trifluoromethyl)-2*H*-indazole (2c): Yellow Solid (27 mg, 37%), mp 42-44 ℃; IR (MIR-ATR, 4000–600 cm^{-1}): *υ*max = 2116, 2032, 1596, 1540, 1502, 1462, 1432, 1305, 1220, 1179, 1127, 1106, 998, 934, 798, 768, 692, 571, 515; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.04 - 7.98 (m, 1H), 7.71 (dd, 1H, J_a = 1.5 and J_b= 9.8 Hz), 7.62 - 7.51 (m, 5H), 7.38 (dd, 1H, J_a = 1.7 and J_b = 9.0 Hz); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ = 148.7, 139.2, 129.8 (q, $J_{C\text{-}F}$ = 42.0 Hz), 128.9, 126.0, 121.9 (q, $J_{C\text{-}F}$ = 268.0 Hz), 120.7, 120.0, 119.2; ^{19}F NMR ($CDCl_3$, 376 MHz): −54.7; HR-MS (ESI-TOF) m/z: $[M+H]^+$ calcd for $[C_{14}H_9BrF_3N_2]^+$ = 340.9896; found: 340.9914.

5-bromo-2-phenyl-3-(trifluoromethyl)-2*H*-indazole (2d): Dark yellow Solid (31 mg, 43%), mp 52-54 ℃; IR (MIR-ATR, 4000–600 cm^{-1}): *υ*max = 3648, 3588, 3547, 3070, 2924, 2321, 1735, 1596, 1502, 1420, 1271, 1216, 1169, 1124, 1107, 1043, 996, 861, 804, 768, 692, 634, 596; ^{1}H NMR ($CDCl_3$, 400 MHz) δ_H = 8.01 (s, 1H), 7.70 (d, 1H, *J* = 9.3 Hz), 7.62 - 7.50 (m, 4H), 7.50 - 7.42 (m, 2H); $^{13}C\{^1H\}$

NMR ($CDCl_3$, 100 MHz): δ = 146.6, 139.3, 137.9, 132.5, 129.8 (q, $J_{C\text{-}F}$ = 36.0 Hz), 124.6, 123.0, 122.6, 121.9 (q, $J_{C\text{-}F}$ = 248.0 Hz), 120.1, 118.6, 116.5, 112.7; ^{19}F NMR ($CDCl_3$, 376 MHz): −54.6; HR-MS (ESI-TOF) m/z: $[M+H]^+$ calcd for $[C_{14}H_9BrF_3N_2]^+$ = 340.9896; found: 340.9900.

2-(4-fluorophenyl)-3-(trifluoromethyl)-2*H*-indazole (2e): Yellow Solid (50 mg, 45%), mp 52-54 ℃; IR (MIR-ATR, 4000–600 cm^{-1}): υmax = 3689, 3620, 3568, 3036, 2938, 2321, 1717, 1540, 1502, 1454, 1252, 1216, 1156, 1118, 1107, 1032, 987, 861, 767, 659, 631; ^1H NMR ($CDCl_3$, 400 MHz): δ_H = 7.86 - 7.75 (m, 2H), 7.62 - 7.53 (m, 2H), 7.45 - 7.39 (m, 1H), 7.31 (dd, 1H, J_a = 6.8 and J_b = 8.3 Hz,), 7.26 - 7.21 (m, 2H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ = 164.5 (d, $J_{C\text{-}F}$ = 249.0 Hz), 149.7, 148.2, 135.6 (d, $J_{C\text{-}F}$ = 2.0 Hz), 128.1 (d, $J_{C\text{-}F}$ = 9.0 Hz), 127.4, 125.5, 123.6 (q, $J_{C\text{-}F}$ = 40.0 Hz), 121.5, 121.0 (q, $J_{C\text{-}F}$ = 268.0 Hz), 119.4, 118.4, 116.5 (d, $J_{C\text{-}F}$ = 24.0 Hz); ^{19}F NMR ($CDCl_3$, 376 MHz): −54.5, -110.2; HR-MS (ESI-TOF) m/z: $[M+H]^+$ calcd for $[C_{14}H_9F_4N_2]^+$ = 281.0696; found: 281.0690.

2-(4-chlorophenyl)-3-(trifluoromethyl)-2*H*-indazole (2f): Dark yellow solid (35 mg, 53%), mp 46-48 ℃; IR (MIR-ATR, 4000–600 cm^{-1}): υmax = 3673, 3613, 3547, 3068, 2317, 2089, 1552, 1522, 1498, 1432, 1298, 1220, 1176, 1118, 1089, 1017, 998, 929, 832, 746, 728, 583, 537; ^1H NMR ($CDCl_3$, 400 MHz): δ_H = 7.76 - 7.68 (m, 2H), 7.49 - 7.39 (m, 4H), 7.34 - 7.29 (m, 1H), 7.24 - 7.17 (m, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ = 148.4, 138.0, 136.1, 129.8 (q, $J_{C\text{-}F}$ = 47.0 Hz), 127.5, 127.4, 125.7, 123.9, 122.3, 122.2, 121.7, 119.9 (q, $J_{C\text{-}F}$ = 231.0 Hz), 118.4; ^{19}F NMR ($CDCl_3$, 376 MHz): −54.3; HR-MS (ESI-TOF) m/z: $[M+H]^+$ calcd for $[C_{14}H_9ClF_3N_2]^+$ = 297.0401; found: 297.0401.

2-(4-bromophenyl)-3-(trifluoromethyl)-2*H*-indazole (2g): Dark yellow (45 mg, 62%), mp 44-46 ℃; IR (MIR-ATR, 4000–600 cm^{-1}): υmax = 3673, 3613, 3547, 3068, 1521, 1495, 1432, 1298, 1222, 1176, 1119, 1099, 1068, 1015, 996, 929, 829, 743, 711, 576, 535; ^1H NMR ($CDCl_3$, 400 MHz): δ_H = 7.84 - 7.78 (m, 2H), 7.70 - 7.64 (m, 2H), 7.46 (d, 2H, J = 8.3 Hz), 7.43 - 7.37 (m, 1H), 7.31 - 7.25 (m, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ = 148.4, 138.6, 132.8 (q, $J_{C\text{-}F}$ = 43.0 Hz), 127.8, 127.6, 125.3, 124.2, 123.9, 122.5 (q, $J_{C\text{-}F}$ = 223.0 Hz), 119.4, 118.4; ^{19}F NMR ($CDCl_3$, 376 MHz): −54.3; HR-MS (ESI-TOF) m/z: $[M+H]^+$ calcd for $[C_{14}H_9BrF_3N_2]^+$ = 340.9896; found: 340.9900.

2-(4-iodophenyl)-3-(trifluoromethyl)-2*H*-indazole (2h): Light yellow (40 mg, 68%), mp 100-102 ℃; IR (MIR-ATR, 4000–600 cm^{-1}): υmax = 3736, 3547, 3462, 3032, 2917, 2356, 2154, 1716, 1683, 1556, 1540, 1509, 1362, 1257, 999, 821, 800, 740, 521; ^1H NMR ($CDCl_3$, 400 MHz): δ_H = 7.94 - 7.86 (m, 2H), 7.85 - 7.78 (m, 2H), 7.45 - 7.38 (m, 1H), 7.38 - 7.28 (m, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ = 148.4, 139.3, 138.8 (q, $J_{C\text{-}F}$ = 43.0 Hz), 127.7, 125.3, 123.8, 122.7, 122.2, 121.7, 119.5 (q, $J_{C\text{-}F}$ = 224.0 Hz), 118.4, 95.8; ^{19}F NMR ($CDCl_3$, 376 MHz): −54.3; HR-MS (ESI-TOF) m/z: $[M+H]^+$ calcd for $[C_{14}H_9F_3IN_2]^+$ = 388.9757; found: 388.9756.

2-(*o*-tolyl)-3-(trifluoromethyl)-2*H*-indazole (2i): Dark yellow Solid (30 mg, 45%), mp 52-54 ℃; IR (MIR-ATR, 4000–600 cm^{-1}): υmax =3057, 2927, 1603, 1564, 1501, 1386, 1337, 1306, 1158,

1114, 1039, 969, 957, 863, 810, 751, 716, 663, 605, 573; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 7.90 - 7.78 (m, 2H), 7.51 - 7.28 (m, 6H), 2.02 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ = 148.1, 139.6, 138.3, 137.1, 135.8, 130.5, 127.3 (q, $J_{C\text{-}F}$ = 36.0 Hz), 125.0, 122.1, 119.4 (q, $J_{C\text{-}F}$ = 228.0 Hz), 116.0, 114.9, 16.8; ^{19}F NMR ($CDCl_3$, 376 MHz): −56.2; HR-MS (ESI-TOF) m/z: $[M+H]^+$ calcd for $[C_{15}H_{12}F_3N_2]^+$ = 277.0947; found: 277.0952.

2-(2-methoxyphenyl)-3-(trifluoromethyl)-2*H*-indazole (2j): Yellow Solid (27 mg, 42%), mp 40-42 ℃; IR (MIR-ATR, 4000–600 cm^{-1}): υmax = 3673, 3614, 3525, 2930, 2846, 2316, 1603, 1510, 1437, 1335, 1283, 1202, 1120, 1093, 1021, 966, 804, 753, 653, 603; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.03 (d, J = 8.8 Hz, 1H), 7.74 (d, J = 6.8 Hz, 1H), 7.53 (dt, J_a = 1.7 and J_b = 7.9 Hz, 1H), 7.44 (dd, J_a = 1.5 and J_b = 7.8 Hz, 1H), 7.38 - 7.32 (m, 1H), 7.13 - 7.04 (m, 2H), 3.74 (m, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ =154.8, 143.5, 132.0, 128.7, 127.9 (q, $J_{C\text{-}F}$ = 42.0 Hz), 125.3, 124.8, 123.9, 123.2, 121.8 (q, $J_{C\text{-}F}$ = 267.0 Hz), 119.0, 112.0, 55.7; ^{19}F NMR ($CDCl_3$, 376 MHz): −54.3; HR-MS (ESI-TOF) m/z: $[M+H]^+$ calcd for $[C_{15}H_{12}F_3N_2O]^+$ = 293.0896; found: 293.0901.

2-(*m*-tolyl)-3-(trifluoromethyl)-2*H*-indazole (2k): Brown oil (43 mg, 64%). IR (MIR-ATR, 4000–600 cm^{-1}): υmax = 3648, 3565, 3525, 3065, 2924, 2322, 1611, 1592, 1495, 1476, 1431, 1302, 1221, 1202, 1169, 1118, 1016, 880, 787, 745, 693, 693, 627, 605, 521; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 7.74 (d, 2H J = 8.8 Hz), 7.39 - 7.24 (m, 5H), 7.20 (dd, 1H, J_a = 7.8 and J_b = 15.2 Hz), 2.37 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ = 148.2, 139.3, 130.7, 129.5, 128.8, 127.1, 126.7, 125.3, 123.1 (q, $J_{C\text{-}F}$ = 44.0 Hz), 119.6 (q, $J_{C\text{-}F}$ = 250.0 Hz), 118.3, 21.2; ^{19}F NMR ($CDCl_3$, 376 MHz): −54.2; HR-MS (ESI-TOF) m/z: $[M+H]^+$ calcd for $[C_{15}H_{12}F_3N_2]^+$ = 277.0947; found: 277.0960.

2-(3-methoxyphenyl)-3-(trifluoromethyl)-2*H*-indazole (2l): Brownish yellow Solid (53 mg, 80%), mp 74-76 ℃; IR (MIR-ATR, 4000–600 cm^{-1}): υmax = 3614, 3547, 2925, 2846, 2323, 2134, 1734, 1593, 1498, 1468, 1288, 1250, 1201, 1163, 1122, 1044, 976, 885, 755, 688, 521; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.04 (d, J = 8.8 Hz, 1H), 7.75 (d, J = 6.8 Hz, 1H), 7.45 (t, J = 8.3 Hz, 1H), 7.40 - 7.32 (m, 1H), 7.19 (d, J = 7.3 Hz, 1H), 7.15 - 7.08 (m, 2H), 3.87 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ = 160.0, 143.4, 140.0, 129.9, 125.6 (q, $J_{C\text{-}F}$ = 40.0 Hz), 123.7, 122.4, 122.1 (q, $J_{C\text{-}F}$ = 268.0 Hz), 118.5, 116.4, 112.0, 55.6; ^{19}F NMR ($CDCl_3$, 376 MHz): −54.7; HR-MS (ESI-TOF) m/z: $[M+H]^+$ calcd for $[C_{15}H_{12}F_3N_2O]^+$ = 293.0896; found: 293.0901.

2-(*p*-tolyl)-3-(trifluoromethyl)-2*H*-indazole (2m): Yellow Solid (50 mg, 83%), mp 42-44 ℃; IR (MIR-ATR, 4000–600 cm^{-1}): υmax = 3673, 3614, 3043, 2925, 2324,1553, 1515, 1471, 1431, 1383, 1298, 1219, 1174, 1117, 1100, 999, 930, 820, 745, 610, 547; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 7.86 - 7.78 (m, 2H), 7.50 - 7.42 (m, 2H), 7.42 - 7.36 (m, 1H), 7.36 - 7.25 (m, 3H), 2.48 - 2.44 (m, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ = 148.1, 140.2, 137.2, 130.2, 128.2, 127.1, 125.9 (q, $J_{C\text{-}F}$ = 39.0 Hz), 123.8, 122.3, 121.5 (q, $J_{C\text{-}F}$ = 267.0 Hz), 119.6, 118.4, 21.3; ^{19}F NMR ($CDCl_3$, 376 MHz): −54.5; HR-MS (ESI-TOF) m/z: $[M+H]^+$ calcd for $[C_{15}H_{12}F_3N_2]^+$ = 277.0947; found: 277.0948.

2-(4-methoxyphenyl)-3-(trifluoromethyl)-2*H*-indazole (2n): Yellow Solid (53 mg, 83%), mp 74-76 ℃; IR (MIR-ATR, 4000–600 cm^{-1}): *v*max = 2969, 2887, 2839, 2303, 2043, 1608, 1513, 1433, 1299, 1252, 1175, 11148, 1030, 1015, 998, 928, 834, 736, 703, 611, 557, 536; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 7.85 - 7.79 (m, 2H), 7.53 - 7.47 (m, 2H), 7.43 - 7.37 (m, 1H), 7.32 - 7.24 (m, 1H), 7.07 - 6.99 (m, 2H), 3.89 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ = 160.6, 148.0, 132.5, 127.4 (q, $J_{C\text{-}F}$ = 39.0 Hz), 124.9, 123.5, 122.7, 122.3, 121.4, 119.6 (q, $J_{C\text{-}F}$ = 244.0 Hz), 114.8, 55.6; ^{19}F NMR ($CDCl_3$, 376 MHz): −54.6; HR-MS (ESI-TOF) m/z: $[M+H]^+$ calcd for $[C_{15}H_{12}F_3N_2O]^+$ = 293.0896; found: 293.0891.

1-(3-(3-(trifluoromethyl)-2*H*-indazol-2-yl)phenyl)ethanone (2o): Light brown Solid (25 mg, 40%), mp 74-76 ℃; IR (MIR-ATR, 4000–600 cm^{-1}): *v*max = 3648, 3589, 3504, 3074, 2925, 2323, 1716, 1690, 1589, 1522, 1493, 1430, 1359, 1302, 1256, 1222, 1178, 1149, 1012, 748, 691, 587, 562; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.23 - 8.12 (m, 2H), 7.88 - 7.76 (m, 3H), 7.72 - 7.64 (m, 1H), 7.47 - 7.40 (m, 1H), 7.36 - 7.29 (m, 1H), 2.66 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ = 196.4, 148.4, 140.0, 138.0, 130.3, 129.5, 128.2, 127.6, 126.1, 125.4, 123.6 (q, $J_{C\text{-}F}$ = 40.0 Hz), 120.5, 119.5 (q, $J_{C\text{-}F}$ = 209.0 Hz), 118.4, 26.7; ^{19}F NMR ($CDCl_3$, 376 MHz): −54.2; HR-MS (ESI-TOF) m/z: $[M+H]^+$ calcd for $[C_{16}H_{12}F_3N_2O]^+$ = 305.0896; found: 305.0914.

3-(trifluoromethyl)-2-(3,4,5-trimethoxyphenyl)-2*H*-indazole (2p): Yellow Solid (48 mg, 78%), mp 126-128 ℃; IR (MIR-ATR, 4000–600 cm^{-1}): *v*max = 3673, 3648, 3565, 2971, 2881, 2835, 1596, 1556, 1505, 1462, 1415, 1307, 1265, 1233, 1170, 1125, 1106, 1016, 945, 897, 837, 794, 733, 702, 613; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 7.87 - 7.78 (m, 2H), 7.46 - 7.38 (m, 1H), 7.31 (dd, 1H, J_a = 6.8 and *Jb* = 8.3 Hz,), 6.83 (s, 2 H), 3.93 (s, 3H), 3.90 (s, 6H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ_H = 153.2, 148.0, 139.3, 134.9, 127.3, 125.1 (q, $J_{C\text{-}F}$ = 42.0 Hz), 121.5, 119.6 (q, $J_{C\text{-}F}$ = 215.0 Hz), 03.8, 61.0, 56.3; ^{19}F NMR ($CDCl_3$, 376 MHz): −54.5; HR-MS (ESI-TOF) m/z: $[M+H]^+$ calcd for $[C_{17}H_{16}F_3N_2O_3]^+$ = 353.1108; found: 353.1104.

6-bromo-2-(o-tolyl)-3-(trifluoromethyl)-2*H*-indazole (2q): Pale yellow Solid (48 mg, 78%), mp 82-84 ℃; IR (MIR-ATR, 4000–600 cm^{-1}): *v*max = 2116, 2032, 1596, 1540, 1502, 1462, 1432, 1305, 1220, 1179, 1127, 1106, 998, 934, 798, 768, 692, 571, 515; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.00 (d, 1H, *J* = 1.0 Hz), 7.88 - 7.79 (m, 1H), 7.77 - 7.70 (m, 1H), 7.67 (d, 1H, *J* = 7.8 Hz), 7.40 - 7.27 (m, 3H), 2.63 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ = 158.3, 150.9, 148.8, 138.9, 129.1, 124.8 (q, $J_{C\text{-}F}$ = 44.0 Hz), 122.1, 121.7 (q, $J_{C\text{-}F}$ = 246.0 Hz), 120.9, 119.4, 115.6, 23.9; ^{19}F NMR ($CDCl_3$, 376 MHz): −54.5; HR-MS (ESI-TOF) m/z: $[M+H]^+$ calcd for $[C_{15}H_{11}BrF_3N_2]^+$ = $[M+H]^+$: 355.0052; found: 355.0063.

2-benzyl-3-(trifluoromethyl)-2*H*-indazole (2r): Yellow Solid (29 mg, 55%), mp 42-44 ℃; IR (MIR-ATR, 4000–600 cm^{-1}): *v*max =3673, 3614, 3547, 3067, 3035, 2926, 2323, 1521, 1483, 1436, 1327, 1286, 1219, 1165, 1112, 1036, 970, 881, 746, 706, 627; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 7.82

- 7.72 (m, 2H), 7.39 - 7.19 (m, 7H), 5.73 (s, 2H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100 MHz): δ_H = 147.8, 135.2, 128.9 (q, $J_{C\text{-}F}$ = 42.0 Hz), 127.7 (d, $J_{C\text{-}F}$ = 8.0 Hz), 126.7, 124.7, 123.7 (q, $J_{C\text{-}F}$ = 207.0 Hz), 121.2, 120.0, 119.2, 118.3, 56.3; ^{19}F NMR ($CDCl_3$, 376 MHz): −55.8; HR-MS (ESI-TOF) m/z: $[M+H]^+$ calcd for $[C_{15}H_{12}F_3N_2]^+$ = 277.0947; found: 277.0943.

2-(4-methylbenzyl)-3-(trifluoromethyl)-2*H*-indazole (2s): Brown oil (29 mg, 45%), mp 90-92 ℃; IR (MIR-ATR, 4000–600 cm^{-1}): *v*max = 3673, 3648, 3613, 2925, 2858, 2359, 1717, 1969, 1622, 1539, 1511, 1475, 1433, 1385, 1337, 1305, 1201, 1160, 1123, 1015, 967, 813, 749, 689, 608; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 7.73 - 7.63 (m, 2H), 7.26 (ddd, 1H, J_a = 1.2, J_b = 7.0 and J_c = 8.4 Hz), 7.20 - 7.00 (m, 5H), 5.61 (s, 2H), 2.24 (s, 3H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100 MHz): δ = 147.8, 138.2, 132.2, 129.4 (q, $J_{C\text{-}F}$ = 44.0 Hz), 127.7 (q, $J_{C\text{-}F}$ = 9.0 Hz), 124.6, 122.6, 121.2 (q, $J_{C\text{-}F}$ = 266.0 Hz), 119.2, 118.3, 56.1, 21.1; ^{19}F NMR ($CDCl_3$, 376 MHz): −55.8; HR-MS (ESI-TOF) m/z: $[M+H]^+$ calcd for $[C_{16}H_{14}F_3N_2]^+$ = 291.1104; found: 291.1110.

Supporting Information

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

Cyclic Voltammetry data, Copies of NMR (PDF).

AUTHOR INFORMATION

Corresponding Author

* E-mail: *sharada@iith.ac.in*

*E-mail: E-mail: *bhakthadoss@yahoo.com*

ORCID

Duddu S. Sharada: 0000-0001-5861-4126

Manickam Bakthadoss: 0000-0003-4184-3947

Notes

The authors declare no competing financial interest

ACKNOWLEDGMENT

We gratefully acknowledge the Department of Science and Technology-Science and Engineering Research Board (DST-SERB-EMR/2016/000952) New Delhi, India and Indian Institute of Technology Hyderabad (IITH) for financial support. AVM and VNB thanks to UGC, AP thanks to DST-SERB, New Delhi, India for the award of research fellowship. We thank Prof. Ch. Subrahmanyam and Mr. Palyam Subramanyam, IIT Hyderabad, India, for their help in cyclic voltammetry. We would like to thank the reviewer for his/her comments which helped us to improve our manuscript.

References:

1. For selected examples, see: (a) Zhou, Y.; Wang, J.; Gu, Z.; Wang, S.; Zhu, W.; Acen˜a, V. J. L.; Soloshonok, A.; Izawa, K.; Liu, H. Next Generation of Fluorine-Containing Pharmaceuticals, Compounds Currently in Phase II-III Clinical Trials of Major Pharmaceutical Companies: New Structural Trends and Therapeutic Areas. *Chem. Rev*. **2016**, *116*, 422-518. (b) Cametti, M.; Crousse, B.; Metrangolo, P.; Milani, R.; Resnati, G. The fluorous effect in biomolecular applications. *Chem. Soc. Rev.* **2012**, *41*, 31-42. (c) Meanwell, N. A. Synopsis of some recent tactical application of bioisosteres in drug design. *J. Med. Chem.* **2011**, *54*, 2529-2591. (d) Hagmann, W. K. The many roles for fluorine in medicinal chemistry. *J. Med. Chem.* **2008**, *51*, 4359-4569. (e) Clark, T.; Hennemann, M.; Murray, J. S.; Politzer. P. Halogen bonding: the sigma-hole. Proceedings of "Modeling interactions in biomolecules II. *J. Mol. Model*. **2007**, *13*, 291-296. (f) Nakamoto, K.; Margoshes, M.; Rundle, R. E. Stretching Frequencies as a Function of Distances in Hydrogen Bonds. *J. Am. Chem. Soc*. **1955**, *77*, 6480-6486. (g) Schleyer, P. V. R.; West, R. Novel Heterocyclo Pentadienes. *J. Am. Chem. Soc*. **1959**, *81*, 3163-3164. (h) Metrangolo, P.; Resnati, G. Metal-bound halogen atoms in crystal engineering. *Chem. Commun*. **2013**, *49*, 1783-1795.
2. O'Hagan, D. Understanding organofluorine chemistry. An introduction to the C–F bond. *Chem. Soc. Rev*. **2008**, *37*, 308-319.
3. (a) Müller, K.; Faeh, C.; Diederich, F. Fluorine in pharmaceuticals: looking beyond intuition. *Science*. **2007**, *317*, 1881-1886. (b) Purser, S.; Moore, P. R.; Swallow. S.; Gouverneur, V. Fluorine in medicinal chemistry. *Chem. Soc. Rev*. **2008**, *37*, 320-330. (c) Meanwell, N. A. Synopsis of some recent tactical application of bioisosteres in drug design. *J. Med. Chem*., **2011**, *54*, 2529-2591. (d) Schlosser, M. CF_3-bearing aromatic and heterocyclic building blocks. *Angew. Chem. Int. Ed*., **2006**, *45*, 5432-5446. (e) Furuya, T.; Kamlet, A. S.; Ritter, T. Catalysis for fluorination and trifluoromethylation. *Nature.* **2011**, *473*, 470-477. (f) Kirsch, P. Modern Fluoroorganic Chemistry: Synthesis, Reactivity, Applications; Wiley-VCH: Weinheim, **2004**.
4. (a) Pham, P. V.; Nagib, D. A.; MacMillan, D. W. C. Photoredox Catalysis: A Mild, Operationally Simple Approach to the Synthesis of α-Trifluoromethyl Carbonyl Compounds.

Angew. Chem., Int. Ed, **2011**, *50*, 6119-6122. (b) Iqbal, N.; Jung, J.; Park, S.; Cho, E. J. Controlled trifluoromethylation reactions of alkynes through visible-light photoredox catalysis. *Angew. Chem., Int. Ed*. **2014**, *53*, 539-542. (c) Natte, K.; Jagadeesh, R. V.; He, L.; Rabeah, J.; Chen, J.; Taeschler, C.; Ellinger, S.; Zaragoza.; Neumann, H.; Brükner. A.; Beller, M. Palladium-Catalyzed Trifluoromethylation of (Hetero)Arenes with CF_3Br. *Angew. Chem., Int. Ed*. **2016**, *55*, 2782-2786. (d) Straathof, N. J. W.; Cramer, S. E.; Hessel. V.; Noël, T. Practical photocatalytic trifluoromethylation and hydrotrifluoromethylation of styrenes in batch and flow. *Angew. Chem. Int. Ed.* **2016**, *55*, 15549-15553.

5. (a) Cai, S.; Chen, C.; Sun, Z.; Xi, C. CuCl-catalyzed ortho trifluoromethylation of arenes and heteroarenes with a pivalamido directing group. *Chem. Commun*. **2013**, *49*, 4552-4554. (b) Zhang, L.-S.; Chen, K.; Chen, B. Li, Luo, S.; Guo, Q.; Wei, v.; Shi, Z. Palladium-Catalyzed Trifluoromethylation of Aromatic C–H Bond Directed by an Acetamino Group. *Org. Lett*. **2013**, *15*, 10-13; (c) Bagal, D. B.; Kachkovskyi, G.; Knorn, M.; Rawner, T.; Bhanage, B. M.; Reiser, O. Trifluoromethylchlorosulfonylation of alkenes: evidence for an inner-sphere mechanism by a copper phenanthroline photoredox catalyst. *Angew. Chem., Int. Ed*. **2015**, *54*, 6999-7002.
6. (a) Langlois B. R.; Roques, N. Nucleophilic trifluoromethylation of aryl halides with methyl trifluoroacetate. *J. Fluorine Chem*. **2007**, *128*, 1318-1325. (b) Shi, G.-F.; Shao, C.-D.; Pan, S.-L.; Yu, J.-X.; Zhang, Y.-H. Silver-Catalyzed C–H Trifluoromethylation of Arenes Using Trifluoroacetic Acid as the Trifluoromethylating Reagent. *Org. Lett*. **2015**, *17*, 38-41. (c) Kawamura, S.; Sodeoka, M. Perfluoroalkylation of Unactivated Alkenes with Acid Anhydrides as the Perfluoroalkyl Source. *Angew. Chem., Int. Ed.* **2016**, *55*, 8740-8743. (d) Guo, J.-Y.; Wu, R.-X.; Jin, J.-K.; Tian, S.-K. TfNHNHBoc as a Trifluoromethylating Agent for Vicinal Difunctionalization of Terminal Alkenes. *Org. Lett*. **2016**, *18*, 3850-3853. (e) Yang, B.; Yu, D.; Xu, X-H.; Qing, F-L. Visible-Light Photoredox Decarboxylation of Perfluoroarene Iodine(III) Trifluoroacetates for C–H Trifluoromethylation of (Hetero)arenes, *ACS Catal*. **2018**, *8*, 2839-2843.
7. (a)Ruppert, I.; Schlich, K.; Volbach, W. Die ersten CF_3-substituierten organyl(chlor)silane. *Tetrahedron Lett*. **1984**, *25*, 2195-2198. (b) Prakash, G. K. S.; Krishnamurti, R.; Olah, G. A. Synthetic methods and reactions. 141. Fluoride-induced trifluoromethylation of carbonyl compounds with trifluoromethyltrimethylsilane (TMS-CF_3). A trifluoromethide equivalent. *J. Am. Chem. Soc*. **1989**, *111*, 393-395. (c) Liu, J.-B.; Chen, C.; Chu, L.-L.; Chen, Z.-H.; Xu, X.-H.; Qing, F.-L. Silver-Mediated Oxidative Trifluoromethylation of Phenols: Direct Synthesis of Aryl Trifluoromethyl Ethers. *Angew. Chem., Int. Ed*. **2015**, *54,* 11839-11842. (d) Nagase, M.; Kuninobu, Y.; Kanai, M. 4-Position-Selective C–H Perfluoroalkylation and Perfluoroarylation of Six-Membered Heteroaromatic Compounds. *J. Am. Chem. Soc*. **2016**, *138*, 6103-6106. (e) Chu, L. L.; Qing, F. L. Copper-Catalyzed Direct C–H Oxidative

Trifluoromethylation of Heteroarenes. *J. Am. Chem. Soc*. **2012**, *134*, 1298- 1304. (f) Shang, M.; Sun, S.-Z.; Wang, H.-L.; Laforteza, B. N.; Dai, H.-X.; Yu, J.-Q. Exceedingly fast copper(II)-promoted ortho C-H trifluoromethylation of arenes using $TMSCF_3$. *Angew. Chem., Int. Ed*. **2014**, *53*, 10439-*10442*.

8. (a) Eisenberger, P.; Gischig, S.; Togni, A. Novel 10-I-3 Hypervalent Iodine-Based Compounds for Electrophilic Trifluoromethylation. *Chem. – Eur. J*. **2006**, *12*, 2579-2586. (b) Kieltsch, I.; Eisenberger P.; Togni, A. Mild electrophilic trifluoromethylation of carbon- and sulfur-centered nucleophiles by a hypervalent iodine(III)-CF_3 reagent. *Angew. Chem., Int. Ed*. **2007,** *46*, 754-757. (c) Charpentier, J.; Früh, N.; Togni, A. Electrophilic Trifluoromethylation by Use of Hypervalent Iodine Reagents. *Chem. Rev*. **2015**, *115*, 650-682. (d) Xie, J.; Yuan, X.; Abdukader, A.; C. Zhu, J. Ma. Visible-Light-Promoted Radical C–H Trifluoromethylation of Free Anilines. .
9. (a) Umemoto T.; Ishihara, S. Power-variable electrophilic trifluoromethylating agents. S-, Se-, and Te-(trifluoromethyl)dibenzothio-, -seleno-, and -tellurophenium salt system. *J. Am. Chem. Soc*. **1993**, *115*, 2156-2164. (b) Wilger, D. J.; Gesmundo, N. J.; Nicewicz, D. A. Catalytic hydrotrifluoromethylation of styrenes and unactivated aliphatic alkenes via an organic photoredox system, *Chem. Sci.* **2013**, *4*, 3160-3165. (c) Jana, S.; Ashokan, A.; Kumar, S.; Verma, A.; Kumar, S. Copper-catalyzed trifluoromethylation of alkenes: synthesis of trifluoromethylated benzoxazines. *Org. Biomol. Chem*., **2015**, *13*, 8411-8415. (d) Tomita, R.; Koike, T.; Akita, M. Photoredox-catalyzed oxytrifluoromethylation of allenes: stereoselective synthesis of 2-trifluoromethylated allyl acetates. *Chem. Commun*. **2017**, *53*, 4681-4684. (e) Xu, Y.; Wu, Z.; Jiang, J.; Ke, Z.; Zhu, C. Merging Distal Alkynyl Migration and Photoredox Catalysis for Radical Trifluoromethylative Alkynylation of Unactivated Olefins. *Angew. Chem., Int. Ed*. **2017**, *56*, 4545-4548.
10. (a) Fujiwara, Y.; Dixon, J. A.; Hara, F. O'.; Funder, E. D.; Dixon, D. D.; Rodriguez, R. A.; Baxter, R. D.; Herle, B.; Sach, N.; Collins, M. R.; Ishihara, Y.; Baran, P. S. Practical and innate carbon–hydrogen functionalization of heterocycles. *Nature*, **2012**, *492*, 95-99.
11. (a) Langlois, B. R.; Laurent, E.; Roidot. Trifluoromethylation of aromatic compounds with sodium trifluoromethanesulfinate under oxidative conditions. *Tetrahedron Lett*, **1991**, *32*, 7525-7528. (b) Billard, T.; Roques, N.; Langlois, B. R. Synthetic Uses of Thio- and Selenoesters of Trifluoromethylated Acids. 1. Preparation of Trifluoromethyl Sulfides and Selenides. *J. Org. Chem.* **1999**, *64*, 5332-5332.
12. (a) Yang, Y.-D.; Iwamoto, K.; Tokunaga, E.; Shibata, N. Transition-metal-free oxidative trifluoromethylation of unsymmetrical biaryls with trifluoromethanesulfinate. *Chem. Commun.* **2013**, *49*, 5510-5512. (b) Presset, M.; Oehlrich, D.; Rombouts, F.; Molander, G. A. Synthesis and Minisci Reactions of Organotrifluoroborato Building Blocks. *J. Org. Chem.* **2013**, 78, 4615-4619. (c) Deb, A.; Manna, S.; Modak, A.; Patra, T.; Maity, S.; Maiti, D.; Oxidative

trifluoromethylation of unactivated olefins: an efficient and practical synthesis of α-trifluoromethyl-substituted ketones. *Angew. Chem. Int. Ed.* **2013**, *52*, 9747-1950. (d) Zhang, C. Application of Langlois' Reagent in Trifluoromethylation Reactions. *Adv. Synth. Catal.* **2014**, *356*, 2895-2906. (e) Lu, Q.; Liu, C.; Huang, Z.; Ma, Y.; Zhang, J.; Lei, A. Relay cooperation of $K_2S_2O_8$ and O_2 in oxytrifluoromethylation of alkenes using CF_3SO_2Na. *Chem. Commun.* **2014**, *50*, 14101-14104. (f) Jana, S.; Verma, A.; Kadu, R.; Kumar, S. Visible-light-induced oxidant and metal-free dehydrogenative cascade trifluoromethylation and oxidation of 1,6-enynes with water. *Chem. Sci*. **2017**, *8*, 6633-6644.

13. (a) Nagib, D. A.; MacMillan, D. W. C. Trifluoromethylation of arenes and heteroarenes by means of photoredox catalysis. *Nature.* **2011**, *480*, 224-228. (b) Zhao, L.; Li, P.; Xiea. X.; Wang, L. Selective remote C–H trifluoromethylation of aminoquinolines with CF_3SO_2Na under visible light irradiation in the absence of an external photocatalyst. *Org. Chem. Front.* **2018**, *5*, 1689-1697. (c) Zou, G.; Wang, X. Visible-light induced di- and trifluoromethylation of N-benzamides with fluorinated sulfones for the synthesis of CF_2H/CF_3-containing isoquinolinediones. *Org. Biomol. Chem*. **2017**, *15*, 8748-8754. (d) Gao, G-L.; Yang, C.; Xia. W. Selective C–H trifluoromethylation of benzimidazoles through photoredox catalysis *Chem. Commun*. **2017**, *53*, 1041-1044. (e) Lefebvre, Q.; Hoffmann, N.; Rueping, M. Photoorganocatalysed and visible light photoredox catalysed trifluoromethylation of olefins and (hetero)aromatics in batch and continuous flow. *Chem. Commun*. **2016**, *52*, 2493-2496. (f) Monir, K.; Bagdi, A. K.; Ghosh, M.; Hajra, A. Regioselective oxidative trifluoromethylation of imidazoheterocycles via C(sp2)-H bond functionalization. *J. Org. Chem.* **2015**, *80*, 1332-1337. (g) Furuya, T.; Kamlet, A. S.; Ritter, T. Catalysis for fluorination and trifluoromethylation. *nature*, **2011**, *473*, 470-477.

14. (a) Majek. M.; von Wangelin, A. J.; Mechanistic Perspectives on Organic Photoredox Catalysis for Aromatic Substitutions. *Acc. Chem. Res.* **2016**, *49*, 2316-2327. (b) Narayanam, J. M. R.; Stephenson, C. R. J. Visible light photoredox catalysis: applications in organic synthesis *Chem. Soc. Rev.* **2011**, *40*, 102-113. (c) Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C.; Visible light photoredox catalysis with transition metal complexes: applications in organic synthesis. *Chem. Rev.* **2013**, *113*, 5322-5363; (d) Hopkinson, A.; Tlahuext-Aca Glorius, F. Merging Visible Light Photoredox and Gold Catalysis. *Acc. Chem. Res.* **2016**, *49*, 2261-2272. (e) Staveness, D.; Bosque, I.; Stephenson, C. R. J. Free Radical Chemistry Enabled by Visible Light-Induced Electron Transfer. *Acc. Chem. Res*. **2016**, *49*, 2295-2306. (f) Chatterjee, T.; Iqbal, N.; You, Y.; Cho, E. J. Controlled Fluoroalkylation Reactions by Visible-Light Photoredox Catalysis. *Acc. Chem. Res*.**2016**, *49*, 2284-2294.

15. (a) Shi. L.; Xia, W. Photoredox functionalization of C–H bonds adjacent to a nitrogen atom. *Chem. Soc. Rev.* **2012**, *41*, 7687-7697. (b) Yoon, T. P.; Ischay, M. A.; Du, J. Visible light photocatalysis as a greener approach to photochemical synthesis. *Nat. Chem*. **2010**, *2*, 527-532.

(c) Nagib, D. A.; Scott, M. E.; MacMillan, D. W. C. Enantioselective α-trifluoromethylation of aldehydes via photoredox organocatalysis. *J. Am. Chem. Soc.* **2009**, *131*, 10875-10877. (d) Reckenthler, M.; Griesbeck, A. G. Photoredox catalysis for organic syntheses. *Adv. Synth. Catal.* **2013**, *355*, 2727-2744. (e) Tomita, R.; Yasu, Y.; Koike, T.; Akita, M. Combining photoredox-catalyzed trifluoromethylation and oxidation with DMSO: facile synthesis of α-trifluoromethylated ketones from aromatic alkenes. *Angew. Chem., Int. Ed.* **2014**, *53*, 7144-7148. (f) Hari, D. P.; König B. The photocatalyzed Meerwein arylation: classic reaction of aryl diazonium salts in a new light. *Angew. Chem., Int. Ed.* **2013**, *52*, 4734-4743.

16. (a) Joule. J. A.; Mills, K. in: Heterocyclic Chemistry, Blackwell Science Ltd., *Oxford*, **2000.** (b) Boger, D. L.; Boyce, C. W.; Garbaccio, R. M.; Goldberg, J. A. CC-1065 and the Duocarmycins: Synthetic Studies. *Chem. Rev.* **1997**, *97*, 787-828. (c) Horton, D. A.; Bourne, G. T.; Smythe, M. L. The Combinatorial Synthesis of Bicyclic Privileged Structures or Privileged Substructures. *Chem. Rev,* **2003**, *103*, 893-930. (d) Chen. F.-E.; Huang, J. Reserpine: A Challenge for Total Synthesis of Natural Products.; *Chem. Rev*. **2005**, *105*, 4671-4706. (e) Trost. B. M.; Brennan, M. K.; Asymmetric Syntheses of Oxindole and Indole Spirocyclic Alkaloid Natural Products. *Synthesis*, **2009**, *3003-3025*. (f) Bakthadoss, M.; Kumar, P. V.; Reddy T. T.; Sharada, D. S. Solvent and catalyst free ring expansion of indoles: a simple synthesis of highly functionalized benzazepines. *Org. Biomol. Chem,* **2018**, *16*, 8160-8168.
17. (a) D'Souza. D. M.; Müller, T. J. J. Multi-component syntheses of heterocycles by transition-metal catalysis. *Chem. Soc. Rev.* **2007**, *36*, 1095-1108. (b) Dömling, A.; Wang. W.; Wang, K. Chemistry and Biology of Multicomponent Reactions. *Chem. Rev.* **2012**, *112*, 3083- 3135. (c) Elguero, J.; Comprehensive Heterocyclic Chemistry, ed. A. R. Katrizky and C. W. Rees, Pergamon Press, New York, **1984**, *4*, 167. (d) Gil, C.; Bräse, S.; The Synthesis of 3-Substituted 6-Aryl-3 H-benzo[a] [1,2,3] triazinones Using Polymer-Bound Triazenes. *J. Comb. Chem*. **2004,** *6*, 38-42. (e) Ramachary, D. B.; Jain, S.; Sequential one-pot combination of multi-component and multi-catalysis cascade reactions: an emerging technology in organic synthesis. *Org. Biomol. Chem*, **2011**, *9*, 1277-1300. (f) Andreonati, S. S.; Sava, V.; Makan, S.; Kolodeev, G. *Pharmazie*, **1999**, *54*, 99. (g) Zhang, S-G.; Liang, C-G.; Zhang, W-H. Recent Advances in Indazole-Containing Derivatives: Synthesis and Biological Perspectives. *Molecules,* **2018**, *23*, 2783-2823. (h) Angelis, M.D.; Stossi, F.; Carlson, K. A.; Katzenellenbogen, B. S.; Katzenellenbogen, J. A. Indazole estrogens: highly selective ligands for the estrogen receptor β. *J. Med. Chem.* **2005**, *48*, 1132-1144. (i) Vidyacharan, S.; Adhikari, C.; Krishna, V. S.; Reshma, R. S.; Sriram, D.; Sharada D. S. A robust synthesis of functionalized 2*H*-indazoles via solid state melt reaction (SSMR) and their anti-tubercular activity. *Bioorg. Med. Chem. Lett*. **2017**, *27*, 1593-1597.

18. (a) Baraldi, P. G.; Balboni, G.; Pavani, M. G.; Spalluto, G.; Tabrizi, M. A.; Clercq, E. D.; Balzarini, J.; Bando, T.; Sugiyama, H.; Romagnoli, R. Design, synthesis, DNA binding, and biological evaluation of water-soluble hybrid molecules containing two pyrazole analogues of the alkylating cyclopropylpyrroloindole (CPI) subunit of the antitumor agent CC-1065 and polypyrrole minor groove binders. *J. Med. Chem*. **2001**, *44*, 2536- 2543. (b) Qian, S.; Cao, J.; Yan, Y.; Sun, M.; Zhu, H.; Hu, Y.; He, Q.; Yang, B. SMT-A07, a 3-(Indol-2-yl) indazole derivative, induces apoptosis of leukemia cells in vitro. *Mol. Cell. Biochem*. **2010**, *345*, 13-21.

19. Li, X.; Chu, S.; Feher, A. V.; Khalili, M.; Nie, Z.; Margosiak, S.; Nikulin, V.; Levin, J.; Sprankle, K. G.; Tedder, M. E.; Almassy, R.; Appelt, K.; Yager, K. M. Structure-based design, synthesis, and antimicrobial activity of indazole-derived SAH/MTA nucleosidase inhibitors. *J. Med. Chem*. **2003**, *46*, 5663-5673.

20. Picciola, G.; Ravenna, F.; Carenini, G.; Gentili, P.; Riva, M. Heterocyclic compounds containing the residue of a 4-aminophenylalkanoic acid with potential anti-inflammatory activity. IV. Derivatives of 2-phenyl-2*H*-indazole. *Farmaco Ed. Sci.* **1981**, *36*, 1037-1056.

21. Han, W.; Pelletier. J. C.; and Hodge, C. N. Tricyclic ureas: a new class of HIV-1 protease inhibitors. *Bioorg. Med. Chem. Lett.* **1998**, *8*, 3615-3620.

22. Lee, F-Y.; Lien, J-C.; Huang, L-J.; Huang, T-M.; Tsai, S-C.; Teng, C-M.; Wu, C-C.; Cheng, F-C.; Kuo, S-C. Synthesis of 1-benzyl-3-(5'-hydroxymethyl-2'-furyl) indazole analogues as novel antiplatelet agents. *J. Med. Chem.* **2001**, *44*, 3746-3749.

23. (a) Sun, J.-H.; Teleha, C. A.; Yan, J.- S.; Rodgers, J. D.; Nugiel, D. A. Efficient Synthesis of 5-(Bromomethyl)- and 5-(Aminomethyl)-1-THP-Indazole. *J. Org. Chem.* **1997**, *62*, 5627-5629.

24. (a) Halland, N.; Nazare, M.; kyek,O.R´'; Alonso, J.; Urmann, M.; Lindenschmidt, A. A General and Mild Palladium-Catalyzed Domino Reaction for the Synthesis of 2*H*-Indazoles. *Angew. Chem. Int. Ed.* **2009**, *48*, 6879- 6882. (b) Haag, B.; Peng, Z.; Knochel, P. Preparation of Polyfunctional Indazoles and Heteroarylazo Compounds Using Highly Functionalized Zinc Reagents. *Org. Lett*. **2009**, *11*, 4270-4273. (c) Hu, J.; Cheng, Y.; Yang, Y.; Rao, Y. A general and efficient approach to 2*H*-indazoles and 1*H*-pyrazoles through copper-catalyzed intramolecular N–N bond formation under mild conditions. *Chem. Commun*. **2011**, *47*, 10133-10135. (d) Kumar, M. R.; Park, A.; Park, N.; Lee, S. Consecutive Condensation, C–N and N–N Bond Formations: A Copper- Catalyzed One-Pot Three-Component Synthesis of 2*H*-Indazole. *Org. Lett.* **2011**, *13*, 3542-3545. (e) Stokes, B. J.; Vogel, C. V.; Urnezis, L. K.; Pan, M.; Driver, T. G. Intramolecular Fe(II)-catalyzed N-O or N-N bond formation from aryl azides. *Org. Lett*. **2010**, *12*, 2884-2887. (f) Wu, C.; Fang, Y.; Larock, R. C.; Shi, F. Synthesis of 2*H*-Indazoles by the [3+2] Cycloaddition of Arynes and Sydnones. *Org. Lett*. **2010**, *12*, 2234-2237. (g) Yang, W.; Yang, Z.; Xu, L.; Zhang, L.; Xu, X.; Miao, M.; Ren, H. Surfactant-type Brønsted acid catalyzed stereoselective synthesis of trans-3-alkenyl indazoles from triazenylaryl allylic alcohols in water. *Angew. Chem. Int. Ed.* **2013**, *52*, 14135-14139. (h) Laleu, B.; Lautens, M.

Synthesis of Annulated 2*H*-Indazoles and 1,2,3- and 1,2,4-Triazoles via a One-Pot Palladium-Catalyzed Alkylation/Direct Arylation Reaction. *J. Org. Chem.* **2008**, *73*, 9164-9167.

25. (a) Bogonda, G.; Kim, H. Y.; Oh, K. Direct Acyl Radical Addition to 2*H*-Indazoles Using Ag-Catalyzed Decarboxylative Cross-Coupling of α-Keto Acids. *Org. Lett*. **2018**, *20*, 2711-2715. (b) Singsardar, M.; Dey, A.; Sarkar, R.; Hajra, A. Visible-Light-Induced Organophotoredox-Catalyzed Phosphonylation of 2*H*-Indazoles with Diphenylphosphine Oxide. *J. Org. Chem*. **2018**, *83*, 12694-12701. (c) Dey, A.; Hajra, A. Potassium Persulfate-Mediated Thiocyanation of 2*H*-Indazole under Iron-Catalysis. *Adv. Synth. Catal.* **2019**, *361,* 842-849; (d) Ghosh, P.; Mondal, S.; Hajra, A. Metal-Free Trifluoromethylation of Indazoles. *J. Org. Chem*. **2018**, *83*, 13618- 13623.
26. (a) Yi, H.; Zhang, G.; Wang, H.; Huang, Z.; Wang, J.; Singh. A. K.; Aiwen Lei. A. Recent Advances in Radical C-H Activation/Radical Cross-Coupling. *Chem. Rev.* **2017**, *117*, 9016-9085. (b) Banerjee, A.; Santra, S. K.; Mishra, A.; Khatun, N.; Patel, B. K. Copper(I)-promoted cycloalkylation–peroxidation of unactivated alkenes via sp3 C–H functionalization. *Org. Biomol. Chem.* **2015**, *13*, 1307-1312. (c) Banerjee, A.; Santra, S. K.; A. Mishra, Khatun, N.; Ali. W.; Patel, B. K.; Oxidant controlled regioselective mono- and di-functionalization reactions of coumarins. *Chem. Commun*. **2015**, *51*, 15422-15425. (d) Tang, S.; Deng, Y-L.; Li, J.; Wang, W-X.; Wang, Y-C.; Li, Z-Z.; Yuan, L.; Chen S-L.; Sheng, R-L. Aerobic oxidative cyclization of benzamides via meta-selective C-H tert-alkylation: rapid entry to 7-alkylated isoquinolinediones. *Chem. Commun*. **2016**, *52*, 4470-4473.
27. (a) Murugan, A.; Gorantla, K. R.; Mallik B. S.; Sharada, D. S. Iron promoted C3–H nitration of 2*H*-indazole: direct access to 3-nitro-2*H*-indazoles. *Org. Biomol. Chem.* **2018**, *16*, 5113-5118. (b) Murugan, A.; Vidyacharan S.; Ghosh, R.; Sharada, D. S. Metal-Free Regioselective Dual C-H Functionalization in a Cascade Fashion: Access to Isocryptolepine Alkaloid Analogues. *ChemistrySelec*t, **2017**, *2*, 3511-3515. (c) Vidyacharan S. Murugan, A.; Sharada, D. S. C(sp^2)–H Functionalization of 2*H*-Indazoles at C3-Position via Palladium(II)-Catalyzed Isocyanide Insertion Strategy Leading to Diverse Heterocycles. *J. Org. Chem*. **2016**, *81*, 2837-2848. (d) Shinde, A. H.; Vidyacharan, S.; Sharada, D. S. $BF_3{\cdot}OEt$ mediated metal-free one-pot sequential multiple annulation cascade (SMAC) synthesis of complex and diverse tetrahydroisoquinoline fused hybrid molecules. *Org. Biomol. Chem*. **2016,** *14*, 3207-3211. (e) Sagar, A.; Babu, V. N.; Sharada, D. S. Silica gel promoted environment-friendly synthesis of α-amino amidines and regioselective transformation of α-amino amidines into amidino substituted indazoles. *RSC Adv*. **2015**, *5*, 29066-29071. (f) Vidyacharan, S.; Sagar, A.; Chaitra C.; Sharada, D. S. A facile synthesis of 2*H*-indazoles under neat conditions and further transformation into aza-g-carboline alkaloid analogues in a tandem one-pot fashion. *RSC Adv*. **2014**, *65*, 34232-34236.

28. Murugan, A.; Babu, V. N.; Sabarinathan, N.; Sharada D. S. Regioselective C3-H Trifluoromethylation of 2*H*-Indazole Under Transition-Metal-Free Photoredox Catalysis. *ChemRxiv*., **2019**, 10.26434/chemrxiv.7796603.v1.

29. Romero, N. A.; Nicewicz, D. A.; Organic Photoredox Catalysis. *Chem. Rev*. **2016**, *116*, 10075−10166. (b) Prier, C. K.; Danica, D. A.; MacMillan, D. W. C. Visible Light Photoredox Catalysis with Transition Metal Complexes: Applications in Organic Synthesis. *Chem. Rev*. **2013**, *113*, 5322−5363.

30. (a) Stokes, B. J.; Vogel, C. V.; Urnezis, L. K.; Pan, M.; Driver, T. G. Intramolecular Fe(II)-Catalyzed N−O or N−N Bond Formation from Aryl Azides. *Org Lett*, **2010**, *12*, 2884-2887. (b) Hu. J.; Cheng. Y.; Yang. Y.; Rao. Y. A general and efficient approach to 2*H*-indazoles and 1*H*-pyrazoles through copper-catalyzed intramolecular N–N bond formation under mild conditions. *Chem. Commun*., **2011**, *47*, 10133-10135. (c) Caron, S.; Vazquez, E.; Stevens, R. W.; Nakao, K.; Koike, H.; Murata, Y. Efficient Synthesis of [6-Chloro-2-(4-chlorobenzoyl)-1*H*-indol-3-yl]-acetic Acid, a Novel COX-2 Inhibitor. *J. Org. Chem*. **2003**, *68*, 4104-4107.