CHEMISTRY
AN ASIAN JOURNAL
www.chemasianj.org

Accepted Article

Title: TM Free Chemoselective Oxidative C-C Coupling of sp3 C-H Bond of Oxindoles with Arenes and Addition to Alkene: Synthesis of 3-Aryl Oxindoles, Benzofuro- and Indolo-indoles

Authors: Sangit Kumar, Moh. Sattar, Vandana Rathore, and Ch. Durga Prasad

To be cited as: *Chem. Asian J.* 10.1002/asia.201601647

Link to VoR: http://dx.doi.org/10.1002/asia.201601647

A Journal of

ACES
Asian Chemical Editorial Society

A sister journal of Angewandte Chemie and Chemistry – A European Journal

WILEY-VCH

10.1002/asia.201601647

WILEY-VCH

FULL PAPER

TM Free Chemoselective Oxidative C-C Coupling of sp^3 C-H Bond of Oxindoles with Arenes and Addition to Alkene: Synthesis of 3-Aryl Oxindoles, Benzofuro- and Indolo-indoles

Moh. Sattar,[a] Vandana Rathore,[a] Ch. Durga Prasad,[a] and Sangit Kumar[a]*

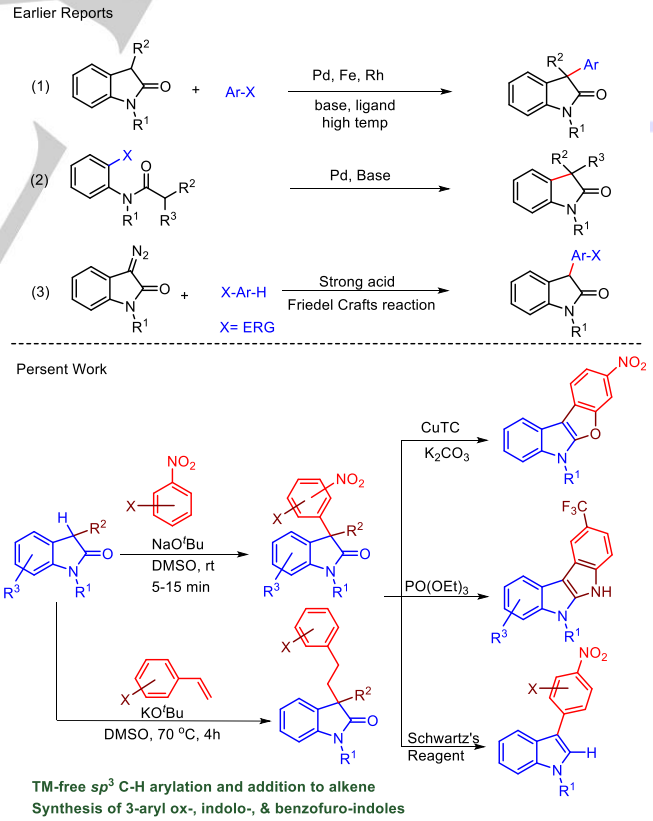
Abstract: A transition-metal (TM) and halogen free NaO^{t}Bu–mediated oxidative cross coupling between sp^3 C-H bond of oxindoles and sp^2 C-H bond of nitroarenes has been developed to access 3-aryl substituted and 3,3-aryldisubstituted oxindoles in DMSO at room temperature in short time. Interestingly, sp^3 C-H bond of oxindoles has also been added to styrene under TM-free conditions for the practical synthesis of quaternary 3,3-disubstituted oxindoles. Synthesized 3-oxindoles have also been further transformed into advanced heterocycles, benzofuroindoles, indoloindoles, and substituted indoles. Mechanistic understanding of the reaction suggests the formation of an anion intermediate from sp^3 C-H bond of oxindole by *tert*-butoxide base in DMSO. The addition of nitrobenzene to in-situ generated carbanion led to the 3-(nitrophenyl)oxindolyl carbanion in DMSO which subsequently oxidizes to 3-(nitro-aryl) oxindole by DMSO.

Introduction

Transition metal (TM)-free strategy for C-C coupling reactions has brought considerable interest in the scientific community since last decade.TM-free oxidative cross coupling of C-H bonds is a straightforward and atom-economical approach for the construction of C-C bond.[1] This approach avoids expensive metal catalysts, ligands, toxic waste, pre-functionalized substrates, additional steps[2] and generates water as only by product in the reactions. Moreover, mild reaction conditions tolerate sensitive functional groups namely halogens, *N*H, CN which are crucial for the late stage elaboration for the synthesis of complex molecules.

tert-Butoxide with or without organic additives has been used for the coupling of aryl halides with inactive arenes, and heteroarenes leading a new carbon-carbon bond and thus produce pivotal biaryls as studied by various research groups.[3-5] This methodology has been further extended to Heck type coupling of aryl halides with alkenes,[5a-5b] intramolecular cyclization of aryl halides with sp^2 C-H, *sec* and *tert*-sp^3 C-H bonds.[4a-4b, 5c-5f] Also strong bases such as *tert*-butoxide known to generate carbanion from acidic carbon-hydrogen bond. The generated carbanion substitutes the carbon-halogen bond of electron-deficient arenes by following S_NAr pathway and also substitution of C-H bond by VNSH pathway.[6] Nitroarenes are the viable aromatic substrates as they are readily available aromatic molecules and also many of them are economical than other substituted benzenes. Moreover, the nitro group has broad potential in synthetic chemistry and the chemical industry as this can be easily transformed into various functionalities and manipulated by various methods into important indole and carbazole heterocyclic rings.[6b-6i]

3-Substituted and 3,3-disubstituted oxindoles are the prominent structural motifs that feature in many biologically active natural products and pharmaceutical compounds.[7] Various 3-substituted oxindoles consisting unprotected *N*-H bonds, display biological activities against a variety of neurodegenerative disorders,[7c] tumors,[7d] HIV,[7e] and anticancer.[7f]



Scheme 1. Literature reports for the synthesis of 3-arylated and 3,3-disubstituted oxindoles.

[a] M. Sattar, V. Rathore, C. D. Prasad, Dr. S Kumar
Department of Chemistry
Indian Institute of Science Education and Research, Bhopal
Bhopal Bypass Road, Bhauri Bhopal, Madhya Pradesh, 462066
India
E-mail: sangitkumar@iiserb.ac.in

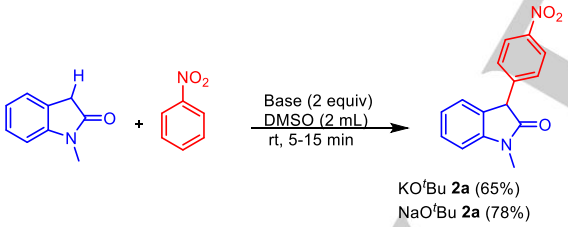
Supporting information for this article is given via a link at the end of the document.((Please delete this text if not appropriate))

10.1002/asia.201601647

In this context, arylation of oxindoles *via* inter[8a-8k] and intra molecular[8l-8p] C-C coupling using aryl halide partners catalyzed by TM-catalysts have been well explored (Scheme 1). Hg(II)-Catalyzed Friedel-Crafts reaction of *N*-protected-3-substituted-3-hydroxyoxindoles with electron rich *N*-methyl indoles and electron rich phenols,[8e] Fe(III)-catalyzed cross coupling reaction of an excess amount of activated arenes such as anisole and thiophenes with 3-benzyl/phenyl substituted oxindoles,[8i] Rh-catalyzed arylation of imines based oxindoles with arylboronic acid have been reported in the literature.[8j]

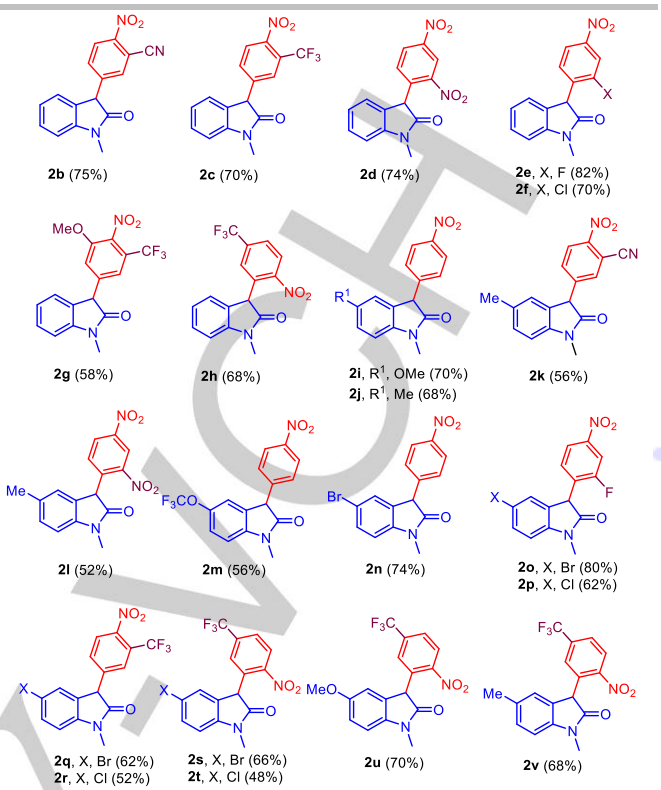
Under TM-free conditions, the synthesis of 3-aryl-oxindoles have been exploited, [8h-8k] where prefunctionalized oxindoles such as 3-diazo-2-oxindoles,[8h] 1,3-diacyloxy[8k] were coupled with activated arenes. Despite the enlisted achievements, they suffer from harsh reaction conditions and/or involve prefunctionalized coupling partners. Also, the reported methodologies involve the protection of *N*-H bond in order to achieve desired C-C coupled product, as the protons of nitrogen-1 and carbon-3 atoms in oxindole moiety have almost similar *p*Ka (~18.5).[8l] Therefore, unprotected *N*-H oxindoles may give *N*-arylated products with aryl halides and boronic acids, instead of C-arylated products in presence of metal catalysts.[8a,8d]

In continuation of our work on TM-free C-C coupling reactions[4] herein, we disclose; a) the chemoselective coupling of sp^3 C-H bond over unprotected *N*-H bond of oxindole with sp^2 C-H bond of nitroarenes by the generation of a carbanion from carbon-hydrogen bond of oxindole utilizing *tert*-butoxide base in DMSO at room temperature for the synthesis of 3-arylated and 3,3-diarylated oxindoles having a quaternary carbon center, b) an addition of sp^3 C-H bond of oxindole to the sp^2 C-H bond of styrene to obtain quaternary carbon centered 3-oxindoles in practical yields, c) 3-substituted oxindoles have been further transformed into benzofuroindoles, indoles and indoloindoles.



Scheme 2. Optimized reaction scheme for C-3 arylation of oxindole

We started with KO^{t}Bu base for the optimization of reaction conditions (SI please see S20-S21) which provided 65% yield of the 3-arylated oxindole **2a** (Scheme 2). Lithium *tert*-butoxide, carbonate bases such as K_2CO_3, Na_2CO_3, Cs_2CO_3, hydride bases; NaH, KH, and alkoxide bases NaOMe, NaOEt bases were noticed to be ineffective for the coupling of oxindole with nitrobenzene. Detailed optimization of conditions is enlisted in SI (please see page S20-S21). NaO^{t}Bu gave better yield (78%) of **2a** in DMSO.

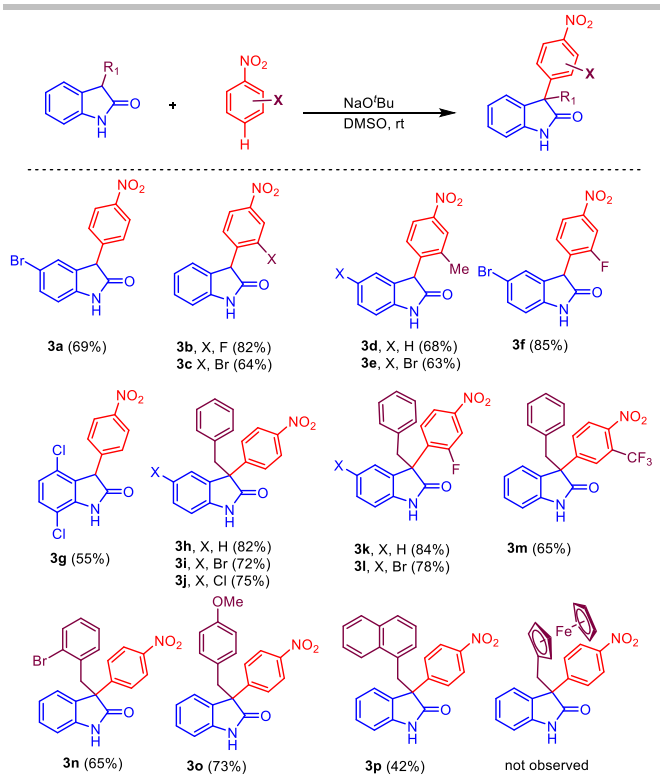


Scheme 3 Scope for *N*-Me-oxindoles with nitrobenzenes

With the optimized conditions in our hand, initially we explored *N*-methyl-substituted oxindoles with substituted nitrobenzenes and resulted 3-aryl oxindoles **2a-2v** are summarized in Scheme 3. A variety of substituents on nitrobenzene having electron withdrawing groups such as CN, CF_3, NO_2, electron donating OMe substituent showed the compatibility with the optimized reaction conditions to provide 3-(nitrophenyl)oxindoles **2b-2d**, and **2g** in 58 to 75% yields. Furthermore, *meta*-fluoro/ chloro substituted nitrobenzenes also underwent C-H coupling reaction with oxindoles chemoselectively to give chloro and fluoro substituted 3-aryloxindoles in 82 and 72% yields, respectively (**2e-f**, **2o-p**). Interestingly, the formation of C-C coupled product by the coupling of C-H and C-F/Cl/Br bond was not observed (Scheme 3,4). Halogen substituents are vital for *post*-modification of 3-aryl-oxindoles and could be readily transformed into advanced heterocycles (*vide infra*). When *para*-position of nitrobenzene is blocked by suitable trifluoromethyl group, the desired *ortho*-nitroaryl indoles **2h**, **2s-2v** were realized under the reaction conditions.

Next, substituted oxindoles having electron donating -CH_3, -OCH_3, OCF_3, electron withdrawing Br and Cl functionalities afforded coupled 3-aryl oxindoles **2i-2m, 2u-2v** and **2n-2t** with various substituted nitrobenzenes in 48-80% yields.

10.1002/asia.201601647



Scheme 4. Substrate scope for *N*-unprotected oxindoles with nitrobenzenes

Next, an exploration of C-H functionalization in *N*-unprotected oxindoles have been carried out (Scheme 4). To our delight, chemoselective C-H coupling of oxindoles over *N*-H coupling with nitroarenes were observed under optimized reaction conditions. *N*-unprotected oxindoles bearing halogens such as chloro, bromo and even dichloro substrates smoothly underwent chemoselective C-H functionalization to afford desired 3-aryl oxindoles **3a**, **3e**-**3g**, **3i**-**3j**, and **3l** in 42-85% yields. In addition, *tert*-C-H bond of *N*-unprotected oxindoles can be arylated under optimized reaction conditions. 3-Benzyl and 3-(bromo and methoxy substituted)-benzyl oxindoles were also tolerated well and afforded respective 3-(nitroaryl)-3-benzyloxindoles **3h**-**3o** in good yields (65-82%). 3-Naphthyl substituted oxindole was also realized with low yield (42%) of 3-nitroaryl-3-naphthyl oxindole **3p**. However, 3-ferrocenyl oxindole failed to yield any 3-arylated oxindole.

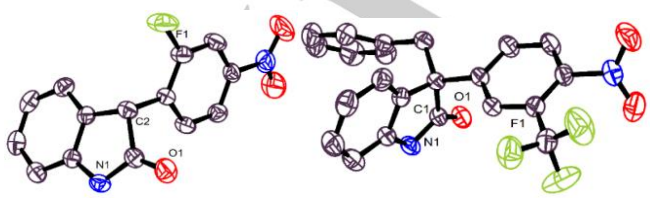
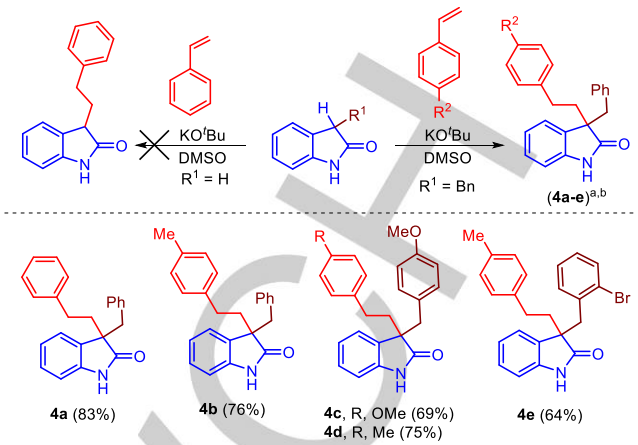


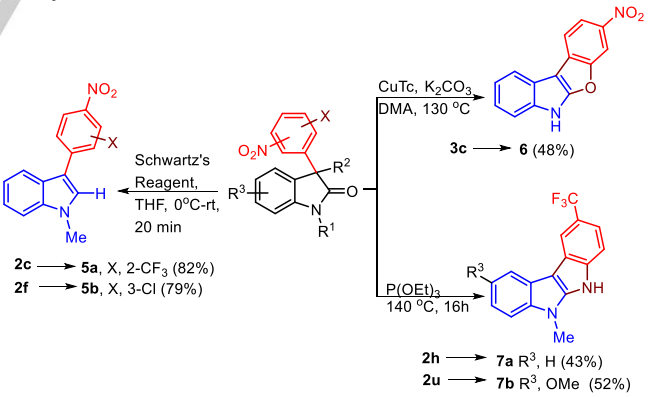
Figure 1. Crystal structures of 3-nitroaryl indoles **3b** (CCDC No. **1474932**) and **3m** (CCDC No. **1474930**). For crystallographic details and crystal structure of **3h** (CCDC No. 1474931), please See SI, S126-S146.

Structures of fluoro, trifluoromethyl substituted 3-(nitroaryl)oxindoles **3b** and **3m** and 3-(nitroaryl)-3-benzyloxindole



Scheme. **5** Substrate scope of 3-substituted oxindoles with styrenes. Reaction was carried out using oxindole (0.44 mmol, 100 mg), styrene (5 equiv., 2.24 mmol, 256 µL), KO^{t}Bu (3 equiv., 1.34 mmol, 151 mg) and DMSO (2 mL) under nitrogen atmosphere at 70 °C for 4h. [a] isolated yield[b]

3h are also studied by single crystal X-ray crystallography (Figure 1). Hayashi[5a] and Shi[5b] *et al*. have accomplished Mizoroki-Heck type coupling reaction of aryl halides with styrene utilizing potassium *tert*-butoxide base under TM-free conditions. We envisaged the coupling of 3-C-H bond of oxindole with styrene under optimized oxidative *tert*-butoxide mediated reaction (Scheme 5). To our surprise, reaction of 3-unsubstituted oxindole with styrene failed to yield any coupled product under various optimized reaction conditions. However, 3-substituted oxindoles reacted with styrene smoothly under heating conditions to yield 3-quaternary substituted oxindole **4a**. Methoxy and methyl substituted styrenes have also been coupled with 3-benzyl oxindoles to afford 3-benzyl-3-phenethyloxindoles **4b**-**4e** in 64-76% yields.



Scheme 6. Further functionalization of oxindoles

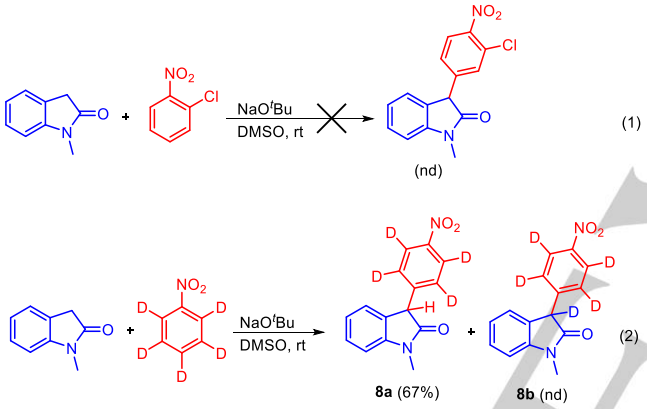
Further, transformation of synthesized 3-aryl oxindoles into advanced heterocycles has been studied (Scheme 6). 3-Arylated oxindoles **2c** and **2f** could be readily reduced into respective indoles **5a** and **5b** using Schwartz's reagent in promising yields. 3-Arylated oxindole **3c** has been transformed into benzofuroindole **6** using copper complex. Also, 3-(2-nitroaryl)-substituted oxindoles **2h** and **2u** could be converted into

10.1002/asia.201601647

indoloindoles **7a** and **7b** having two adjacent pyrrole rings by heating in triethylphosphite [$P(OEt)_3$].

Mechanistic Consideration

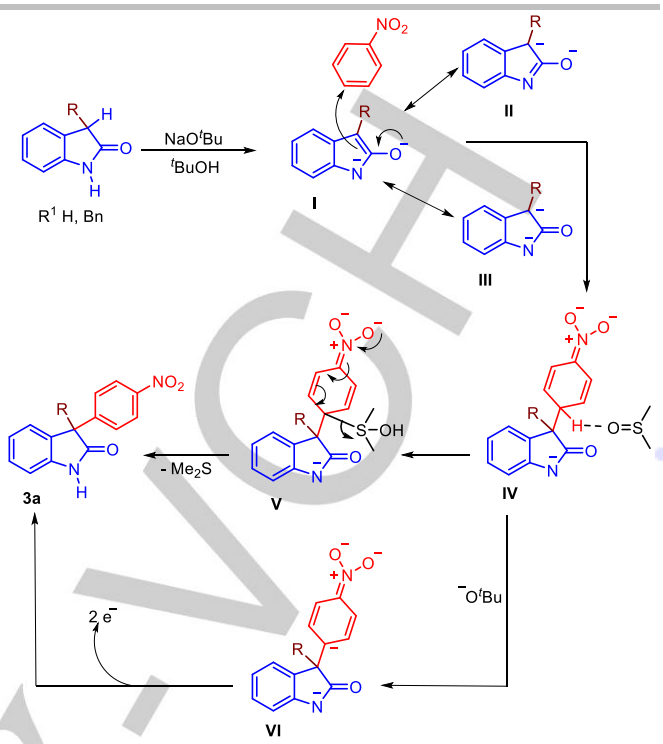
EPR Experiment on the NaO^{t}Bu-mediated reaction of 3-unsubstituted oxindole in the presence of NaO^{t}Bu in DMSO afforded a sharp singlet (SI, please see page S115-117). Addition of nitrobenzene to the equimolar solution of unsubstituted oxindole and NaO^{t}Bu lead to complete disappearance of EPR singlet and a new triplet was observed. Intrigued by this finding, we decided to perform ^{1}H NMR on the reaction mixture using DMSO-d_6. The reddish reaction mixture of oxindole and NaO^{t}Bu and dark blue colored reaction mixture of oxindole, NaO^{t}Bu and nitrobenzene in DMSO-d_6 provided clean NMR spectra without any signal broadening, which generally occurs due to presence of radicals in the sample (SI, pages S121-S123). ^{1}H NMR experiments on the reaction mixture indicated lack of radicals in the reaction mixture in significant concentration and therefore, reaction less likely to proceed by radical pathway.



Scheme 7. Control experiment between nitrobenzene and oxindole

The reactivity of 3-oxindolyl carbanion was studied in S_NAr vs VNSH reaction by taking 2-chloro-nitrobenzene substrate which could provide S_NAr C-C coupled product by the substitution of C-Cl bond and VNSH product by the substitution of hydrogen bond in nitrobenzene.[9] The reaction of *N*-methyloxindole with 2-choro-nitrobenzene in the presence of *tert*-butoxide base gave 3-(2-nitro)phenyl-oxindole as the sole S_NAr C-C coupled product and even traces of the expected VNSH[6] 3-(3-chloro-4-nitro)phenyl-oxindole product was not observed after several repeated attempts.

Next, reaction was performed in deuterated nitrobenzene-d_5 neither show any noticeable difference in the reaction time nor incorporation of deuterium into 3-aryl oxindole was observed which suggests the nitrobenzene does not involve in the rate determining step of the reaction.



Scheme 8. Proposed mechanism for C-3 arylation of oxindoles

In the proposed mechanism, we believe that oxindole provides carbanion intermediate **I** in the presence of NaO^{t}Bu. The intermediate can be stabilized *via* intermediates **II** and **III**. The Intermediate **I** may add to nitrobenzene to form 3-(4-nitrocyclohexa-2,5-dien-1-yl)indolin-2-one anion **IV** which lead to intermediate **V** by DMSO under basic conditions would furnish desired C-C couple 3-nitroaryl oxindole and itself reduce to dimethyl sulfide. The formation of DMS has also been established by ^{1}H NMR and GC-mass analysis of the reaction mixture (see SI, page S121-SI123). Oxidation of 3-(4-nitrocyclohexa-2,5-dien-1-yl)indolin-2-one anion **IV** is also possible by aerial oxygen,[4d,6f] however, substantial decrease in the yield of desired 3-aryl oxindole was noticed when reaction performed in an open flask. Alternatively, intermediate **IV** may be deprotonated by NaO^{t}Bu or by the dimsyl anion and the resulting polyanionic species **VI**, which would be a reasonable electron donor, may be oxidised to 3-nitroaryl oxindole by electron transfer.

Conclusion

In summary, a regioselective NaO^{t}Bu mediated protocol for the synthesis of C-3 arylated oxindoles and 3,3-disubstituted oxindoles has been developed at room temperature in short time without employing external oxidant, TM-catalytic system, and halogen. This reaction was chemoselective towards sp^3 C-H bond over *N*-H bond even in 3-substituted oxindoles. The presented methodology tolerates various functionalities such as bromo, chloro, fluoro, methyl, methoxy, trifluoromethyl groups, on the framework of nitrobenzene. Moreover, substituted oxindoles and 3-alkylated oxindoles having functionalities on the benzene ring

such as 5-chloro, bromo, methoxy, methyl, OCF_3 groups were compatible in the metal free oxidative coupling. Oxindoles have also been coupled with styrene to form quaternary carbon containing 3,3-disubstituted oxindoles. Synthesized 3-aryl-oxindoles can be further functionalized into indoles by using Schwartz's reagent in an excellent yield. Further, 3-Aryl oxindoles can be transformed into benzofuroindole and indoloindoles. Overall, we have developed a metal free, eco-friendly and sustainable method for the synthesis of biologically active substituted oxindoles which could serve as building blocks in pharmaceuticals, agrochemicals and drug chemistry.

Experimental Section

Typical Procedure for C-3 Arylation of Oxindole. Oxindoles and their precursors were prepared by following known methods and synthesis and analytic data are presented in SI (page S2-S19).[10] Oxindole (100 mg, 0.68 mmol) was dissolved in dry DMSO in a 10 mL round bottom flask having stirrer bar under nitrogen atmosphere. Nitrobenzene (1.2 equiv., 84 µL, 0.82 mmol) was added to the mixture, after that NaO^{t}Bu (2 equiv., 130 mg, 1.36 mmol) portion wise dissolved to the reaction mixture. Reaction progress was checked through silica gel thin layer chromatography. After completion of the reaction, the mixture was dissolved in 20 mL of water and 5 mL x 3 of ethyl acetate, further the organic layer was separated and treated with Na_2SO_4 and dried over rotary evaporator. Then, the crude product was purified through flash column chromatography using 3:7 (EA:Hex) solvent mixture as a eluent.

1-Methyl-3-(4-nitrophenyl)indolin-2-one (2a) Light yellow solid; yield: 142 mg (78%); R_f 0.25 in 3:7 (EA:Hex). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, J = 8.7 Hz, 2H), 7.38 (t, J = 8.8 Hz, 3H), 7.15 (d, J = 7.2 Hz, 1H), 7.10 (t, J = 7.4 Hz, 1H), 6.93 (d, J = 7.8 Hz, 1H), 4.71 (s, 1H), 3.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.4, 147.4, 144.4, 143.8, 129.4, 129.1, 127.2, 125.0, 124.0, 123.1, 108.6, 51.6, 26.6; HRMS (ESI) m/z calcd for $C_{15}H_{12}N_2O_3$ $[M+H]^+$ 269.0921, found 269.0909.

5-(1-Methyl-2-oxoindolin-3-yl)-2-nitrobenzonitrile (2b) Yellow solid; yield: 150 mg (75%); R_f 0.2 in 3:7 (EA:Hex) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, J = 8.5 Hz, 1H), 7.73 (dd, J = 11.2, 2.6 Hz, 1H), 7.46 – 7.39 (m, 1H), 7.18 – 7.11 (m, 1H), 6.96 (d, J = 7.9 Hz, 1H), 3.25 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.3, 147.6, 144.5, 144.2, 135.2, 133.9, 129.8, 125.9, 125.6, 125.1, 123.5, 114.7, 109.1, 108.5, 50.9, 26.8; HRMS (ESI)- m/z calcd for $C_{15}H_{12}N_2O_3$ $[M-H]^-$ 292.0717, found 292.0704.

1-Methyl-3-(4-nitro-3-(trifluoromethyl)phenyl)indolin-2-one (2c) Light yellow; yield: 160 mg (70%); R_f 0.27 in 3:7 (EA:Hex) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 8.3 Hz, 1H), 7.68 (s, 1H), 7.58 (dd, J = 8.3, 1.5 Hz, 1H), 7.45 – 7.36 (m, 1H), 7.19 – 7.08 (m, 2H), 6.95 (d, J = 7.9 Hz, 1H), 4.73 (s, 1H), 3.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.8, 147.3, 144.5, 142.1, 133.0, 129.5, 128.0 (q, J = 5.2 Hz), 126.1, 125.6, 125.0, 124.0, 123.3, 120.4, 108.9, 51.2, 26.7; HRMS (ESI) m/z calcd for $C_{16}H_{11}F_3N_2O_3$ $[M+H]^+$ 337.0795, found 337.0813.

3-(2,4-Dinitrophenyl)-1-methylindolin-2-one (2d) Dark brown solid; yield: 158 mg (74%); R_f 0.18 in 3:7 (EA:Hex) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (d, J = 2.2 Hz, 1H), 8.35 (dd, J = 8.5, 2.0 Hz, 1H), 7.40 (dd, J = 17.5, 8.7 Hz, 1H), 7.11 (dt, J = 14.9, 7.3 Hz, 1H), 6.95 (d, J = 7.8 Hz, 1H), 5.56 (s, 1H), 3.27 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.3, 149.6, 147.3, 144.4, 138.1, 132.5, 129.5, 127.3, 125.8, 124.5, 123.3, 121.0, 108.9, 48.7, 26.7; HRMS (ESI) m/z calcd for $C_{15}H_{11}N_3O_5$ $[M+H]^+$ 314.0771, found 314.0785.

3-(2-Fluoro-4-nitrophenyl)-1-methylindolin-2-one (2e) Sienna solid; yield: 160 mg (82%); R_f 0.32 in 3:7 (EA:Hex) ^{1}H NMR (400 MHz, CDCl3) δ 7.97 (dd, J = 9.7, 1.9 Hz, 6H), 7.39 – 7.31 (m, 3H), 7.24 (t, J = 7.9 Hz, 4H), 7.06 (q, J = 7.6 Hz, 6H), 6.92 (d, J = 7.8 Hz, 3H), 4.95 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.9, 161.9, 159.4, 148.2 (d, J = 8.7 Hz), 144.3, 132.1 (d, J = 15.4 Hz), 130.8 (d, J = 4.2 Hz), 129.1, 126.8, 124.4, 123.1, 119.6 (d, J = 3.7 Hz), 111.8 (d, J = 27.1 Hz), 108.6, 46.5, 26.6; HRMS (ESI) m/z calcd for $C_{15}H_{11}FN_2O_3$ $[M+H]^+$ 287.0826, found 287.0851.

3-(2-Chloro-4-nitrophenyl)-1-methylindolin-2-one (2f) Firebrick solid; yield: 144 mg (70%); R_f 0.2 in 3:7 (EA:Hex) ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.36 (s, 1H), 8.07 (d, J = 7.5 Hz, 1H), 7.39 (t, J = 7.8 Hz, 1H), 7.27 – 7.01 (m, 3H), 6.96 (d, J = 7.9 Hz, 1H), 5.24 (s, 1H), 3.34 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.05, 147.67, 144.27, 142.54, 135.77, 129.14, 127.16, 127.14, 125.22, 124.36, 123.17, 122.21, 108.63, 49.85, 26.70; HRMS (ESI) m/z calcd for $C_{15}H_{11}ClN_2O_3$ $[M+H]^+$ 303.0535, found 303.0531.

3-(3-Methoxy-4-nitro-5-(trifluoromethyl)phenyl)-1-methylindolin-2-one (2g) Sienna solid; yield: 144 mg (58%); R_f 0.18 in 3:7 (EA:Hex) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (s, 1H), 7.81 (s, 1H), 7.30 (t, J = 7.5 Hz, 1H), 6.96 (t, J = 7.3 Hz, 1H), 6.92 – 6.82 (m, 2H), 4.94 (s, 1H), 3.61 (s, 3H), 3.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7, 159.0, 147.9, 144.6, 132.9, 132.6, 132.2, 128.5, 126.8, 123.3, 122.6, 113.5 (q, J = 6.0 Hz), 109.8, 107.8, 56.9, 46.2, 26.5; HRMS (ESI) m/z calcd for $C_{17}H_{13}F_3N_2O_4$ $[M+H]^+$ 367.0900, found 367.0912.

1-Methyl-3-(2-nitro-5-(trifluoromethyl)phenyl)indolin-2-one (2h) Light yellow solid; yield: 155 mg (68%); R_f 0.27 in 3:7 (EA:Hex) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, J = 8.5 Hz, 1H), 7.73 (dd, J = 8.4, 1.0 Hz, 1H), 7.47 (s, 1H), 7.37 (t, J = 7.7 Hz, 1H), 7.13 (d, J = 7.2 Hz, 1H), 7.07 (t, J = 7.4 Hz, 1H), 6.94 (d, J = 7.8 Hz, 1H), 5.41 (s, 1H), 3.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.8, 151.5, 144.4, 135.0, 134.7, 132.3, 129.2, 128.5, 126.1, 126.06 – 125.9 (m), 124.4, 123.1, 121.3, 108.8, 48.7, 26.7; HRMS (ESI) m/z calcd for $C_{16}H_{11}F_3N_2O_3$ $[M+H]^+$ 337.0795, found 337.0788.

5-Methoxy-1-methyl-3-(4-nitrophenyl)indolin-2-one (2i) Orange red solid; yield: 118 mg (70%); R_f 0.2 in 3:7 (EA:Hex) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, J = 8.8 Hz, 2H), 7.38 (d, J = 8.7 Hz, 2H), 6.89 (dd, J = 8.5, 2.3 Hz, 1H), 6.82 (d, J = 8.5 Hz, 1H), 6.75 (d, J = 1.3 Hz, 1H), 4.68 (s, 1H), 3.75 (s, 3H), 3.22 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.1, 156.3, 147.4, 143.8, 137.9, 129.4, 128.4, 124.0, 113.4, 112.4, 108.9, 55.8, 52.0, 26.7; HRMS (ESI) m/z calcd for $C_{16}H_{14}N_2O_4$ $[M+H]^+$ 299.1026, found 299.1021.

1,5-Dimethyl-3-(4-nitrophenyl)indolin-2-one (2j) Red solid; yield: 119 mg (68%); R_f 0.2 in 3:7 (EA:Hex) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, J = 8.5 Hz, 2H), 7.38 (d, J = 8.5 Hz, 2H), 7.16 (d, J = 7.7 Hz, 1H), 6.95 (s, 1H), 6.81 (d, J = 7.9 Hz, 1H), 4.67 (s, 1H), 3.23 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.50, 147.40, 144.14, 142.06, 132.82, 129.46, 127.33, 125.82, 124.03, 121.99, 108.38, 51.77, 26.68, 21.08; HRMS (ESI) m/z calcd for $C_{16}H_{14}N_2O_3$ $[M+H]^+$ 283.1077, found 283.1089.

5-(1,5-Dimethyl-2-oxoindolin-3-yl)-2-nitrobenzonitrile (2k) Dark brown solid; yield: 107 mg (56%); R_f 0.2 in 3:7 (EA:Hex) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, J = 8.5 Hz, 1H), 7.80 – 7.67 (m, 2H), 7.21 (d, J = 7.9 Hz, 1H), 6.96 (s, 1H), 6.84 (d, J = 8.0 Hz, 1H), 4.69 (s, 1H), 3.23 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.30, 144.44, 142.11, 135.16, 133.96, 133.28, 130.04, 125.93, 125.84, 125.72, 122.95, 114.81, 108.81, 108.53, 51.05, 26.81, 21.10; HRMS (ESI) m/z calcd for $C_{17}H_{13}N_3O_3$ $[M+H]^+$ 308.1030, found 308.1047.

3-(2,4-Dinitrophenyl)-1,5-dimethylindolin-2-one (2l) Yellow solid; yield: 106 mg (52%); R_f 0.18 in 3:7 (EA:Hex) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (s, 1H), 8.34 (d, J = 7.5 Hz, 1H), 7.40 (d, J = 7.2 Hz, 1H), 7.16 (d, J = 7.2 Hz, 1H), 6.94 (s, 1H), 6.82 (d, J = 7.5 Hz, 1H), 5.51 (s, 1H), 3.24 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.37, 147.24, 142.03, 138.42,

133.07, 129.71, 127.38, 126.87, 125.94, 125.36, 120.98, 120.26, 108.67, 48.78, 26.79, 21.07; HRMS (ESI) m/z calcd for $C_{16}H_{13}N_3O_5$ $[M+H]^+$ 328.0928, found 328.0936.

1-Methyl-3-(4-nitrophenyl)-5-(trifluoromethoxy)indolin-2-one (2m) orange solid; yield: 85 mg (56%); R_f 0.2 in 3:7 (EA:Hex) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 8.7 Hz, 2H), 7.37 (d, *J* = 8.7 Hz, 2H), 7.26 (d, *J* = 9.5 Hz, 1H), 7.05 (s, 1H), 6.92 (d, *J* = 8.5 Hz, 1H), 4.73 (s, 1H), 3.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.14, 147.65, 145.02 (q, J = 1.9 Hz), 143.17, 142.77, 129.36, 128.50, 124.21, 122.39, 121.77, 119.11, 109.09, 51.64, 26.83; HRMS (ESI) m/z calcd for $C_{16}H_{11}F_3N_2O_4$ $[M+H]^+$ 353.0744, found 353.0759.

5-Bromo-1-methyl-3-(4-nitrophenyl)indolin-2-one (2n) Dark goldenrod solid; yield: 114 mg (74%); R_f 0.2 in 3:7 (EA:Hex) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 8.6 Hz, 2H), 7.49 (d, *J* = 7.8 Hz, 1H), 7.36 (d, *J* = 8.6 Hz, 2H), 7.25 (d, *J* = 4.7 Hz, 1H), 6.80 (t, *J* = 8.5 Hz, 1H), 4.70 (s, 1H), 3.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.8, 147.6, 143.5, 142.9, 132.0, 129.4, 129.1, 128.2, 124.1, 115.7, 110.0, 51.4, 26.7; HRMS (ESI) m/z calcd for $C_{15}H_{11}BrN_2O_3$ $[M-H]^-$ 344.9869, found 344.9875.

5-Bromo-3-(2-fluoro-4-nitrophenyl)-1-methylindolin-2-one (2o) Peru solid; yield: 129 mg (80%); R_f 0.24 in 3:7 (EA:Hex) ^{1}H NMR (400 MHz, $CDCl_3$ δ 7.98 (dd, *J* = 11.6, 4.4 Hz, 2H), 7.47 (dd, *J* = 8.2, 1.0 Hz, 1H), 7.27 (dd, *J* = 9.4, 4.5 Hz, 1H), 7.18 (s, 1H), 6.80 (d, *J* = 8.3 Hz, 1H), 4.93 (s, 1H), 3.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.38, 160.53 (d, *J* = 252.4 Hz), 148.43 (d, *J* = 8.0 Hz), 143.32, 132.04 (s), 131.20 (d, *J* = 15.2, Hz), 130.93 (d, *J* = 4.1, Hz), 128.75, 127.62, 119.79 (d, *J* = 3.7 Hz), 115.71 (s), 111.96 (d, *J* = 26.95 Hz), 110.03, 46.45, 26.81; HRMS (ESI) m/z calcd for $C_{15}H_{10}BrFN_2O_3$ $[M+H]^+$ 364.9932, found 364.9938.

5-Chloro-3-(2-fluoro-4-nitrophenyl)-1-methylindolin-2-one (2p) Dark goldenrod solid; yield: 110 mg (62%); R_f 0.24 in 3:7 (EA:Hex) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07-7.93 (m, 2H), 7.33-7.25 (m, 2H), 7.05 (s, 1H), 6.84 (d, *J* = 8.4 Hz, 1H), 4.93 (s, 1H), 3.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.47, 161.86, 159.35, 148.43 (d, *J* = 8.7 Hz), 142.84, 131.22 (d, *J* = 15.4 Hz), 130.91 (d, *J* = 4.1 Hz), 129.13, 128.47 (d, *J* = 15.4 Hz), 124.90, 119.78 (d, *J* = 3.7 Hz), 111.94 (d, *J* = 27.1 Hz), 109.54, 46.52 (d, *J* = 1.5 Hz), 26.83; HRMS (ESI) m/z calcd for $C_{15}H_{10}ClFN_2O_3$ $[M+H]^+$ 321.0437, found 321.0451.

5-Bromo-1-methyl-3-(4-nitro-3-(trifluoromethyl)phenyl)indolin-2-one (2q) Bisque solid; yield: 114 mg (62%); R_f 0.22 in 3:7 (EA:Hex) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.3 Hz, 1H), 7.67 (s, 1H), 7.53 (d, *J* = 7.7 Hz, 2H), 7.27 (s, 1H), 6.83 (d, *J* = 8.3 Hz, 1H), 4.73 (s, 1H), 3.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 147.5, 143.5, 141.3, 132.9, 132.4, 128.1 – 127.8 (m), 125.7, 124.6, 124.2, 123.0, 120.3, 115.9, 110.3, 51.1, 26.8; HRMS (ESI) m/z calcd for $C_{16}H_{10}BrF_3N_2O_3$ $[M-H]^-$ 412.9743, found 412.9749.

5-Chloro-1-methyl-3-(4-nitro-3-(trifluoromethyl)phenyl)indolin-2-one (2r) White solid; yield: 106 mg (52%); R_f 0.2 in 3:7 (EA:Hex) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.3 Hz, 1H), 7.67 (s, 1H), 7.53 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.38 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.14 (s, 1H), 6.88 (d, *J* = 8.4 Hz, 1H), 4.73 (s, 1H), 3.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.35, 143.05, 141.33, 132.91, 129.58, 128.78, 128.06 (q, *J* = 5.4 Hz), 127.80, 125.77, 125.47, 120.35, 109.86, 51.17, 26.87; HRMS (ESI) m/z calcd for $C_{16}H_{10}ClF_3N_2O_3$ $[M+H]^+$ 371.0405, found 371.0396.

5-Bromo-1-methyl-3-(2-nitro-5-(trifluoromethyl)phenyl)indolin-2-one (2s) Tan solid; yield: 121 mg (66%); R_f 0.24 in 3:7 (EA:Hex) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8.5 Hz, 1H), 7.77 (d, *J* = 7.7 Hz, 1H), 7.56 – 7.38 (m, 2H), 7.22 (s, 1H), 6.82 (d, *J* = 8.3 Hz, 1H), 5.31 (s, 1H), 3.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.3, 151.0, 143.4, 133.25 (q, J = 33.9 Hz), 132.1, 131.7, 128.0, 127.3, 126.4, 123.9, 121.2, 118.5, 115.7, 110.1, 49.1, 26.8; HRMS (ESI) m/z calcd for $C_{16}H_{10}BrF_3N_2O_3$ $[M+H]^+$ 414.9900, found 414.9897.

5-Chloro-1-methyl-3-(2-nitro-5-(trifluoromethyl)phenyl)indolin-2-one (2t) Peru solid; yield: 98 mg (48%); R_f 0.24 in 3:7 (EA:Hex) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.5 Hz, 1H), 7.77 (d, J = 8.4 Hz, 1H), 7.47 (s, 1H), 7.34 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.10 (s, 1H), 6.86 (d, *J* = 8.4 Hz, 1H), 5.30 (d, *J* = 16.2 Hz, 1H), 3.28 (s, 3H); 13C NMR (126 MHz, $CDCl_3$) δ 173.43, 156.37, 142.99, 137.92, 135.06 (q, *J* = 33.7 Hz), 132.37, 131.71, 129.21, 128.49, 127.27, 126.40, 113.48, 109.67, 109.15, 55.83, 26.84; HRMS (ESI) m/z calcd for $C_{16}H_{10}ClF_3N_2O_3$ $[M+H]^+$ 393.0224, found 393.0210.

5-methoxy-1-methyl-3-(2-nitro-5-(trifluoromethyl)phenyl)indolin-2-one (2u) Brown solid; yield: 145 mg (70%); R_f 0.22 in 3:7 (EA:Hex) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 8.5 Hz, 1H), 7.73 (d, *J* = 7.4 Hz, 1H), 7.46 (s, 1H), 6.97 – 6.81 (m, 2H), 6.74 (s, 1H), 5.38 (s, 1H), 3.74 (s, 3H), 3.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.47, 156.39, 137.95, 134.94 (q, *J* = 33.2 Hz), 132.39, 127.28, 126.17, 126.01 (q, *J* = 3.8 Hz), 124.05, 121.33, 113.49, 111.91, 109.14, 55.84, 49.12, 26.78; HRMS (ESI) m/z calcd for $C_{17}H_{13}F_3N_2O_4$ $[M+Na]^+$ 389.0720, found 389.0725.

1,5-Dimethyl-3-(2-nitro-5-(trifluoromethyl)phenyl)indolin-2-one (2v) Peru solid; yield: 148 mg (68%); R_f 0.22 in 3:7 (EA:Hex) ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8.5 Hz, 1H), 7.77 (dd, *J* = 8.4, 1.1 Hz, 1H), 7.50 (s, 1H), 7.20 (d, *J* = 7.9 Hz, 1H), 6.98 (s, 1H), 6.86 (d, *J* = 8.0 Hz, 1H), 5.40 (s, 1H), 3.30 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.82, 151.51, 142.07, 135.06, 134.80, 132.87, 132.64, 129.50, 126.14, 125.93 (q, *J* = 3.54 Hz), 125.26 – 125.04 (m), 123.79, 121.62, 108.51, 49.17, 26.73 21.08; HRMS (ESI) m/z calcd for $C_{17}H_{13}F_3N_2O_3$ $[M+H]^+$ 351.0951, found 351.0945.

5-Bromo-3-(4-nitrophenyl)indolin-2-one (3a) Dark blue green solid; yield: 108 mg (69%); R_f 0.18 in 3:7 (EA:Hex) ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.96 (s, 1H), 8.29 – 8.23 (m, 2H), 7.49 – 7.39 (m, 3H), 7.27 (s, 1H), 6.90 (d, *J* = 8.3 Hz, 1H), 4.78 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.56, 147.70, 142.70, 140.55, 132.13, 129.96, 129.45, 128.48, 124.30, 115.81, 111.87, 52.14; HRMS (ESI) m/z calcd for $C_{14}H_9BrN_2O_3$ $[M+H]^+$ 332.9869, found 332.9878.

3-(2-Fluoro-4-nitrophenyl)indolin-2-one (3b) Yellow solid; yield: 168 mg (82%); R_f 0.2 in 3:7 (EA:Hex) ^{1}H NMR (400 MHz, DMSO) δ 10.72 (s, 1H), 8.13 – 8.04 (m, 2H), 7.55 (t, *J* = 8.0 Hz, 1H), 7.21 (t, *J* = 7.5 Hz, 1H), 6.98 – 6.87 (m, 3H), 5.14 (s, 1H); ^{13}C NMR (100 MHz, DMSO) δ 176.00, 160.27 (d, *J* = 250.5 Hz), 148.21 (d, *J* = 9.1 Hz), 143.23, 133.23 (d, *J* = 15.1 Hz), 132.77 (d, *J* = 4.6 Hz), 128.83 (d, *J* = 38.8 Hz), 123.45 (d, *J* = 232.1 Hz), 120.35 (d, *J* = 3.3 Hz), 111.96 (d, *J* = 26.89 Hz), 110.16, 47.66; HRMS (ESI) m/z calcd for $C_{14}H_9FN_2O_3$ $[M+H]^+$ 273.0970, found 273.0653.

3-(2-Bromo-4-nitrophenyl)indolin-2-one (3c) Brown solid; yield: 160 mg (64%); R_f 0.18 in 3:7 (EA:Hex) ^{1}H NMR (400 MHz, DMSO) δ 10.75 (s, 2H), 8.63 – 7.81 (m, 5H), 7.22 (s, 2H), 7.20 – 6.51 (m, 8H), 5.27 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 180.54, 152.35, 150.32, 148.04, 141.03, 135.12, 134.01, 132.91, 130.36, 129.57, 128.56, 127.26, 115.14, 56.81; HRMS (ESI) m/z calcd for $C_{14}H_9BrN_2O_3$ $[M+H]^+$ 332.9869, found 332.9869.

3-(2-Methyl-4-nitrophenyl)indolin-2-one (3d) Firebrick solid; yield: 137 mg (68%); R_f 0.2 in 3:7 (EA:Hex) ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.04 (s, 1H), 8.15 (s, 1H), 7.99 (d, *J* = 6.9 Hz, 1H), 7.31 (t, *J* = 7.8 Hz, 1H), 7.09 – 7.02 (m, 2H), 6.99 (d, *J* = 7.8 Hz, 1H), 5.00 (s, 1H), 2.87 – 2.30 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.41, 147.31, 142.61, 141.54, 139.42, 128.96, 125.71, 124.79, 123.99, 123.20, 121.48, 112.49, 110.36, 49.64, 19.97; HRMS (ESI) m/z calcd for $C_{15}H_{12}N_2O_3$ $[M+H]^+$ 269.0921, found 269.0926.

5-Bromo-3-(2-methyl-4-nitrophenyl)indolin-2-one (3e) Brown solid; yield: 103 mg (63%); R_f 0.2 in 3:7 (EA:Hex) ^{1}H NMR (500 MHz, DMSO) δ

10.82 (s, 1H), 8.14 (s, 1H), 8.01 (s, 1H), 7.45 (d, *J* = 8.1 Hz, 1H), 7.2 - 6.8 (m, 3H), 6.92 (d, *J* = 8.3 Hz, 1H), 5.27 (s, 1H), 2.84 – 2.17 (m, 3H); ^{13}C NMR (125 MHz, DMSO) δ 176.23, 168.85, 151.05, 147.10, 143.85, 142.63, 140.08, 131.64, 127.67, 125.52, 121.74, 114.03, 112.09, 55.35, 19.63; HRMS (ESI) m/z calcd for $C_{15}H_{11}BrN_2O_3$ $[M+H]^+$ 344.9869, found 344.9895.

5-Bromo-3-(2-fluoro-4-nitrophenyl)indolin-2-one (3f) Brown solid; yield: 141 mg (85%); R_f 0.22 in 3:7 (EA:Hex) ^{1}H NMR (400 MHz, DMSO) δ 10.85 (s, 1H), 8.09 (t, *J* = 7.0 Hz, 2H), 7.58 (t, *J* = 8.0 Hz, 1H), 7.40 (d, *J* = 7.9 Hz, 1H), 7.14 (s, 1H), 6.86 (d, *J* = 8.3 Hz, 1H), 5.21 (s, 1H); ^{13}C NMR (100 MHz, DMSO) δ 176.60, 176.22, 155.02, 147.09, 142.63, 137.47, 131.63, 127.52, 125.51, 121.73, 113.04 (d, *J* = 195.38 Hz), 112.26 (d, *J* = 71.63 Hz), 109.78, 46.25 (d, *J* = 46.25 Hz); HRMS (ESI) m/z calcd for $C_{14}H_8BrFN_2O_3$ $[M-H]^-$ 348.9619, found 348.9601.

4,7-Dichloro-3-(4-nitrophenyl)indolin-2-one (3g) Dark brown solid; yield: 88 mg (55%); R_f 0.14 in 3:7 (EA:Hex) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (s, 1H), 8.19 (d, *J* = 8.7 Hz, 2H), 7.36 (d, *J* = 8.7 Hz, 2H), 7.27 (d, *J* = 8.7 Hz, 1H), 7.00 (d, *J* = 8.8 Hz, 1H), 4.82 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.51, 147.72, 140.83, 140.75, 130.47, 129.97, 129.29, 126.39, 124.35, 124.16, 114.00, 52.97; HRMS (ESI) m/z calcd for $C_{14}H_8Cl_2N_2O_3$ $[M-H]^-$ 320.9828, found 320.9854.

3-Benzyl-3-(4-nitrophenyl)indolin-2-one (3h) Light yellow solid; yield: 127 mg (82%); R_f 0.2 in 2:8 (EA:Hex) ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (d, *J* = 8.9 Hz, 3H), 7.72 (d, *J* = 8.9 Hz, 2H), 7.25 (td, *J* = 7.7, 1.1 Hz, 1H), 7.20 (d, *J* = 7.0 Hz, 1H), 7.17 – 7.09 (m, 2H), 7.05 (t, *J* = 7.4 Hz, 2H), 6.90 (d, *J* = 7.2 Hz, 2H), 6.78 (d, *J* = 7.7 Hz, 1H), 3.71 (d, *J* = 12.9 Hz, 1H), 3.52 (d, *J* = 12.9 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 178.75, 147.24, 146.86, 140.72, 134.69, 130.39, 130.14, 128.93, 128.39, 127.82, 127.00, 125.91, 123.71, 122.66, 110.29, 58.65, 43.87; HRMS (ESI) m/z calcd for $C_{21}H_{16}N_2O_3$ $[M+H]^+$ 345.1234, found 345.1233.

3-Benzyl-5-bromo-3-(4-nitrophenyl)indolin-2-one (3i) Yellow solid; yield: 101 mg (72%); R_f 0.2 in 2:8 (EA:Hex) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, *J* = 8.9 Hz, 2H), 8.02 (s, 1H), 7.66 (t, *J* = 11.6 Hz, 2H), 7.33 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.29 – 7.24 (m, 1H), 7.14 – 7.02 (m, 3H), 6.86 (d, *J* = 6.9 Hz, 2H), 6.63 (d, *J* = 8.3 Hz, 1H), 3.66 (d, *J* = 12.9 Hz, 1H), 3.46 (d, *J* = 12.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.90, 147.42, 145.97, 139.62, 134.19, 132.62, 131.84, 130.09, 128.95, 128.26, 128.02, 127.24, 123.89, 115.25, 111.61, 58.80, 43.83; HRMS (ESI) m/z calcd for $C_{21}H_{15}BrN_2O_3$ $[M+H]^+$ 423.0339, found 423.0320.

3-Benzyl-5-chloro-3-(4-nitrophenyl)indolin-2-one (3j) Yellow solid; yield: 110 mg (75%); R_f 0.2 in 2:8 (EA:Hex) ^{1}H NMR (400 MHz, DMSO) δ 10.59 (s, 1H), 8.21 (d, *J* = 8.9 Hz, 2H), 7.70 (d, *J* = 8.9 Hz, 1H), 7.54 (d, *J* = 1.9 Hz, 1H), 7.16 (dd, *J* = 8.3, 2.0 Hz, 1H), 7.09 – 7.02 (m, 3H), 6.95 – 6.87 (m, 2H), 6.65 (d, *J* = 8.3 Hz, 1H), 3.67 (d, *J* = 12.8 Hz, 1H), 3.55 (d, *J* = 12.8 Hz, 1H); ^{13}C NMR (125 MHz, DMSO) δ 178.01, 148.04, 147.13, 141.23, 135.86, 133.50, 130.39, 128.91, 128.76, 128.14, 127.17, 126.28, 126.27, 124.19, 111.55, 59.24, 41.99; HRMS (ESI) m/z calcd for $C_{21}H_{15}ClN_2O_3$ $[M+Na]^+$ 401.0663, found 401.0671.

3-Benzyl-3-(2-fluoro-4-nitrophenyl)indolin-2-one (3k) Light goldenrod solid; yield: 136 mg (84%); R_f 0.22 in 2:8 (EA:Hex) ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (s, 1H), 8.15 (dd, *J* = 8.7, 1.8 Hz, 1H), 7.93 – 7.85 (m, 2H), 7.19 – 7.10 (m, 3H), 7.06-7.02 (m, 3H), 6.83 (d, *J* = 7.2 Hz, 2H), 6.63 (d, *J* = 7.8 Hz, 1H), 5.31 (s, 1H), 3.70 – 3.63 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.04, 160.22 (d, *J* = 253.6 Hz), 148.07 (d, *J* = 9.3 Hz), 141.26, 135.73 (d, *J* = 13.1 Hz), 133.45, 130.88, 130.23, 129.20 (d, *J* = 4.4 Hz), 128.84, 127.70 , 127.06 , 123.86 (d, *J* = 1.6 Hz), 122.65, 119.36 (d, *J* = 3.5 Hz), 111.98 (d, *J* = 27.55 Hz), 109.86, 54.60 (d, *J* = 292.8 Hz), 41.65; HRMS (ESI) m/z calcd for $C_{21}H_{15}FN_2O_3$ $[M+H]^+$ 363.1139, found 363.1163.

3-Benzyl-5-bromo-3-(2-fluoro-4-nitrophenyl)indolin-2-one (3l) Yellow solid; yield: 114 mg (78%); R_f 0.21 in 2:8 (EA:Hex) ^{1}H NMR (500 MHz, DMSO) δ 10.54 (s, 1H), 8.27 – 8.14 (m, 2H), 8.05 (dd, *J* = 11.1, 2.1 Hz, 1H), 7.42 (d, *J* = 1.8 Hz, 1H), 7.29 (dd, *J* = 8.3, 1.9 Hz, 1H), 7.15 – 7.07 (m, 3H), 6.82 (d, *J* = 6.6 Hz, 2H), 6.54 (d, *J* = 8.3 Hz, 1H), 3.88 (d, *J* = 12.2 Hz, 1H), 3.47 (d, *J* = 12.2 Hz, 1H); ^{13}C NMR (125 MHz, DMSO) δ 177.53, 170.80, 159.55 (d, *J* = 247.07 Hz), 148.25 (d, *J* = 9.7 Hz), 142.23, 135.87 (d, *J* = 13.0 Hz), 134.42, 133.81, 131.73, 130.80 (d, *J* = 4.1 Hz), 130.48, 128.00, 127.33 (d, *J* = 7.6 Hz), 120.07 (d, *J* = 2.9 Hz), 113.70, 111.88 (d, *J* = 2.9 Hz), 111.55, 60.22, 55.50; HRMS (ESI) m/z calcd for $C_{21}H_{14}BrFN_2O_3$ $[M+H]^+$ 441.0245, found 441.0256.

3-Benzyl-3-(4-nitro-3-(trifluoromethyl)phenyl)indolin-2-one (3m) Antique white solid; yield: 120 mg (65%); R_f 0.2 in 2:8 (EA:Hex) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (s, 1H), 8.00 (s, 1H), 7.93 – 7.79 (m, 2H), 7.27 – 7.22 (m, 1H), 7.21 – 6.98 (m, 5H), 6.84 (d, *J* = 7.1 Hz, 2H), 6.76 (d, *J* = 7.7 Hz, 1H), 3.66 (d, *J* = 12.9 Hz, 1H), 3.44 (d, *J* = 12.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.13, 147.15, 145.19, 140.68, 134.19, 132.16, 130.09, 129.34, 127.91, 127.18, 126.98 (q, *J* = 5.5 Hz), 125.88, 125.32, 124.03, 123.69, 122.92, 120.52, 110.57, 58.31, 44.33; HRMS (ESI) m/z calcd for $C_{22}H_{15}F_3N_2O_3$ $[M+H]^+$ 413.1108, found 413.1115.

3-(2-Bromobenzyl)-3-(4-nitrophenyl)indolin-2-one (3n) Yellow solid; yield: 91 mg (65%); R_f 0.18 in 2:8 (EA:Hex) ^{1}H NMR (400 MHz, DMSO) δ 10.67 (s, 1H), 8.20 (d, *J* = 8.9 Hz, 2H), 7.67 (d, *J* = 8.9 Hz, 2H), 7.39 (dd, *J* = 7.9, 1.0 Hz, 1H), 7.19 (d, *J* = 7.4 Hz, 1H), 7.14 (td, *J* = 7.7, 0.9 Hz, 1H), 7.08 (td, *J* = 7.5, 1.1 Hz, 1H), 7.00 (td, *J* = 7.7, 1.7 Hz, 1H), 6.92 (dd, *J* = 7.6, 6.8 Hz, 2H), 6.74 (d, *J* = 7.7 Hz, 1H), 3.78 (q, *J* = 13.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.93, 152.90, 151.87, 147.02, 140.57, 137.85, 135.42, 134.98, 134.10, 134.08, 133.58, 132.46, 131.30, 130.59, 128.89, 126.80, 115.03, 62.86, 46.13; HRMS (ESI) m/z calcd for $C_{21}H_{16}BrN_2O_3$ $[M+H]^+$ 423.0339, found 423.0320.

3-(4-Methoxybenzyl)-3-(4-nitrophenyl)indolin-2-one (3o) Light yellow solid; yield: 108 mg (73%); R_f 0.19 in 2:8 (EA:Hex) ^{1}H NMR (400 MHz, DMSO) δ 10.43 (s, 1H), 8.18 (d, *J* = 8.9 Hz, 2H), 7.68 (d, *J* = 8.9 Hz, 2H), 7.35 (d, *J* = 7.4 Hz, 1H), 7.12 (t, *J* = 7.3 Hz, 1H), 6.98 (t, *J* = 7.4 Hz, 1H), 6.77 (d, *J* = 8.6 Hz, 2H), 6.67 (d, *J* = 7.7 Hz, 1H), 6.57 (d, *J* = 8.6 Hz, 2H), 3.58 (s, 3H), 3.54 – 3.44 (m, 2H); ^{13}C NMR (100 MHz, DMSO) δ 178.28, 158.33, 148.75, 146.95, 142.37, 131.46, 131.39, 128.95, 128.75, 127.86, 126.06, 124.00, 122.13, 113.40, 110.20, 58.96, 55.24, 41.78; HRMS (ESI) m/z calcd for $C_{22}H_{18}N_2O_4$ $[M+H]^+$ 375.1339, found 375.1330.

3-(Naphthalen-1-ylmethyl)-3-(4-nitrophenyl)indolin-2-one (3p) Yellow solid; yield: 61 mg (42%); R_f 0.2 in 2:8 (EA:Hex) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (s, 1H), 8.18 (d, *J* = 8.9 Hz, 2H), 7.95 – 7.89 (m, 1H), 7.76 – 7.66 (m, 3H), 7.60 (d, *J* = 8.2 Hz, 1H), 7.33 – 7.28 (m, 2H), 7.14 – 7.04 (m, 2H), 6.98 (dd, *J* = 14.5, 7.2 Hz, 2H), 6.87 (t, *J* = 7.3 Hz, 1H), 6.66 (d, *J* = 7.8 Hz, 1H), 4.21 (d, *J* = 13.8 Hz, 1H), 3.94 (d, *J* = 13.8 Hz, 1H); ^{13}C NMR (125 MHz, DMSO) δ 178.51, 149.00, 147.02, 142.34, 133.61, 132.53, 132.45, 131.24, 129.01, 128.96, 128.55, 128.39, 127.78, 126.67, 125.73, 125.27, 125.11, 124.03, 121.92, 110.04, 58.87, 37.78; HRMS (ESI) m/z calcd for $C_{25}H_{18}N_2O_3$ $[M+H]^+$ 393.1234, found 393.1257.

Typical procedure for reductive addition of styrene with 3-substituted oxindoles. 3-Benzyl oxindole (0.44 mmol, 100 mg) was dissolved in dry DMSO (2 mL) in a 15 mL well dried sealed tube having magnetic bead. Styrene (5 equiv, 2.2 mmol, 256 µL) was added to the mixture, after that KO^{t}Bu (3 equiv, 1.32 mmol, 148 mg) was added over portion wise. Reaction progress was checked through thin layer chromatography, after completion of the reaction, reaction mixture was dissolved in 20 mL of water and organic layer was extracted with (5 mL × 3) of ethyl acetate, treated with Na_2SO_4 and dried over rota evaporator. Purified through flash column chromatography using 3:7 (EA:Hex) solvent mixture as a eluent.

3-Benzyl-3-phenethylindolin-2-one (4a) Bisque solid ; yield: 122 mg (83%) R_f 0.5 in 3:7 (EA:Hex) ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.63 (s, 1H), 7.27 – 7.17 (m, 5H), 7.14 – 7.04 (m, 6H), 6.94 – 6.90 (m, 2H), 6.82 (d, *J* = 7.6 Hz, 1H), 3.20 (d, *J* = 13.1 Hz, 1H), 3.11 (d, *J* = 13.1 Hz, 1H), 2.48 – 2.39 (m, 2H), 2.23 – 2.15 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 181.58, 141.49, 141.20, 135.72, 131.40, 130.04, 128.36, 128.33, 128.00, 127.66, 126.56, 125.93, 123.88, 122.27, 109.77, 55.19, 44.13, 39.31, 30.83; HRMS (ESI) m/z calcd for $C_{23}H_{21}NO$ $[M+H]^+$ 328.1696, found 328.1705.

3-Benzyl-3-(4-methylphenethyl)indolin-2-one (4b) Green yellow solid; yield: 116 mg (76%) R_f 0.5 in 3:7 (EA:Hex). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24 (s, 1H), 7.21 (dd, *J* = 11.7, 4.3 Hz, 2H), 7.13 – 7.04 (m, 6H), 6.98 (d, *J* = 7.9 Hz, 2H), 6.91 (dd, *J* = 7.7, 1.5 Hz, 2H), 6.78 (d, *J* = 7.6 Hz, 1H), 3.19 (d, *J* = 13.1, Hz, 1H), 3.10 (d, *J* = 13.1 Hz, 1H), 2.44 – 2.36 (m, 2H), 2.32 (s, 3H), 2.19 – 2.10 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 181.30, 141.05, 138.42, 135.73, 135.38, 131.43, 130.04, 129.01, 128.22, 127.95, 127.64, 126.53, 123.90, 122.26, 109.63, 55.14, 44.13, 39.52, 30.35, 20.99; HRMS (ESI) m/z calcd for $C_{24}H_{23}NO$ $[M+H]^+$ 342.1852, found 342.1868.

3-(4-Methoxybenzyl)-3-(4-methoxyphenethyl)indolin-2-one (4c) Light yellow solid; yield: 106 mg (69%); R_f 0.5 in 3:7 (EA:Hex) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.23 – 7.16 (m, 2H), 7.10 (t, *J* = 7.5 Hz, 1H), 6.99 (d, *J* = 8.4 Hz, 2H), 6.79 (dt, *J* = 16.2, 8.1 Hz, 5H), 6.59 (d, *J* = 8.3 Hz, 2H), 3.78 (s, 3H), 3.68 (s, 3H), 3.11 (d, *J* = 13.3 Hz, 1H), 3.03 (d, *J* = 13.3 Hz, 1H), 2.41 – 2.30 (m, 2H), 2.15 – 2.07 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 181.20, 158.18, 157.82, 141.03, 133.61, 131.59, 131.00, 129.24, 127.88, 127.81, 123.86, 122.23, 113.71, 113.03, 109.59, 55.24, 55.20, 55.00, 43.35, 39.48, 29.90; HRMS (ESI) m/z calcd for $C_{25}H_{25}NO_3$ $[M+H]^+$ 388.1907, found 388.1904.

3-(4-methoxybenzyl)-3-(4-methylphenethyl)indolin-2-one (4d) Antique white solid; yield: 110 mg (75%); R_f 0.5 in 3:7 (EA:Hex) ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.62 (s, 1H), 7.25 – 7.19 (m, 2H), 7.14 – 7.10 (m, 1H), 7.06 (d, *J* = 7.9 Hz, 2H), 6.97 (d, *J* = 8.0 Hz, 2H), 6.85 – 6.80 (m, 3H), 6.60 – 6.55 (m, 2H), 3.64 (s, 3H), 3.12 (d, *J* = 13.3 Hz, 1H), 3.05 (d, *J* = 13.3 Hz, 1H), 2.42 – 2.34 (m, 2H), 2.32 (s, 3H), 2.18 – 2.09 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 181.73, 158.17, 141.25, 138.51, 135.33, 131.66, 131.00, 129.00, 128.23, 127.91, 127.82, 123.83, 122.23, 113.04, 109.78, 55.31, 54.95, 43.30, 39.41, 30.36, 21.00; HRMS (ESI) m/z calcd for $C_{21}H_{16}NO_2$ $[M+H]^+$ 372.1958, found 372.1969.

3-(2-Bromobenzyl)-3-(4-methylphenethyl)indolin-2-one (4e) Goldenrod solid; yield: 89 mg (64%); R_f 0.5 in 3:7 (EA:Hex) ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.70 (s, 1H), 7.40 (dd, J = 5.4, 2.6 Hz, 1H), 7.22 – 7.15 (m, 3H), 7.09 – 7.03 (m, 4H), 7.00 – 6.94 (m, 3H), 6.86 (d, J = 7.7 Hz, 1H), 3.47 (d, J = 13.9, Hz, 1H), 3.38 (d, J = 13.8, Hz, 1H), 2.49 – 2.36 (m, 2H), 2.31 (s, 3H), 2.26 - 2.19 (m, 1H), 2.13 – 2.07 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 181.73, 140.89, 138.32, 135.99, 135.40, 132.80, 131.23, 130.80, 129.02, 128.25, 128.23, 128.07, 126.91, 125.87, 124.67, 122.23, 109.58, 54.58, 42.04, 39.45, 30.18, 21.00; HRMS (ESI) m/z calcd for $C_{24}H_{22}BrNO$ $[M+H]^+$ 420.0958, found 420.0947.

General procedure for the synthesis of indoles. To a single neck round bottom flask, Schwartz's reagent ($Cp_2Zr(H)Cl$, 1.1 equiv) was added to the solution of oxindole (100 mg, 1 equiv) in dry THF under inert atmosphere at 0 °C temperature. After addition, reaction mixture was kept at room temperature for 15-20 min and reaction progress was checked by thin layer chromatography. After completion of the reaction, saturated aqueous $NaHCO_3$ solution (15 mL) was added and the resulting mixture was extracted with ethyl acetate (20 mL×3). The organic layers were combined, dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by column chromatography by using ethyl acetate/hexane (10/90).

1-Methyl-3-(4-nitro-3-(trifluoromethyl)phenyl)-1H-indole (5a) Red solid; yield: 78 mg (82%); R_f 0.3 in 1:9 (EA:Hex) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 1.1 Hz, 1H), 8.01 (d, *J* = 8.5 Hz, 1H), 7.92 (dd, *J* = 13.9, 5.0 Hz, 2H), 7.42 (d, *J* = 8.2 Hz, 2H), 7.38 – 7.32 (m, 1H), 7.32 – 7.25 (m, 1H), 3.89 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.58, 141.55, 137.84, 129.48, 128.62, 126.39, 125.43 (q, 5.8 Hz), 124.86, 124.52, 123.04, 123.62, 121.40, 119.25, 113.46, 110.24, 33.27; HRMS (ESI) m/z calcd for $C_{16}H_{11}F_3N_2O_2$ $[M+H]^+$ 321.0845, found 321.0822.

3-(2-Chloro-4-nitrophenyl)-1-methyl-1H-indole (5b) Orange solid; yield: 75 mg (79%); R_f 0.3 in 1:9 (EA:Hex) ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.43 (d, *J* = 2.4 Hz, 1H), 8.20 (dd, *J* = 8.6, 2.4 Hz, 1H), 7.83 (d, *J* = 8.6 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.58 (s, 1H), 7.45 (d, *J* = 8.2 Hz, 1H), 7.39 – 7.35 (m, 1H), 7.28 (d, J = 8.3 Hz, 1H), 3.93 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.68, 140.93, 136.91, 132.90, 131.28, 130.38, 126.48, 125.75, 122.66, 121.80, 120.83, 119.71, 111.18, 109.96, 33.26.

Synthetic procedure for the synthesis of benzofuroindole (6) To a sealed tube containing stirrer bar oxindole (**3c**, 1 equiv, 0.30 mmol, 100 mg), Cu(I)TC (Copper(I)-thiophene-2-carboxylate, 1.1 equiv, 0.33 mmol, 63 mg) and K_2CO_3 (2 equiv, 0.60 mmol, 83 mg) were dissolved in dimethylacetamide (DMA) under inert atmosphere. The resulted reaction mixture was stirred at 130 °C for 3h. Upon completion of the reaction, the mixture was cooled to room temperature, passed through celite pad, and poured into H_2O and extracted with ethyl acetate (15 mL×4). The combined organic layers were dried over anhydrous Na_2SO_4, and concentrated in vacuo. The crude product was purified by column chromatography by using ethyl acetate/hexane as an eluent.

3-Nitro-6H-benzofuro[2,3-b]indole (6) Brown solid; yield: 36 mg (48%); R_f 0.5 in 4:6 (EA:Hex) ^{1}H NMR (400 MHz, DMSO) δ 10.81 (s, 1H), 8.91 (d, *J* = 2.0 Hz, 1H), 8.05 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.17 (t, *J* = 7.8 Hz, 1H), 7.10 (d, *J* = 7.3 Hz, 1H), 6.97 (t, *J* = 7.5 Hz, 1H), 6.68 (dd, *J* = 11.8, 8.2 Hz, 2H); ^{13}C NMR (100 MHz, DMSO) δ 174.67, 148.61, 143.03, 141.67, 135.77, 130.36, 128.50, 127.08, 125.15, 124.34, 122.83, 119.88, 110.47, 57.72.

General procedure for the synthesis of indolo indoles Triethyl phosphite $P(OEt)_3$ (0.5 mL) and oxindole (100 mg, 1 equiv) were added to a sealed tube (10 mL) containing stirrer bar. The resulted reaction mixture was stirred at 150 °C for 16-20 h, Progress of the reaction was monitored by TLC. Upon completion of the reaction, the mixture was cooled to room temperature, poured into 5N HCl solution and extracted with ethyl acetate (15 mL×4). The combined organic layers were dried over anhydrous Na_2SO_4, and concentrated in *vacuo*. The crude product was purified by column chromatography by using ethyl acetate/hexane as an eluent.

6-Methyl-2-(trifluoromethyl)-5,6-dihydroindolo[2,3-b]indole (7a)[4d] Cream viscous liquid; yield: 37 mg (43%); R_f 0.34 in 3:7 (EA:Hex) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (s, 1H), 8.09 (s, 1H), 7.90 (s, 1H), 7.45 – 7.28 (m, 4H), 3.84 (s, 3H); HRMS (ESI) m/z calcd for $C_{16}H_{11}F_3N_2$ $[M+H]^+$ 289.0947, found 289.0971.

2-Methoxy-5-methyl-9-(trifluoromethyl)-5,6-dihydroindolo[2,3-b]indole (7b)[4d] Brown viscous liquid; yield: 45 mg (52%); R_f 0.34 in 3:7 (EA:Hex) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (s, 1H), 8.05 (s, 1H), 7.36 (d, *J* = 14.6 Hz, 3H), 7.19 (d, *J* = 8.8 Hz, 1H), 6.85 (d, *J* = 8.5 Hz, 1H), 3.95 (s, 3H), 3.73 (s, 3H); HRMS (ESI) m/z calcd for $C_{17}H_{15}F_3N_2O$ $[M-H]^-$ 319.1053, found 319.1070.

1-Methyl-3-(4-nitrophenyl-2,3,5,6-*d*$_4$)indolin-2-one (8a) Brown solid; yield: 124 mg (67%); R_f 0.25 in 3:7 (EA:Hex) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (t, *J* = 7.7 Hz, 1H), 7.19 (d, *J* = 7.3 Hz, 1H), 7.14 (td, *J* = 7.5, 0.7 Hz, 1H), 6.97 (d, *J* = 7.9 Hz, 1H), 4.75 (s, 1H), 3.29 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.51, 147.33, 144.49, 143.70, 129.16, 129.03 (t, *J* = 25.4 Hz), 127.19, 125.07, 123.67 (t, *J* = 26.0 Hz), 123.14, 108.67, 51.55, 26.65.

Acknowledgements

SK thanks IISER Bhopal and DST-SERB New Delhi (EMR/2015/000061) for generous funding. MS and VR, CDP, acknowledge CSIR and CSIR-UGC New Delhi, respectively for fellowship .

Keywords: TM-free C-C Coupling • Oxindole • nitrobenzene • styrene • tert-butoxide • carbanion

[1] Transition metal free C-H functionalization based reviews a) J. Seayad, A. Tillack, C. G. Hartung, M. Beller, *Adv. Synth. Catal.* **2002**, *344*, 795-813; b) S. Yanagisawa, K. Itami, *ChemCatChem* **2011**, *3*, 827-829; c) W. Shi, C. Liu, A. Lei, *Chem Soc Rev.* **2011**, *40*, 2761-2776; d) A. Studer, D. P. Curran, *Angew. Chem. Int. Ed.* **2011**, *50*, 5018-5022; e) E. Shirakawa, T. Hayashi, *Chem. Lett.* **2012**, *41*, 130-134; f) T. L. Chan, Y. Wu, P. Y. Choy, F. Y. Kwong, *Chem. Eur. J.* **2013**, *19*, 15802-15814; g) A. Studer, D. P. Curran, *Nat. Chem.* **2014**, *6*, 765-773; h) C. L. Sun, Z. J. Shi, *Chem. Rev.* **2014**, *114*, 9219-9280; i) C. Liu, J. Yuan, M. Gao, S. Tang, W. Li, R. Shi, A. Lei *Chem. Rev.* **2015**, *115*, 12138−12204; Transition metal free based research articles j) D. Tzalis, P. Knochel, *Angew. Chem. Int. Ed.* **1999**, *38*, 1463-1465; k) A. L. Rodriguez, T. Bunlaksananusorn, P. Knochel, *Org. Lett.* **2000**, *2*, 3285-3287; l) T. Bunlaksananusorn, P. Knochel *Tetrahedron Lett.* **2002**, *43*, 5817–5819; m) Q. Liu, Q. Y. Zhao, J. Liu, P. Wu, H. Yi, A. Lei, *Chem. Commun.* **2012**, *48*, 3239-3241; n) K. Matcha, R. Narayan, A. P. Antonchick, *Angew. Chem. Int. Ed.* **2013**, *52*, 7985-7989; o) Y. Wu, F. Y. Kwong, P. Li, A. S. C. Chan, *Synlett.* **2013**, *24*, 2009-2013; p) H. Gao, D. H. Ess, M. Yousufuddin, L. Kürti, *J. Am. Chem. Soc.* **2013**, *135*, 7086-7089; q) R. Sword, S. OÏSullivan, J. A. Murphy, *Aust. J. Chem.* **2013**, *66*, 314 –322; r) S. M. Kim, D. W. Kim, J. W. Yang, *Org. Lett.* **2014**, *16*, 2876-2879; s) J. Yuan, X. Ma, H. Yi, C. Liu, A. Lei, *Chem. Commun.* **2014**, *50*, 14386-14389; t) R. Narayan, A. P. Antonchick, *Chem. Eur. J.* **2014**, *20*, 4568-4572; u) S. Manna, K. Matcha, A. P. Antonchick, *Angew. Chem. Int. Ed.* **2014**, *53*, 8163-8166; v) Y. Wu, P. Y. Choy, F. Y. Kwong, *Asian J. Org. Chem.* **2014**, *3*, 1262-1265; w) R. Samanta, R. Narayan, J. O. Bauer, C. Strohmann, S. Sievers, A. P. Antonchick, *Chem. Commun.* **2015**, *51*, 925-928; x) M. Pichette Drapeau, I. Fabre, L. Grimaud, I. Ciofini, T. Ollevier, M. Taillefer, *Angew. Chem. Int. Ed.* **2015**, *54*, 10587-10591; y) Z. Huang, D. Zhang, X. Qi, Z. Yan, M. Wang, H. Yan, A. Lei, *Org. Lett.* **2016**, *18*, 2351-2354; z) J. P. Barham, M. P. John, J. A. Murphy, *J. Am. Chem. Soc.* **2016**, *138*, 15482-15487.

[2] a) P. T. Anastas, J. C. Warner, *Green Chemistry: Theory and Practice*, Oxford University Press, Oxford, **1998**; b) J. A. Murphy, *Pure Appl. Chem*. **2000**, *72*, 1327–1334; c) K. Sanderson, *Nature*, **2011**, *469*, 18-20; d) Ö. Usluer, M. Abbas, G. Wantz, L. Vignau, L. Hirsch, E. Grana, C. Brochon, E. Cloutet, G. Hadziioannou, *ACS Macro Letters* **2014**, *3*, 1134-1138.

[3] a) M. D. Roydhouse, J. C. Walton, *Chem. Commun.* **2005**, *41*, 4453-4455; b) S. Yanagisawa, K. Ueda, T. Taniguchi, K. Itami, *Org. Lett.* **2008**, *10*, 4673-4676; c) C. L. Sun, H. Li, D. G. Yu, M. Yu, X. Zhou, X. Y. Lu, K. Huang, S. F. Zheng, B. J. Li, Z. J. Shi, *Nat. Chem*. **2010**, *2*, 1044-1049; d) W. Liu, H. Cao, H. Zhang, H. Zhang, K. H. Chung, C. He, H. Wang, F. Y. Kwong, A. Lei, *J. Am. Chem. Soc.* **2010**, *132*, 16737–16740; e) E. Shirakawa, K.-I. Itoh, T. Higashino, T. Hayashi, *J. Am. Chem. Soc.* **2010**, *132*, 15537–15539; f) C.-L. Sun, Y.-F. Gu, W.-P. Huang, Z.-J. Shi, *Chem. Commun.* **2011**, *47*, 9813-9815 g) H. Li, C.-L. Sun, M. Yu, D.-G. Yu, B.-J. Li, Z.-J. Shi, *Chem. Eur. J.* **2011**, *17*, 3593-3597; h) H. Liu, B. Yin, Z. Gao, Y. Li, H. Jiang, *Chem. Commun.* **2012**, *48*, 2033-2035; i) Y. Wu, S. M. Wong, F. Mao, T. L. Chan, F. Y. Kwong, *Org. Lett*. **2012**, *14*, 5306-5309; j) H. Zhang, R. Shi, A. Ding, L. Lu, B. Chen, A. Lei, *Angew. Chem. Int. Ed.* **2012**, *51*, 12542-12545; k) A. Dewanji, S. Murarka, D. P. Curran, A. Studer, *Org. Lett.* **2013**, *15*, 6102-6105; l) Y. Wu, P. Y. Choy, F. Y. Kwong, *Org. Biomol. Chem.* **2014**, *12*, 6820-6823; m) S. Zhou, G. M. Anderson, B. Mondal, E. Doni, V. Ironmonger, M. Kranz, T. Tuttle, J. A. Murphy, *Chem. Sci.* **2014**, *5*, 476-482; n) S. Zhou, E. Doni, G. M. Anderson, R. G. Kane, S. W. MacDougall, V. M. Ironmonger, T. Tuttle, J. A. Murphy, *J. Am. Chem. Soc.* **2014**, *136*, 17818-17826; o) J. Ballester, A.-M. Caminade, J.-P. Majoral, M. Taillefer, A. Ouali, *Catalysis Commun.* **2014**, *47*, 58-62; p) H. Yi, A. Jutand, A. Lei, Chem. Comm. **2015**, *51*, 545-548; q) E. Doni, S. Zhou, J. A. Murphy, *Molecules* **2015**, *20*, 1755-1774; r) J. P. Barham, G. Coulthard, K. J. Emery, E. Doni, F. Cumine, G. Nocera, M. P. John, L. E. A. Berlouis, T. McGuire, T. Tuttle, J. A. Murphy, *J. Am. Chem. Soc.* **2016**, *138*, 7402-7410; s) H. Wang, Z. Wang, H. Huang, J. Tan, K. Xu, *Org. Lett.* **2016**, *18*, 5680-5683; t) K. J. Emery, T. Tuttle, A. R. Kennedy, J. A. Murphy, *Tetrahedron* **2016**, *72*, 7875-7887; u) J. P. Barham, G. Coulthard, R. G. Kane, N. Delgado, M. P. John, J. A. Murphy, *Angew. Chem. Int. Ed.* **2016**, *55*, 4492-4496.

[4] Our group publications on C-H functionalization a) B. S. Bhakuni, A. Kumar, S. J. Balkrishna, J. A. Sheikh, S. Konar, S. Kumar, *Org. Lett.* **2012**, *14,* 2838-2841; b) B. S. Bhakuni, A. Yadav, S. Kumar, S. Patel, S. Sharma, S. Kumar, *J. Org. Chem*. **2014**, *79*, 2944-2954; c) A. Kumar, A. Yadav, A. Verma, S. Jana, M. Sattar, S. Kumar, D. Prasad Ch, S. Kumar, *Chem. Comm.* **2014**, *50*, 9481-9484; d) S. Kumar, V. Rathore, A. Verma, D. Prasad Ch, A. Kumar, A. Yadav, S. Jana, M. Sattar, Meenakshi, S. Kumar, *Org. Lett.* **2015**, *17*, 82-85; e) V. Rathore, M. Sattar, R. Kumar, S. Kumar, *J. Org. Chem.* **2016**, *81*, 9206-9218.

[5] a) E. Shirakawa, X. Zhang, T. Hayashi, *Angew. Chem. Int. Ed.* **2011**, *50*, 4671-4674; b) C. L. Sun, Y. F. Gu, B. Wang, Z. J. Shi, *Chem. Eur. J.* **2011**, *17*, 10844-10847; c) D. S. Roman, Y. Takahashi, A. B. Charette; *Org. Lett.* **2011**, *13*, 3242- 3245; d) C. L. Sun, Y. F. Gu, W. P. Huang, Z. J. Shi, *Chem. Comm.* **2011**, *47*, 9813-9815; e) M. Rueping, M. Leiendecker, A. Das, T. Poisson, L. Bui, *Chem. Commun.* **2011**, *47*, 10629-10631; f) R. Singha, A. Ahmed, Y. Nuree, M. Ghosh, J. K. Ray, *RSC Adv.* **2015**, *5*, 50174-50177.

[6] a) M. Makosza, J. Winiarski, *Acc. Chem. Res.* **1987**, *20*, 282-289; b) M. Makosza, K. Wojciechowski, *Chem. Rev.* **2004**, *104*, 2631-2666; c) M. Makosza, *Chem. Soc. Rev.* **2010**, *39*, 2855-2868; d) M. Makosza, *Synthesis* **2011**, *15*, 2341-2356; e) H. Gao, D. H. Ess, M. Yousufuddin, L. Kurti, *J. Am. Chem. Soc.* **2013**, *135*, 7086-7089; TM free α-arylation of ketone f) Q. L. Xu, H. Gao, M. Yousufuddin, D. H. Ess, L. Kürti, *J. Am. Chem. Soc.* **2013**, *135*, 14048-14051; g) H Gao, Q. L. Xu, M. Yousufuddin, D. H. Ess, L. Kurti, *Angew. Chem. Int. Ed.*, **2014**, *53*, 2701-2705; h) K. Blaziak, M. Makosza, W. Danikiewicz, *Chem. Eur. J.* **2015**, *21*, 6048-6051; i) K. Blaziak, W. Danikiewicz, M. Makosza, *J. Am. Chem. Soc.* **2016**, *138*, 7276-7281.

[7] Biologically active oxindole based drug molecules and activity a) C. V. Galliford, K. A. Scheidt, *Angew. Chem. Int. Ed.* **2007**, *46*, 8748–8758; b) B. Trost, M. Brennan, *Synthesis* **2009**, 3003-3025; c) F. Zhou, Y.-L. Liu, J. Zhou, *Adv. Synth. Cat.* **2010**, *352*, 1381-1407; d) M. K. Christensen, *et al. J. Med. Chem.* **2010**, *53*, 7140-7145; e) A. Millemaggi, R. J. K. Taylor, *Eur. J. Org. Chem.* **2010**, 4527-4547; f) S. Denoyelle, T. Chen, H. Yang, L. Chen, Y. Zhang, J. A. Halperin, B. H. Aktas, M. Chorev, *Eur. J. Med. Chem.* **2013**, *69*, 537-553.

[8] a) R. A. Altman, A. M. Hyde, X. Huang, S. L. Buchwald, *J. Am. Chem. Soc.* **2008,** *130*, 9613-9620; b) M. J. Durbin, M. C. Willis, *Org. Lett.* **2008**, *10*, 1413-1415; c) C.-K. Mai, M. F. Sammons, T. Sammakia *Org. Lett.* **2010**, *12*, 2306-2309; d) P. Li, S. L. Buchwald, *Angew. Chem. Int. Ed.* **2011**, *50*, 6396-6400; e) F. Zhou, Z. Y. Cao, J. Zhang, H. B. Yang, J. Zhou, *Chem. Asian J.* **2012**, *7*, 233-241; f) C. Piemontesi, Q. Wang, J. Zhu, *Org. Biomol. Chem.* **2013**, *11*, 1533-1536; g) Z.-K. Xiao, H.-Y. Yin, L.-X. Shao *Org. Lett*. **2013**, *15*, 1254-1257; h) C. Zhai, D. Xing, C. Jing, J. Zhou, C. Wang, D. Wang, W. Hu, *Org. Lett.* **2014**, *16*, 2934-2937; i) H. R. Wu, H. Y. Huang, C. L. Ren, L. Liu, D. Wang, C. J. Li, *Chem. Eur. J.* **2015**, *21*, 16744-16748; j) C. S. Marques, A. J. Burke, *Eur. J. Org. Chem.* **2016,** 806–812; k) X. Li, W. Ni, F. Mao, W. Wang, J. Li, *Chem. Asian J*. **2016**, *11*, 226 references for intramolecular coupling of substituted oxindoles l) F. G. Bordwell, H. E. Fried, *J. Org. Chem.* **1991**, *56*, 4218-4223; m) K. H. Shaughnessy, B. C. Hamann, J. F. Hartwig, *J. Org. Chem.* **1998**, *63*, 6546-6553; n) S. Lee, J. F. Hartwig, *J. Org. Chem.* **2001**, *66*, 3402-3415; o) Y. X. Jia, D. Katayev, E. P. Kündig, *Chem. Commun.* **2010**, *46*, 130-132; p) A. Beyer, J. Buendia, C. Bolm, *Org. Lett.* **2012**, *14*, 3948-3951.

10.1002/asia.201601647

[9] a) J. F. Bunnett *Acc. Chem. Res*. **1978**, *11*, 413-420. (b) J. F. Bunnett, *Acc. Chem. Res.* **1992**, *25*, 2-9.

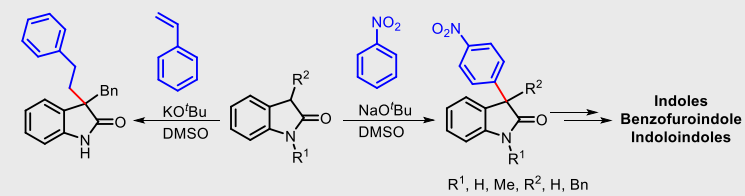
[10] a) X.-H. Xu, X. Wang, G.-k. Liu, E. Tokunaga, N. Shibata, *Org. Lett.* **2012**, *14*, 2544-2547; b) Z. Lian, S. D. Friis, T. Skrydstrup, *Angew. Chem. Int. Ed.* **2014**, *53*, 9582-9586; c) Lai, Y.; Ma, L.; Huang, W.; Yu, X.; Zhang, Y.; Ji, H.; Tian, J. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 7349-7353; d) L. Cheng, L. Liu, D. Wang, Y.-J. Chen, *Org. Lett.* **2009**, *11*, 3874-3877; e) T. Jensen, R. Madsen, *J. Org. Chem.* **2009**, *74*, 3990-3992; f) P. Galzerano, G. Bencivenni, F. Pesciaioli, A. Mazzanti, B. Giannichi, L. Sambri, G. Bartoli, P. Melchiorre, *Chem. Eur. J.* **2009**, *15*, 7846-7849.

10.1002/asia.201601647

WILEY-VCH

FULL PAPER

FULL PAPER



TM and halogen free sp^3 C-H arylation & addition to alkene
Synthesis of 3-aryl ox-, indolo-, & benzofuro-indoles
Over all 49 examples, upto 84% yields

*M. Sattar, V. Rathore, C. D. Prasad, Dr. S Kumar **

Page No. – Page No.

TM Free Chemoselective Oxidative C-C Coupling of sp^3 C-H Bond of Oxindoles with Arenes and Addition to Alkene: Synthesis of 3-Aryl Oxindoles, Benzofuro- and Indolo-indoles

A transition-metal (TM) and halogen free NaO^{t}Bu–mediated oxidative cross coupling between sp^3 C-H bond of oxindoles and sp^2 C-H bond of nitroarenes has been developed to access 3-aryl substituted and 3,3-aryldisubstituted oxindoles in DMSO at room temperature in short time. Interestingly, sp^3 C-H bond of oxindoles has also been added to styrene under TM-free conditions for the practical synthesis of quaternary 3,3-disubstituted oxindoles. Synthesized 3-oxindoles have also been further transformed into advanced heterocycles; benzofuroindoles, indoloindoles, and substituted indoles. Mechanistic understanding of the reaction suggests the formation of an anion intermediate from sp^3 C-H bond of oxindole by *tert*-butoxide base in DMSO. The addition of nitrobenzene to in-situ generated carbanion led to the 3-(nitropheny)oxindolyl carbanion in DMSO which subsequently oxidizes to 3-(nitro-aryl) oxindole by DMSO.