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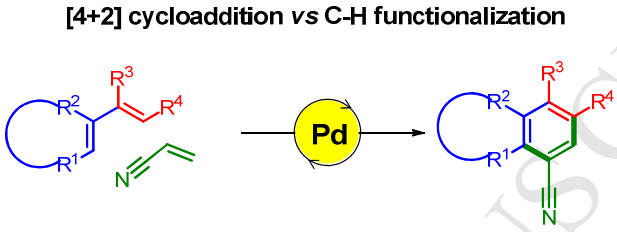

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Regioselective Preferential C-H Activation of Sterically Hindered 1,3-Dienes over [4+2] cycloaddition

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ABSTRACT

The study of Pd-catalyzed preferential C-H activation of sterically hindered α, β-olefinic indoles onto alkenes beyond [4+2] cycloaddition has been described. The carbazole derivatives were readily synthesized via activation of vinylic C−H bonds with excellent regioselectivity. Further, the one-pot strategy has been employed for the synthesis of tricyclic carbazoles. The double and triple C-H activation followed by concomitant Michael addition provides an economical approach for the synthesis of *N*-protected carbazole. A wide range of alkenes at the α- and β-position are compatible with this reaction. The mechanistic and X-ray crystallographic studies supported the designed chemistry of C-H activation.

1. Introduction

In recent years significant progress in metal-catalyzed C-H activation has been observed.[1] The regioselective functionalization of sterically hindered arenes at different sites of organic molecules provides an opportunity for the introduction of structural modifications and in the development of fused carbazoles. However, the extensive application of C–H functionalization in organic synthesis is inferior due to lack of methodologies that enable the site-selective activation of C–H bonds, which often have subtle distinction in the intrinsic reactivity. For instance, Pd(II)-catalyzed C-H bond metalation resulted in the general application as robust catalysts for the direct synthesis of (hetero)arenes.[2] Owing to geometric strain, we mainly focused on the development of metal-catalyzed C–H activation reactions that are directed by sterically hindered functional groups. It is believed that the proximity-driven metalation type of tactic enables the selective functionalization of C–H bonds that are few bonds away from the directing atom via cyclometalation.

The carbazole core moiety is present in various natural products which show enormous pharmaceutical significance.[3,4] The Ellipticine exhibit Topoisomerase II inhibitor, Glycoborine act as anti-HIV agent, Phosphorescence OLEDs, Epocarbazolin A is an inhibitor of 5-lipoxygenase enzyme, sPLA2 inhibitor, and Hepatitis C virus replication inhibitor are few remarkable applications of carbazole derivatives (Figure 1).[5]

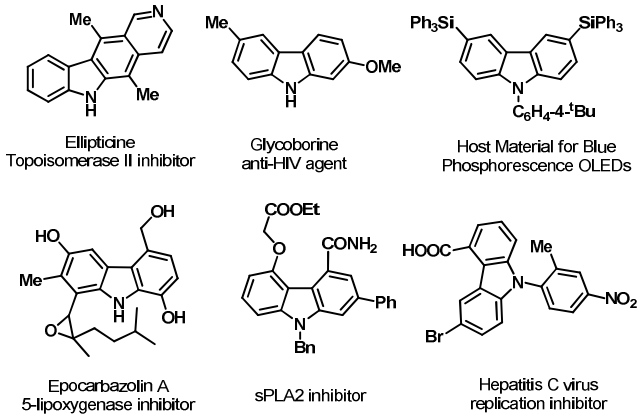

Figure 1. Biologically active carbazole derivatives.

The C-H activation directed through Pd-catalyst, perhaps the most common method used for the alkenylation[6] of the indole-containing directing group (DG) with an alkene. The C−H functionalization involving the syntheses of *N*-protected carbazoles has been extensively exploited; for example, Itami[7] and Yu[8] reported the synthesis of carbazole from *N*-methylindole using Pd–Cu–Ag and Pd-Cu metallic system respectively; however C-H activation of indoles with sterically hindered crotonate has not been much explored. Recently, Pelkey, Kartika, Argade, Chang, Zhao and Tang co-workers[9,10] have contributed significantly in the field of carbazole synthesis using protected amine.

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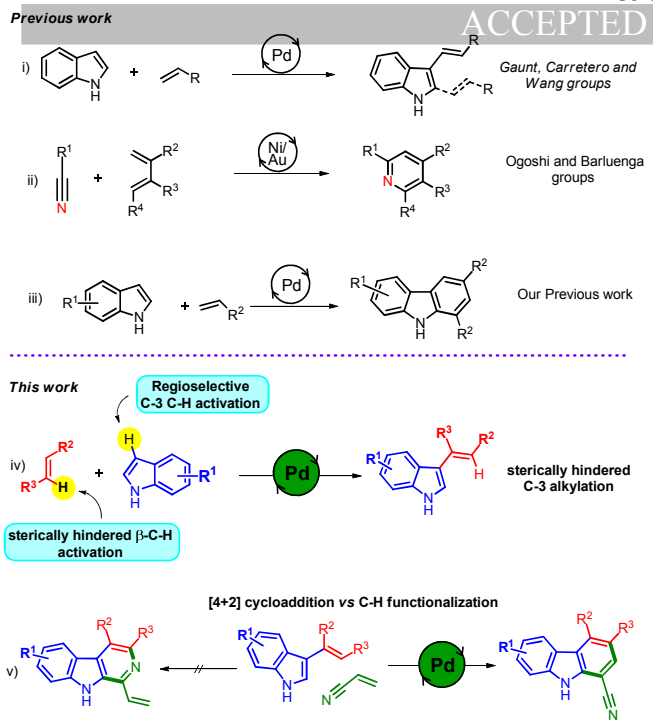


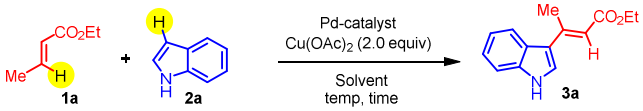
Scheme 1. Regioselective C-H activation

In past few years, Gaunt,[11] Carretero,[12] Wang[13] and co-workers demonstrated selective C-2 and C-3 functionalization of indoles by using Pd-catalyst (Scheme 1, i). In literature, [4+2] cycloaddition chemistry of 1,3-dienes with nitriles has been reported by Ogoshi and Barluenga group using nickel and gold catalyst respectively for the synthesis of pyridine (Scheme 1, ii).[14] Recently, our group have also explored the double C-H activation chemistry via oxidative Heck palladation from indole acrylates (Scheme 1, iii).[15a-b] Inspired by our previous work and in contradict to the [4+2] cycloaddition reaction herein we report a novel Pd-Cu bimetallic system catalyzed regioselective C-3 functionalization of indoles with β-steric hindered crotonates (Scheme 1, iv). The literature survey depicted the formation of [4+2] cycloaddition product. However the experimental analysis illustrated the synthesis of carbazoles via C-H functionalization.

2. Results and Discussion

Initially, we optimized the reaction condition for C-C coupling of β-steric hindered alkenes with C-3 indoles (for detail see supporting information). A variety of Pd-catalysts, along with various combinations of organic solvents were examined in the reaction of ethyl (*E*)-but-2-enoate **1a** with indole **2a** (Table 1). Using Gaunt conditions[11a] of 10 mol % $Pd(OAc)_2$ with 1.8 equiv of $Cu(OAc)_2$ as an oxidant in DMF/DMSO (9:1) at 70°C for 18 h, the desired product **3a** was obtained in 65% yield (Table 1, entry 1). Elevating the reaction temperature from 70 °C to 100 °C declined the yield of product **3a** (Table 1, entry 2). It is interesting to note that use of DMF/DMSO in different ratios, for instance, 7:1, 6:1, 5:1, 4:1 influenced the yield of product **3a** (Table 1, entries 3–6). The reaction of **1a** with indole using 10 mol% of catalyst, 2.0 equiv of oxidant in DMF/DMSO (5:1) at 70 °C for 18 h was found to the suitable reaction condition for oxidative Heck coupling reaction (Table 1, entry 5). On running the reaction for 24 h have not affected the yield of the coupled product **3a** (Table 1, entry 7). Use of $PdCl_2(PPh_3)_2$ provided the product **3a** in deteriorate yield (Table 1, entry 8).

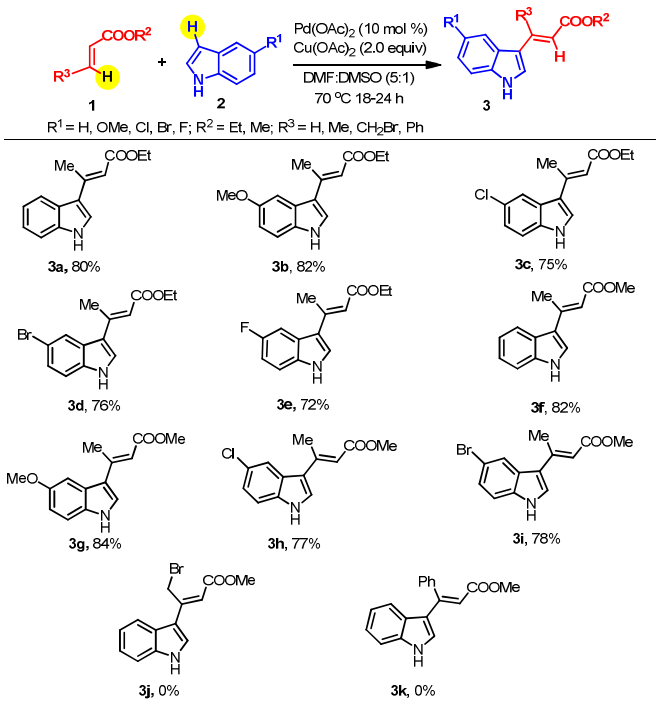
Table 1. Optimization of reaction conditions [a]



Entry	Catalyst (mol%)	Solvent	T °C/ time (h)	Yield (%)[b] **3a**
1[11a]	$Pd(OAc)_2$/10	DMF/DMSO (9:1)	70/18	65
2	$Pd(OAc)_2$/10	DMF/DMSO (9:1)	100/18	55
3	$Pd(OAc)_2$/10	DMF/DMSO (7:1)	70/18	70
4	$Pd(OAc)_2$/10	DMF/DMSO (6:1)	70/18	76
5	**$Pd(OAc)_2$/10**	**DMF/DMSO (5:1)**	**70/18**	**80**
6	$Pd(OAc)_2$/10	DMF/DMSO (4:1)	70/18	78
7	$Pd(OAc)_2$/10	DMF/DMSO (5:1)	70/24	80
8	$PdCl_2(PPh_3)_2$/ 10	DMF/DMSO (5:1)	70/18	30

[a] Reactions were performed using 4.0 mmol (*E*)-ethyl but-2-enoate **1a**, indole **2a** (2.0 mmol), catalyst, $Cu(OAc)_2$ (2.0 equiv) in 2.0 mL of solvent.
[b] Isolated yield.

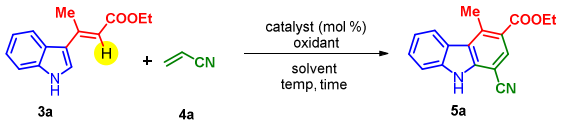
After optimizing the reaction condition for the oxidative Heck, we explore the generality and scope of hindered C-H activation of crotonate derivative (Scheme 2). A variety of crotonates (**1**) and indoles (**2**), bearing electron-neutral and electron-deficient substituents were reacted with each other to provide functionalized vinyl indoles **3a**–**i** in 72–84% yield with excellent functional group tolerance. The reaction of ethyl (*E*)-but-2-enoate **1a** with a variety of C-5 substituted indoles containing R = H, OMe, Cl, Br and F (**2a-e**) successfully provided the coupled products **3a-e** in good yields.



Scheme 2. Pd (II) catalyzed regioselective β-sterically hindered C-H activation of crotonate derivative.

When methyl-group was used as R^2, the reactions were well implemented to form the intriguing coupled products **3f-i** in 77-84% yields. However, on performing the reaction of β-substituted alkene using R^3 as $–CH_2Br$ and –Ph with indole **2a**, failed to provide the alkenyleted products **3j-k** (Scheme 2).

Table 2. Optimization for Carbazole Synthesis[a]

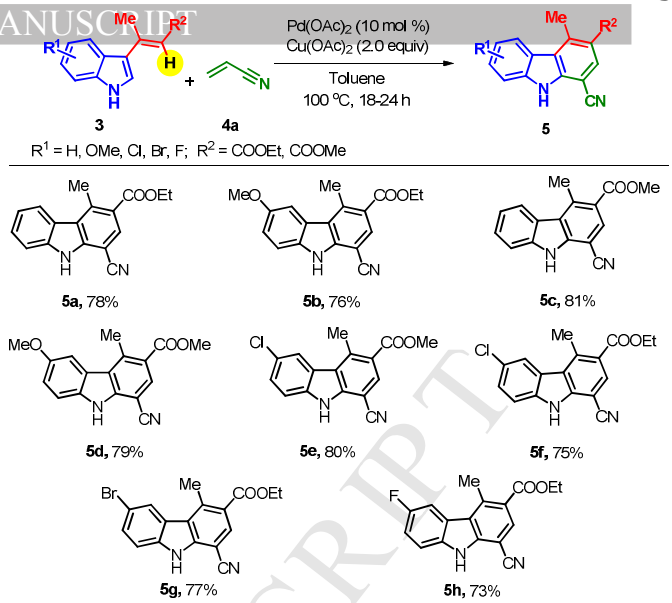


Entry	Catalyst	Solvent	T °C/ time (h)	Yield (%)[b] **5a**
1[c]	$PdCl_2(PPh_3)_2$	DMF/DMSO (5:1)	100/18	40
2	$PdCl_2(PPh_3)_2$	DMF/DMSO (5:1)	80/18	35
3	$PdCl_2(PPh_3)_2$	DMF/DMSO (5:1)	120/18	30
4	$PdCl_2(PPh_3)_2$	DMF/DMSO (5:1)	100/24	30
5	$Pd(OAc)_2$	DMF/DMSO (5:1)	100/18	75
6	**$Pd(OAc)_2$**	**Toluene**	**100/18**	**78**
7	$Pd(OAc)_2$	DMF	100/40	23
8	$Pd(OAc)_2$	NMP	100/40	00
9	$Pd(OAc)_2$	DMA	100/40	15
10	$Pd(OAc)_2$	DMSO	100/40	trace

[a] Reactions were performed using 0.5 mmol of ethyl-(*E*)-3-(1*H*-indol-3-yl)but-2-enoate **3a**, acrylonitrile **4a** (1.0 mmol), catalyst (10 mol %), $Cu(OAc)_2$ (1.5 equiv) in 2.0 mL of solvent.
[b] Isolated yield.
[c] $Cu(OAc)_2$ (1.8 equiv)

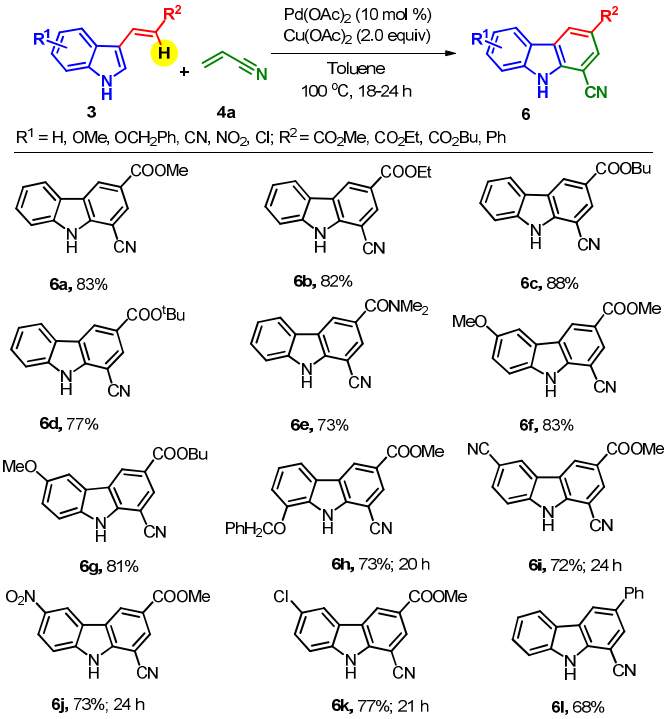
After synthesizing starting compound, we next examine the optimal conditions for carbazole synthesis, by choosing ethyl (*E*)-3-(1*H*-indol-3-yl)but-2-enoate **3a** and acrylonitrile **4a** as model compounds (Table 2). Using our previously optimized reaction condition of 10 mol % $PdCl_2(PPh_3)_2$ with 1.8 equiv of oxidant in DMF/DMSO (5:1) at 100°C for 18 h, the desired product **5a** was obtained in 40% yield (Table 2, entry 1). Altering the reaction temperature from 80 °C to 120 °C was incapable of providing the desired product **5a** in moderate yields (Table 2, entries 2–3). No significant change was observed on increasing the reaction time (Table 2, entry 4). When 10 mol % of $Pd(OAc)_2$ was used in DMF/DMSO (5:1), product **5a** was obtained in 75% yield (Table 2, entry 5). When toluene was used as a solvent, the desired product **5a** was obtained in 78% yield (Table 2, entry 6). Inferior results were obtained when DMF, NMP, DMA, and DMSO have been used as solvents (Table 2, entries 7–10).

It is interesting to note that C-H activation is preferred over [4+2] cycloaddition product; therefore we explore the concept to examine the scope of hindered vinyl indoles with acrylonitrile **4a** (Scheme 3). When ethyl (*E*)-3-(1*H*-indol-3-yl)but-2-enoate **3a** and its derivative **3b** (R^1 = OMe**)** were reacted with acrylonitrile **4a** the desired carbazole products **5a-b** were obtained in 78% and 76% yields respectively. Vinylindole bearing electron-neutral (R^1 = H) and electron-releasing (R^1 = OMe) substituents **3f–g** were successful in providing the functionalized carbazoles **5c–d** in 81–79% yields. The reaction of halogen substituted alkyl (*E*)-3-(5-halo-1*H*-indol-3-yl) but-2-enoate (R^1 = Cl, Br, F) **3h, 3c-e** with vinyl cyanide **4a** afforded the tri-substituted carbazoles **5e–h** in good yields.



Scheme 3. Preferential C-H activation over [4+2] cycloaddition of hindered vinyl indole

Encouraged by above results, we performed the reaction of alkylindoloacrylate **3l–o** with electron-deficient alkene **4a** provided the bi-substituted carbazoles **6a–d** in 77-88% yields; however the reaction of the (*Z*)-3-(1*H*-indol-3-yl)-*N*,*N*-dimethyl acrylamide **3p** provided the desired products **6e** in lower yield. C-5 (R^1 = OMe) and C-2 (R^1 = OCH_2Ph) substituted vinyl indoles **3q–s** were capable in providing the cyclized product **6f-h** in 73-83% yields. It was interesting to note that the substrate **3t-v**; bearing strong electron-withdrawing R^1 = CN, NO_2, Cl groups (**3t-3v**), provided the corresponding carbazoles **6i-k** in profitable yields. The reaction of electron-rich vinyl indole (R^2 = Ph) **3w** with electron-deficient alkene fruitfully afforded the fused product **6l** in 68% yield (Scheme 4).



Scheme 4. Synthesis of disubstituted carbazoles

The X-ray crystallographic studies of **5c** and **6b** further supported in elucidating the cyclized products (Figure 2).[16]

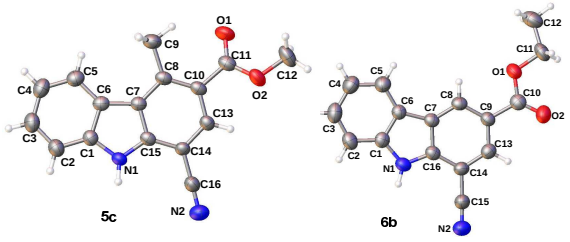
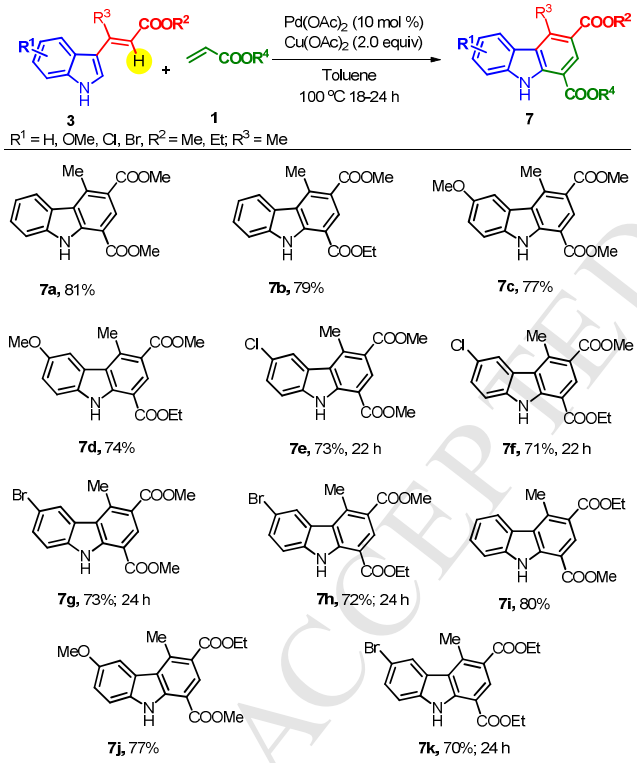


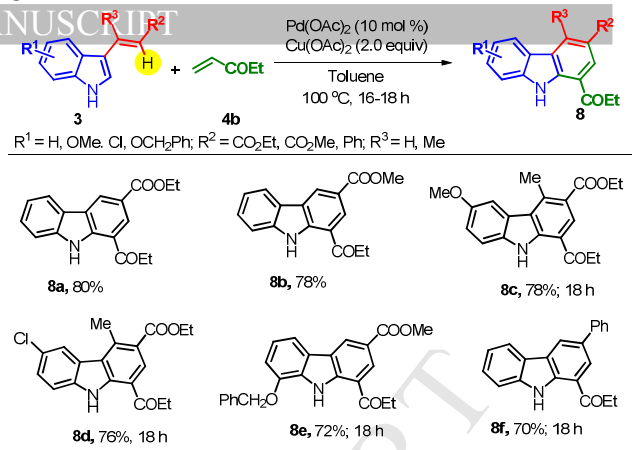
Figure 2. X-ray crystallographic structure of **5c** and **6b** with thermal ellipsoid 50% probability level

Inspired by the former results, we aimed to further explore the C-H activation chemistry with a variety of indole acrylates **3** and electron-deficient alkenes **1** for the synthesis of functionalized carbazoles **7a–k** (Scheme 5). Alkyl (*E*)-3-(1*H*-indol-3-yl)but-2-enoate bearing electron-neutral, (R^1 = H) electron-releasing (R^1 = OMe) and electron-deficient (R^1 = Cl, Br) substituents at C-5 position when reacted with methyl- and ethyl acrylate **1e–f** afforded the fused carbazoles **7a–h** in 81–71% yields with excellent regioselectivity. When ethyl group was used as R^2, the reaction underwent smoothly to give the expected cyclized products **7i-k** in good yields.



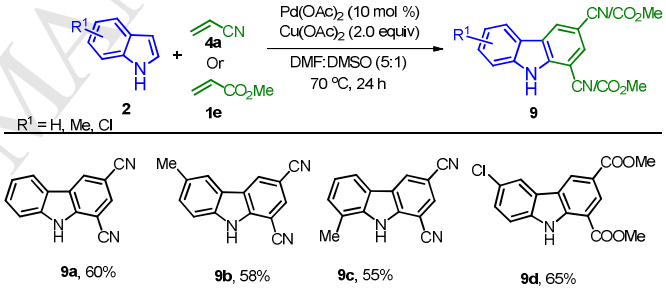
Scheme 5. Scope of C-H activation with acrylates

Further, we employed vinyl ketones **4b** instead of acrylates **1** for the construction of carbazole derivatives (Scheme 6). The reaction of ethyl/methyl (*E*)-3-(1*H*-indol-3-yl)acrylate **3m**/**3l** with ethyl vinyl ketone **4b** provided the desired products **8a-b** in 80% and 78% yields respectively. Sterically hindered vinyl indoles C-5 (R^1 = OMe, Cl) **3b-c** were also competent in providing the tri-substituted carbazoles **8c-d** in good yields. Electronically biased vinyl indoles such as methyl (*E*)-3-(7-(phenoxymethyl)-1*H*-indol-3-yl)acrylate **3s** and (*E*)-3-styryl-1*H*-indole **3w** fruitfully provided the carbazole derivatives **8e-f** in satisfactory yields.



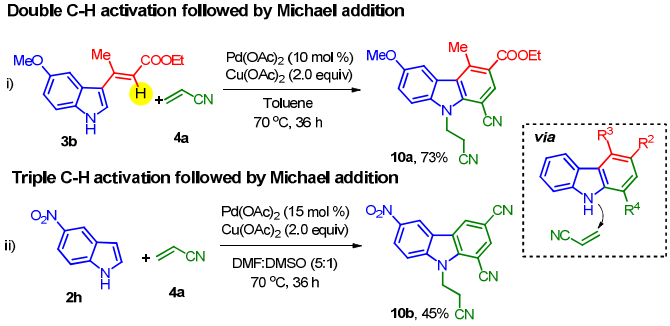
Scheme 6. Scope of C-H activation with vinyl ketones

After attaining successful results with vinyl indoles, we endeavor to attain the one pot synthesis of carbazole using substituted indoles **2** with acrylonitrile **4a** and methyl acrylate **1e** (Scheme 7). It was worthy to note that the one pot carbazole synthesis occurred in DMF:DMSO (5:1) indeed it is necessary due to the first-Heck coupling reaction. Indole **2a** and its C-5 and C-2 methyl derivatives **2f-g** underwent triple successive Heck coupling to give the expected carbazole products **9a-c** in good yields. The reaction of 5-chlorolindole **2c** with methyl acrylate **1e** using Pd-Cu bimetallic system afforded the dimethyl 6-chloro-9*H*-carbazole-1,3-dicarboxylate **9d** in 65% yield (Scheme 7).



Scheme 7. One pot carbazoles synthesis

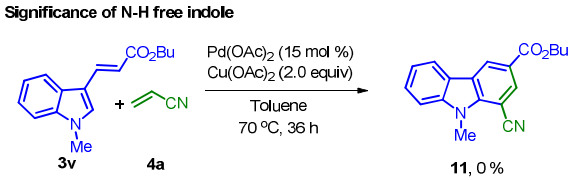
In addition to the carbazole synthesis through C-H activation using vinyl indoles with acrylonitrile **4a** in one pot, we observed a unique finding of *N*-protected indoles via Michael addition (Scheme 8). When we performed the reaction of (*E*)-ethyl 3-(5-methoxy-1*H*-indol-3-yl)but-2-enoate **3b** and 5-nitroindole **2h** with **4a** an unusual carbazole synthesis followed by concomitant Michael addition products **10a-b** were observed in 73 and 45% yields, respectively.



Scheme 8. Carbazole synthesis followed by concomitant Michael addition

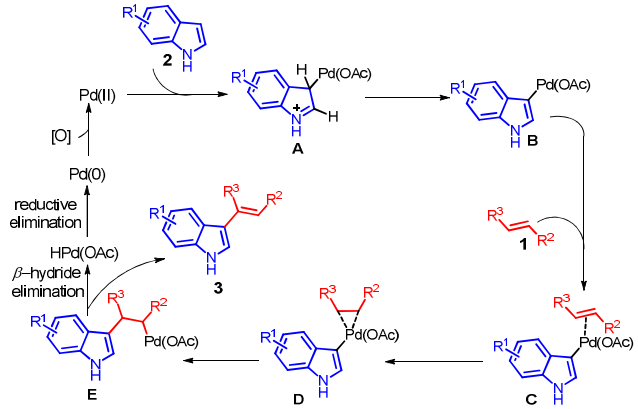
After attaining successful results with free (NH) –indole we endeavor to perform the reaction with *N*-protected indole. We

performed the reaction of *N*-methyl indole **3v** with acrylonitrile **4a**. However we failed to obtained the desired carbazole **11**. The studies revealed that the free -NH group in indole ring is crucial for the synthesis of carbazole (Scheme 9).

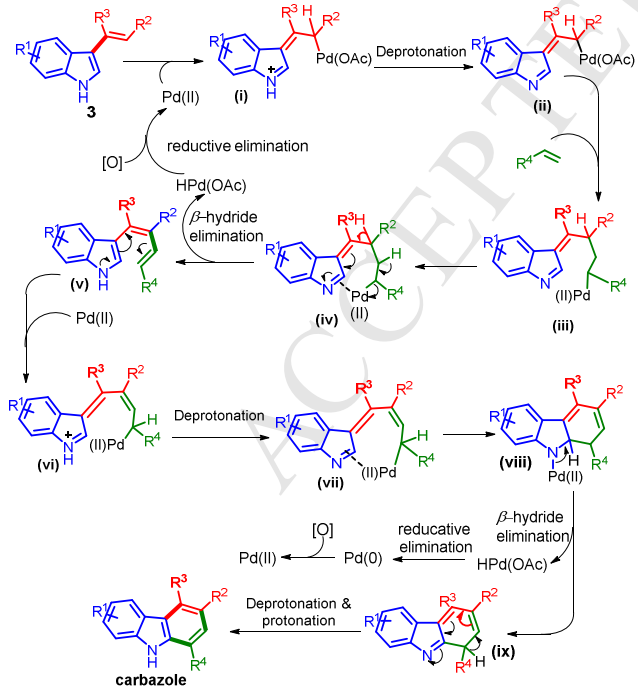


Scheme 9. Control experiment

Based on our report and literature survey,[11a] we proposed a possible mechanistic pathway in Scheme 10. The mechanism begins with the C-3 functionalization of indoles **2** generating C3-palladated species (**A**) which coordinates with alkenes (**1**). Due to steric hindrance, cis-trans isomerization (**C**) occurs followed by β-hydride and reductive elimination (**E**) which leads to the Heck-type reaction forming C3-functionalized indole **3** (Scheme 10).



Scheme 10. Plausible reaction mechanism of sterically hindered C-H activation



Scheme 11. Plausible reaction mechanism of carbazole synthesis

The next phase of the mechanism is based on the formation of an enamine like motif (**i**), the electron current would be dependable with an attack on the carbon next to R^2 palladium and loss of -NH proton leads to the construction of palladium allyl system (**ii**). This curial step of the mechanism has been designed on the basis of the control experiment performed in scheme 9 which clearly reveals the significance of free –NH group over –NMe group.The sterically hindered olefin insertion at the α-position of R^2 generate species (**iii**). The newly produced Pd-C bond would next attack the imine (C=N) to establish the tricyclic core skeleton (**iv**). The di-Heck intermediate **v** would be formed via β-hydride elimination followed by N-protonation/C-H deprotonation at C-H bond next to R^2. The intermediate **v** would undergo the same C-Pd bond forming process as mentioned above with proton loss of the -NH bond and nucleophilic attack of the terminal carbon carrying R^3 to palladium to form skeleton **vii** which will then undergo intramolecular carbopalladation of the C=N bond (**viii**) leading to the formation of carbazoles via β-hydride elimination followed by C-H deprotonation/N-protonation (**ix**). The palladium(II)–hydrido complex reduces into a Pd(0) complex, which is oxidized by $Cu(OAc)_2$ to regenerate Pd(II) species (Scheme 11).

3. Conclusion

In summary, we have developed a regioselective synthesis of highly functionalized carbazoles by using Pd(II)-Cu bimetallic system. The results of the designed protocol suggested that the C-H activation is preferred over [4+2] cycloaddition. The sterically hindered substrate is bearing electron-rich and electron-deficient vinyl indoles with alkenes were examined for the synthesis of the tri- and di-substituted carbazoles. The designed one-pot strategy was also successful in providing the tricyclic *N*-heterocycle. Further *N*-protected carbazoles were prepared by double and triple C-H activation followed by concomitant Michael addition. The C-H activation strategy for the synthesis of carbazole has been well supported by the proposed mechanistic pathway via a di-Heck intermediate.

4. Experimental section

General Experimental

^1H (400 MHz) and ^{13}C (100 MHz) NMR spectra were recorded with Jeol (JNM-ECX400P) spectrometers and Delta 4.3.6 version in $CDCl_3$ and DMSO-d_6 at r.t., referenced to TMS as internal standards. FTIR spectra were measured Zn−Se ATR, cm^{-1} on a Bruker Alpha infrared spectrophotometer. The mass spectra (EI, 74 eV; gas-reactant nitrogen) were obtained with a Agilent 6530 Accurate Mass Q-TOF LC/MS instrument. The analyses of compounds were conducted in USIC, Univesity of Delhi analytical laboratory. Full spectral data for all novel compounds are given below, few previously characterized compounds gave spectra consistent with the literature. All solvents were purified according to standard procedures. All the reactions were performed in an oven-dried Schlenk flask. Column chromatography was performed using silica gel (100-200 mesh). All melting points are uncorrected.

Pd (II) Catalyzed regioselective β-sterically hindered C-H activation of crotonate derivative: In an oven-dried round bottom flask, a solution of (*E*)-alkyl but-2-enoate **1** (4.0 mmol), indole **2** (2.0 mmol), 10 mol % $Pd(OAc)_2$ and $Cu(OAc)_2$ (2.0 equiv) in 2.0 mL of DMF:DMSO (5:1). The resulting reaction mixture was heated at 70 °C for 18-24 h. Progression of the reaction was monitored by TLC analysis; after complete consumption of starting material, the reaction was cooled to room temperature. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL). The layers were separated, and the organic layer was washed with aqueous saturated brine solution

and dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (100−200 mesh) (hexane:ethyl acetate; 90/10). The structure and purity of known starting materials (**3l-r** and **3w**)[11, 13, 15a-b] were confirmed by comparison of their physical and spectral data (^{1}H NMR, ^{13}C NMR, and HRMS) with literature data.

(*E*)-Ethyl 3-(1*H*-indol-3-yl)but-2-enoate **(3a).**

In an oven-dried round bottom flask, a solution of (*E*)-ethyl but-2-enoate **1a** (4.0 mmol), indole **2a** (234.0 mg, 2.0 mmol), 10 mol % $Pd(OAc)_2$ and $Cu(OAc)_2$ (2.0 equiv) in 2.0 mL of DMF:DMSO (5:1). The resulting reaction mixture was heated at 70 °C for 18 h. Progression of the reaction was monitored by TLC analysis; after complete consumption of starting material, the reaction was cooled to room temperature. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL). The layers were separated, and the organic layer was washed with aqueous saturated brine solution and dried over Na_2SO_4. Organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (100−200 mesh) (hexane:ethyl acetate; 90/10) to give the title compound **3a** (366.4 mg, 80%); as a pale yellow needles, mp: 119–121 ^{o}C, FTIR (Zn−Se ATR, cm−1) 3277, 2982, 2926, 2902, 1693, 1677, 1599, 1572, 1523, 1461, 1430, 1364, 1327, 1305, 1263, 1188, 1132, 1050, 1019, 910, 857, 828, 738; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.56 (1H, br s, NH), 7.74–7.68 (2H, m, 2CH), 7.33 (1H, d, J = 8.4 Hz, CH), 7.07–6.99 (2H, m,2CH), 6.17 (1H, s, CH), 3.99 (2H, q, J = 8.4 Hz, OCH_2), 2.49 (3H, s, CH_3), 1.11 (3H, t, J = 6.87, CH_3); ^{13}C NMR ^{13}C (100 MHz, DMSO–d_6) δ 166.8, 161.0, 137.4, 128.4, 124.2, 122.0, 120.7, 120.0, 116.7, 112.4, 110.3, 58.9, 17.7, 14.4. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{14}H_{16}NO_2]$ 230.1181, found 230.1176.

(E)-Ethyl 3-(5-methoxy-1H-indol-3-yl)but-2-enoate **(3b).**

In an oven-dried round bottom flask, a solution of (*E*)-ethyl but-2-enoate **1a** (4.0 mmol), 5-methoxy-1*H*-indole **2b** (294.0 mg, 2.0 mmol), 10 mol % $Pd(OAc)_2$ and $Cu(OAc)_2$ (2.0 equiv) in 2.0 mL of DMF:DMSO (5:1). The resulting reaction mixture was heated at 70 °C for 18 h. Progression of the reaction was monitored by TLC analysis; after complete consumption of starting material, the reaction was cooled to room temperature. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL). The layers were separated, and the organic layer was washed with aqueous saturated brine solution and dried over Na_2SO_4. Organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (100−200) (hexane:ethyl acetate; 90/10) to give the title compound **3b** (424.7 mg, 82%); as a pale brown needles, mp: 140–142 ^{o}C, FTIR (Zn−Se ATR, cm−1) 3268, 2980, 2912, 1698, 1667, 1579, 1533, 1450, 1370, 1315, 1268, 1122, 1060, 915, 860, 748; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (1H, br s, NH), 7.39 (2H, s, 2CH), 7.25(1H, d, J = 9.2 Hz, CH), 6.89–6.86 (1H, m, CH), 6.33 (1H, s, CH), 4.21 (2H, q, J = 7.6 Hz, OCH_2), 3.85 (3H, s, OCH_3), 2.62 (3H, s, CH_3), 1.32–1.29 (3H, m, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 155.0, 150.6, 132.1, 126.4, 125.2, 118.8, 112.34, 112.29, 103.6, 59.5, 56.0, 18.3, 14.4. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{15}H_{18}NO_3]$ 260.1287, found 260.1281.

(E)-Ethyl 3-(5-chloro-1H-indol-3-yl)but-2-enoate **(3c)**

In an oven-dried round bottom flask, a solution of (*E*)-ethyl but-2-enoate **1a** (4.0 mmol), 5-chloro-1*H*-indole **2c** (302.0 mg, 2.0 mmol), 10 mol % $Pd(OAc)_2$ and $Cu(OAc)_2$ (2.0 equiv) in 2.0 mL of DMF:DMSO (5:1). The resulting reaction mixture was heated at 70 °C for 24 h. Progression of the reaction was monitored by TLC analysis; after complete consumption of starting material, the reaction was cooled to room temperature. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL). The layers were separated, and the organic layer was washed with aqueous saturated brine solution and dried over Na_2SO_4. Organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (100−200) (hexane:ethyl acetate; 90/10) to give the title compound **3c** (394.5 mg, 75%); as a yellow needles, mp: 158–160 ^{o}C; FTIR (Zn−Se ATR, cm−1) 3242, 2977, 2924, 2897, 1670, 1600, 1518, 1427, 1373, 1283, 1194, 1138, 752; ^{1}H NMR (400 MHz, DMSO–d_6) δ 11.86 (1H, br s, NH), 7.93 (1H, d, J = 2.2 Hz, CH), 7.55 (1H, d, J = 1.5 Hz, CH), 4.46 (1H, d, J = 8.4 Hz, CH), 7.18 (1H, dd, J = 8.4 and 1.5 Hz, CH), 6.17 (1H, s, CH), 7.13 (2H, q, J = 6.8 Hz, OCH_2), 2.58 (3H, s, CH_3), 1.23 (3H, t, J = 6.9 Hz, CH_3); ^{13}C NMR (100 MHz, DMSO–d_6) δ 166.6, 150.3, 135.8, 129.8, 125.24, 125.21, 122.0, 119.1, 116.4, 113.9, 110.9, 59.0, 17.7, 14.3. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{14}H_{15}ClNO_2]$ 264.0791, found 264.0784.

(E)-Ethyl 3-(5-bromo-1H-indol-3-yl)but-2-enoate **(3d)**.

In an oven-dried round bottom flask, a solution of (*E*)-ethyl but-2-enoate **1a** (4.0 mmol), 5-bromo-1*H*-indole **2d** (2.0 mmol), 10 mol % $Pd(OAc)_2$ and $Cu(OAc)_2$ (2.0 equiv) in 2.0 mL of DMF:DMSO (5:1). The resulting reaction mixture was heated at 70 °C for 24 h. Progression of the reaction was monitored by TLC analysis; after complete consumption of starting material, the reaction was cooled to room temperature. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL). The layers were separated, and the organic layer was washed with aqueous saturated brine solution and dried over Na_2SO_4. Organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (100−200) (hexane:ethyl acetate; 90/10) to give the title compound **3d** (468.1 mg, 76%); as a brown needles, mp: 154–156^{o}C (468.1 mg, 76%); FTIR (Zn−Se ATR, cm−1) 3249, 2967, 2870, 1679, 1567, 1437, 1376, 1273, 1184, 1132, 756; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.87 (1H, br s, NH), 7.92–7.89 (2H, m, 2CH), 7.42 (1H, d, J = 9.2 Hz, CH), 7.28 (1H, dd, J = 8.4 and 1.5 Hz, CH), 6.16 (1H, s,CH), 4.11 (2H, q, J = 6.9 Hz, OCH_2) 2. 58 (3H, s, CH_3), 1.23 (3H, t, J = 7.6 Hz, CH_3); ^{13}C NMR (100 MHz, DMSO–d_6) δ 166.6, 150.3, 136.0, 129.6, 125.9, 124.6, 122.0, 116.4, 114.3, 113.3, 110.9, 59.0, 17.7, 14.3. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{14}H_{15}BrNO_2]$ 308.0286, found 308.0266.

(E)-Ethyl 3-(5-fluoro-1H-indol-3-yl)but-2-enoate **(3e)**.

In an oven-dried round bottom flask, a solution of (*E*)-ethyl but-2-enoate **1a** (4.0 mmol), 5-fluoro-1*H*-indole **2e** (2.0 mmol), 10 mol % $Pd(OAc)_2$ and $Cu(OAc)_2$ (2.0 equiv) in 2.0 mL of DMF:DMSO (5:1). The resulting reaction mixture was heated at 70 °C for 22 h. Progression of the reaction was monitored by TLC analysis; after complete consumption of starting material, the reaction was cooled to room temperature. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL). The layers were separated, and the organic layer was washed with aqueous saturated brine solution and dried over Na_2SO_4. Organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (100−200) (hexane:ethyl acetate; 90/10) to give the title compound **3e** (355.6 mg, 72%); as a dark yellow needles, mp: 130–133^{o}C; FTIR (Zn−Se ATR, cm−1) 3232, 2944, 2887, 1678, 1598, 1523, 1442, 1376, 1263, 1167, 1122, 751; ^{1}H NMR (400 MHz, DMSO–d_6) δ 11.80 (1H, br s, NH), 7.95 (1H, d, J = 3.0 Hz, CH), 7.51 (1H, dd, J = 10.7 and 2.3

Hz, CH), 7.48–7.45 (1H, m, CH), 7.07–7.02 (1H, m, CH), 6.17 (1H, s, CH), 4.13 (2H, q, J = 6.9 Hz, OCH_2), 2.60 (3H, s, CH_3), 1.25 (3H, t, J = 7.2 Hz, CH_3); ^{13}C NMR (100 MHz, DMSO–d_6) δ 166.7, 157.8 (d, J = 231.9 Hz, 1C), 150.6, 134.0, 130.1, 124.4 (d, J = 11.5 Hz, 1C), 116.8 (d, J = 4.5 Hz, 1C), 113.5 (d, J = 10.5 Hz, 1C), 110.4, 110.2 (d, J = 25.9 Hz, 1C), 105.0 (d, J = 24.9 Hz, 1C), 59.0, 17.7, 14.4. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{14}H_{15}FNO_2]$ 248.1087, found 248.1081.

(E)-Methyl 3-(1H-indol-3-yl)but-2-enoate **(3f)**.

In an oven-dried round bottom flask, a solution of (*E*)-methyl but-2-enoate **1b** (4.0 mmol), indole **2a** (2.0 mmol), 10 mol % $Pd(OAc)_2$ and $Cu(OAc)_2$ (2.0 equiv) in 2.0 mL of DMF:DMSO (5:1). The resulting reaction mixture was heated at 70 °C for 18 h. Progression of the reaction was monitored by TLC analysis; after complete consumption of starting material, the reaction was cooled to room temperature. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL). The layers were separated, and the organic layer was washed with aqueous saturated brine solution and dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (100−200) (hexane:ethyl acetate; 90/10) to give the title compound **3f** (352.6 mg, 82%) as a brown needles, mp: 110–112 ^{o}C; FTIR (Zn−Se ATR, cm−1) 3266, 3026, 2924, 2855, 1683, 1599, 1519, 1494, 1429, 1202, 1136, 826; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (1H, br s, NH), 7.97 (1H, d, J = 6.9 Hz, CH), 7.45 (1H, d, J = 2.3 Hz, CH), 7.40 (1H, dd, J = 6.9 and 1.5 Hz, CH), 7.27–7.20 (2H, m, CH), 6.40 (1H, s, CH), 3.78 (3H, s, OCH_3), 2.67 (3H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 150.8, 137.0, 128.1, 127.6, 125.8, 122.8, 121.1, 120.8, 112.3, 111.7, 50.9, 18.2. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{13}H_{14}NO_2]$ 216.1025, found 216.1020.

(E)-Methyl 3-(5-methoxy-1H-indol-3-yl)but-2-enoate **(3g)**.

In an oven-dried round bottom flask, a solution of (*E*)-methyl but-2-enoate **1b** (4.0 mmol), 5-methoxy-1*H*-indole **2b** (2.0 mmol), 10 mol % $Pd(OAc)_2$ and $Cu(OAc)_2$ (2.0 equiv) in 2.0 mL of DMF:DMSO (5:1). The resulting reaction mixture was heated at 70 °C for 18 h. Progression of the reaction was monitored by TLC analysis; after complete consumption of starting material, the reaction was cooled to room temperature. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL). The layers were separated, and the organic layer was washed with aqueous saturated brine solution and dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (100−200) (hexane:ethyl acetate; 90/10) to give the title compound **3g** (411.6 mg, 84%) as a brown needles, mp: 147–150 ^{o}C; FTIR (Zn−Se ATR, cm−1) 3255, 2934, 2865, 1680, 1600, 1523, 1480, 1212, 1126; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (1H, br s, NH), 7.39–7.37 (2H, m, 2CH), 7.25 (1H, d, J = 8.4 Hz, CH), 6.88 (1H, dd, J = 9.2 and 2.3 Hz, CH), 6.35 (1H, s, CH), 3.84 (3H, s, OCH_3), 3.74 (3H, s, OCH_3), 2.62 (3H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 155.0, 151.1, 132.1, 126.5, 125.1, 118.6, 112.5, 112.4, 111.7, 103.3, 56.0, 50.8, 18.3. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{14}H_{16}NO_3]$ 246.1130, found 246.1120.

(E)-Methyl 3-(5-chloro-1H-indol-3-yl)but-2-enoate **(3h).**

In an oven-dried round bottom flask, a solution of (*E*)-methyl but-2-enoate **1b** (4.0 mmol), 5-chloro-1*H*-indole **2c** (2.0 mmol), 10 mol % $Pd(OAc)_2$ and $Cu(OAc)_2$ (2.0 equiv) in 2.0 mL of DMF:DMSO (5:1). The resulting reaction mixture was heated at 70 °C for 24 h. Progression of the reaction was monitored by TLC analysis; after complete consumption of starting material, the reaction was cooled to room temperature. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL). The layers were separated, and the organic layer was washed with aqueous saturated brine solution and dried over Na_2SO_4. Organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (100−200) (hexane:ethyl acetate; 90/10) to give the title compound **3h** (383.4 mg, 77%) as a yellow needles, mp: 184–186^{o}C; FTIR (Zn−Se ATR, cm−1) 3300, 2926, 2855, 1688, 1600, 1517, 1460, 1425, 1334, 1282, 1190, 1136, 1028, 784; ^{1}H NMR (400 MHz, DMSO–d_6) δ 11.86 (1H, br s, NH), 7.94 (1H, d, J = 3.0 Hz, CH), 7.76 (1H, d, J = 1.5 Hz, CH), 7.46 (1H, d, J = 8.4 Hz, CH), 7.18 (1H, dd, J = 8.3 and 2.3 Hz, CH), 6.19 (1H, s, CH), 3.56 (3H, s, OCH_3), 2.58 (3H, s, CH_3); ^{13}C NMR (100 MHz, DMSO–d_6) δ 167.0, 150.6, 135.8, 129.9, 125.3, 125.2, 122.1, 119.1, 116.4, 113.9, 110.5, 50.6, 17.7. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{13}H_{13}ClNO_2]$ 250.0635, found 250.0644.

(E)-methyl 3-(5-bromo-1H-indol-3-yl)but-2-enoate **(3i).**

In an oven-dried round bottom flask, a solution of (*E*)-methyl but-2-enoate **1b** (4.0 mmol), 5-bromo-1*H*-indole **2d** (2.0 mmol), 10 mol % $Pd(OAc)_2$ and $Cu(OAc)_2$ (2.0 equiv) in 2.0 mL of DMF:DMSO (5:1). The resulting reaction mixture was heated at 70 °C for 24 h. Progression of the reaction was monitored by TLC analysis; after complete consumption of starting material, the reaction was cooled to room temperature. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL). The layers were separated, and the organic layer was washed with aqueous saturated brine solution and dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (100−200) (hexane:ethyl acetate; 90/10) to give the title compound **3i** (458.6 mg, 78%) as a off-white needles, mp: 187–188 ^{o}C; FTIR (Zn−Se ATR, cm−1) 3320, 2927, 2863, 1692, 1604, 1518, 1428, 1337, 1285, 1029, 762; ^{1}H NMR (400 MHz, DMSO–d_6) δ 11.88 (1H, br s, NH), 7.89 (1H, d, J = 1.5 Hz, CH), 7.41 (1H, d, J = 9.2 Hz, CH), 7.29 (1H, dd, J = 8.4 and 1.5 Hz, CH), 7.22 (1H, t, J = 6.9 Hz, CH), 6.19 (1H, s, CH), 3.64 (3H, s, OCH_3), 2.57 (3H, s, CH_3); ^{13}C NMR (100 MHz, DMSO–d_6) δ 167.0, 150.5, 136.0, 129.8, 128.1, 125.9, 124.6, 122.0, 114.4, 113.3, 110.5, 50.6, 17.7. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{13}H_{13}BrNO_2]$ 294.0130, found 294.0123.

(E)-Methyl 3-(7-(benzyloxy)-1H-indol-3-yl)acrylate (**3s**).

In an oven-dried round bottom flask, a solution of methyl acrylate **1e** (4.0 mmol), 7-(benzyloxy)-1H-indole **2** (2.0 mmol), 10 mol % $Pd(OAc)_2$ and $Cu(OAc)_2$ (2.0 equiv) in 2.0 mL of DMF:DMSO (5:1). The resulting reaction mixture was heated at 70 °C for 20 h. Progression of the reaction was monitored by TLC analysis; after complete consumption of starting material, the reaction was cooled to room temperature. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL). The layers were separated, and the organic layer was washed with aqueous saturated brine solution and dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (100−200) (hexane:ethyl acetate; 90/10) to give the title compound **3q** (429.8 mg, 70%) as a off-white needles, mp: 146–148 ^{o}C; FTIR (Zn−Se ATR, cm−1) 3250, 2939, 2870, 1665, 1589, 1517, 1485, 1209, 1118; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (1H, br s, NH), 7.91 (1H, d, J = 16.0 Hz, CH), 7.51 (1H, d, J = 7.6 Hz, CH), 7.47–7.36 (6H, m, 6CH), 7.15 (1H, t, J = 8.4 Hz, CH), 6.80 (1H, d, J = 7.6 Hz, CH), 6.44 (1H, d, J = 16.0 Hz, CH), 5.20 (2H, s, CH_2), 3.80 (3H, s, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.4, 138.5, 136.6, 128.7, 128.3,

128.1, 127.9, 127.7, 122.0, 114.1, 113.3, 113.1, 104.5, 70.4, 51.4 HRMS (ESI) $[M+H]^+$ Calcd for $[C_{19}H_{18}NO_3]$ 308.1287, found 308.1281.

(E)-Methyl 3-(5-cyano-1H-indol-3-yl)acrylate **(3t).**

In an oven-dried round bottom flask, a solution of methyl acrylate **1e** (4.0 mmol), 1*H*-indole-5-carbonitrile **2** (2.0 mmol), 10 mol % $Pd(OAc)_2$ and $Cu(OAc)_2$ (2.0 equiv) in 2.0 mL of DMF:DMSO (5:1). The resulting reaction mixture was heated at 70 °C for 24 h. Progression of the reaction was monitored by TLC analysis; after complete consumption of starting material, the reaction was cooled to room temperature. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL). The layers were separated, and the organic layer was washed with aqueous saturated brine solution and dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (100−200) (hexane:ethyl acetate; 90/10) to give the title compound **3r** (271.2 mg, 60%); as a yellow needles, mp: 146–148 °C; FTIR (Zn−Se ATR, cm−1) 3233, 2919, 2850, 2231, 1678, 1579, 1514, 1489, 1219, 1128; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.21 (1H, br s, NH), 8.48 (1H, s, CH), 8.13 (1H, d, *J* = 2.3 Hz, CH), 7.87 (1H, d, *J* = 16.0 Hz, CH), 7.60 (1H, d, *J* = 8.4 Hz, CH), 7.53 (1H, dd, *J* = 8.4 and 1.5 Hz, CH), 6.53 (1H, d, *J* = 16.7 Hz, CH), 3.69 (3H, s, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 139.0, 137.5, 133.3, 125.4, 125.3, 124.7, 120.3, 113.5, 112.9, 112.3, 103.0, 51.1. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{13}H_{11}N_2O_2]$ 227.0821, found 227.0823.

(E)-Methyl 3-(5-nitro-1H-indol-3-yl)acrylate **(3u)**

In an oven-dried round bottom flask, a solution of methyl acrylate **1e** (4.0 mmol), 5-nitro-1*H*-indole **2** (2.0 mmol), 10 mol % $Pd(OAc)_2$ and $Cu(OAc)_2$ (2.0 equiv) in 2.0 mL of DMF:DMSO (5:1). The resulting reaction mixture was heated at 70 °C for 24 h. Progression of the reaction was monitored by TLC analysis; after complete consumption of starting material, the reaction was cooled to room temperature. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL). The layers were separated, and the organic layer was washed with aqueous saturated brine solution and dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (100−200) (hexane:ethyl acetate; 85/15) to give the title compound **3s** (319.8 mg, 65%); as a yellow needles, mp: 136–138 °C; FTIR (Zn−Se ATR, cm−1) 3245, 2929, 2836, 1690, 1569, 1544, 1441, 1230, 1216; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.36 (1H, br s, NH), 8.71 (1H, s, CH), 8.19 (s, 1H), 8.07–8.04 (m, 1H), 7.90 (d, J = 16.02 Hz, 1H), 7.61 (d, J = 8.4 Hz, 1H) 6.45 (d, J = 16.02 Hz, 1H), 3.71 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 167.3, 141.9, 140.3, 137.2, 134.2, 13.1, 124.4, 117.8, 116.4, 116.3, 113.5, 51.3 HRMS (ESI) $[M+H]^+$ Calcd for $[C_{12}H_{11}N_2O_4]$ 247.0719, found 247.0720.

(E)-methyl 3-(5-chloro-1H-indol-3-yl)acrylate **(3v)**

In an oven-dried round bottom flask, a solution of methyl acrylate **1e** (4.0 mmol), 5-chloro-1*H*-indole **2** (2.0 mmol), 10 mol % $Pd(OAc)_2$ and $Cu(OAc)_2$ (2.0 equiv) in 2.0 mL of DMF:DMSO (5:1). The resulting reaction mixture was heated at 70 °C for 22 h. Progression of the reaction was monitored by TLC analysis; after complete consumption of starting material, the reaction was cooled to room temperature. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL). The layers were separated, and the organic layer was washed with aqueous saturated brine solution and dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (100−200) (hexane:ethyl acetate; 85/15) to give the title compound **3t** (319.6 mg, 68%); as a yellow needles, mp: 136–138 °C; FTIR (Zn−Se ATR, cm−1) 3233, 2935, 2836, 1695, 1579, 1537, 1449, 1237, 1212; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (1H, br s, NH), 7.85−7.81 (2H, m, 2CH), 7.45 (1H, d, *J* = 3.0 Hz, CH), 7.31 (1H, d, *J* = 9.1 Hz, CH), 7.19 (1H, dd, *J* = 8.4 and 1.5 Hz, CH), 6.37 (1H, d, *J* = 16.0 Hz, CH), 3.80 (3H, s, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7, 137.9, 130.4, 129.9, 127.3, 126.2, 123.6, 119.9, 113.3, 113.0, 112.8, 51.6; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{12}H_{11}ClNO_2]$ 236.0478, found 236.0480.

General procedure and analytical data for [4+2] cycloaddition *vs* C-H activation:

Ethyl 1-cyano-4-methyl-9H-carbazole-3-carboxylate **(5a)**.

In a oven-dried round bottom flask, a solution of (*E*)-ethyl 3-(1*H*-indol-3-yl)but-2-enoate **3a** (114.5 mg, 0.5 mmol) in toluene; 2 mL), $Pd(OAc)_2$ (11.2 mg, 10 mol %), $Cu(OAc)_2$ (2.0 equiv) and acrylonitrile **4a** (1.0 mmol) were added. The resulting reaction mixture was heated at 100 °C for 18 h. Progression of the reaction was monitored by TLC, while noticing complete consumption of (*E*)-ethyl 3-(1*H*-indol-3-yl)but-2-enoate, reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. Organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 95/05) to give the title compound **3a** (108.3 mg, 78%) as a off white crystal, mp 137−139 °C; FTIR (Zn−Se ATR, cm−1) 3282, 2978, 2852, 2227, 1712, 1589, 1240, 1024, 748; ^{1}H NMR (400 MHz, DMSO–d_6) δ 12.52 (br s, 1H), 8.25 (d, *J* = 7.6 Hz, 1H), 8.22 (s, 1H), 7.63 (d, *J* = 7.6 Hz, 1H), 7.53 (t, *J* = 7.6 Hz, 1H), 7.32 (t, *J* = 6.9 Hz, 1H), 4.31 (q, *J* = 6.9 Hz, 2H), 3.08 (s, 3H), 1.35 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, DMSO–d_6) δ 166.2, 141.4, 141.0, 140.6, 131.9, 126.9, 123.1, 122.4, 121.2, 120.8, 116.7, 112.0, 90.6, 60.8, 17.9, 14.1 ; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{17}H_{15}N_2O_2]$ 279.1134 found 279.1128.

Ethyl 1-cyano-6-methoxy-4-methyl-9H-carbazole-3-carboxylate **(5b)**

In a oven-dried round bottom flask, a solution of (*E*)-ethyl 3-(5-methoxy-1*H*-indol-3-yl)but-2-enoate **3b** (129.5 mg, 0.5 mmol) in toluene; 2 mL), $Pd(OAc)_2$ (11.2 mg, 10 mol %), $Cu(OAc)_2$ (2.0 equiv) and acrylonitrile **4a** (1.0 mmol) were added. The resulting reaction mixture was heated at 100 °C for 18 h. Progression of the reaction was monitored by TLC while noticing complete consumption of (*E*)-ethyl 3-(5-methoxy-1*H*-indol-3-yl)but-2-enoate, the reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 95/05) to give the title compound **3a** (117.0 mg, 76%) as a pale yellow needles, mp: 136–139 °C; FTIR (Zn−Se ATR, cm−1) 3287, 2922, 2852, 2222, 1711, 1466, 1194, 767; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (1H, br s, NH), 8.29 (1H, s, CH), 7.76 (1H, s, CH),

7.48 (1H, d, *J* = 9.2 Hz, CH), 7.19 (1H, d, *J* = 9.2 Hz, CH), 4.41 (2H, d, *J* = 6.9 Hz, OCH_2), 3.95 (3H, s, OCH_3), 3.20 (3H s, CH_3), 1.46–1.41 (3H, m, CH_3); ^{13}C NMR (100 MHz, , $CDCl_3$) δ 166.8, 154.8, 150.1, 142.8, 141.8, 134.3, 132.3, 124.2, 122.0, 116.7, 115.6, 111.8, 107.2, 91.1, 61.2, 56.2, 18.4, 14.4. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{18}H_{17}N_2O_3]$ 309.1239, found 309.1234.

Methyl 1-cyano-4-methyl-9H-carbazole-3-carboxylate **(5c)**.

In a oven-dried round bottom flask, a solution of (*E*)-methyl 3-(1*H*-indol-3-yl)but-2-enoate **3f** (107.5 mg, 0.5 mmol) in toluene; 2 mL), $Pd(OAc))_2$ (11.2 mg, 10 mol %), $Cu(OAc)_2$ (2.0 equiv) and acrylonitrile **4a** (1.0 mmol) were added. The resulting reaction mixture was heated at 100 °C for 18 h. Progression of the reaction was monitored by TLC, while noticing complete consumption of (*E*)-methyl 3-(1*H*-indol-3-yl)but-2-enoate, the reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 95/05) to give the title compound **3a** (106.8 mg, 81%) as a colourless needles, mp: 255–257 ^{o}C; FTIR (Zn−Se ATR, cm−1) 3295, 2958, 2926, 2229, 1723, 1332, 1245, 1211, 1029, 826, 759; ^{1}H NMR (400 MHz, DMSO–d_6) δ 12.53 (1H, br s, NH), 8.25 (1H, d, *J* = 7.6 Hz, CH), 8.21 (1H, s, CH), 7.62 (1H, d, *J* = 8.4 Hz, CH), 7.52 (1H, d, *J* = 8.4 Hz, CH), 7.31 (1H, t, *J* = 8.4 Hz, CH), 3.85 (3H, s, OCH_3), 3.07 (3H, s, CH_3); ^{13}C NMR (100 MHz, DMSO–d_6) δ 166.6, 141.5, 131.9, 128.1, 127.4, 126.9, 125.7, 123.1, 122.5, 120.9, 120.7, 116.6, 112.0, 90.6, 52.1, 17.9. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{16}H_{13}N_2O_2]$ 265.0977, found 265.0989.

Methyl 1-cyano-6-methoxy-4-methyl-9H-carbazole-3-carboxylate **(5d)**.

In a oven-dried round bottom flask, a solution of (*E*)-methyl 3-(5-methoxy-1*H*-indol-3-yl)but-2-enoate **3g** (122.5 mg, 0.5 mmol) in toluene; 2 mL), $Pd(OAc)_2$ (11.20 mg, 10 mol %), $Cu(OAc)_2$ (2.0 equiv) and acrylonitrile **4a** (1.0 mmol) were added. The resulting reaction mixture was heated at 100 °C for 20 h. Progression of the reaction was monitored by TLC, while noticing complete consumption of (*E*)-methyl 3-(5-methoxy-1*H*-indol-3-yl)but-2-enoate, the reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane:ethylacetate; 95/05) to give the title compound **3a** (116.1 mg, 79%) as a yellow needles, mp: 164.3–165 ^{o}C (116.1 mg, 79%); FTIR (Zn−Se ATR, cm−1) 3287, 2956, 2926, 2228, 1718, 1608, 1460, 762, 701; ^{1}H NMR (400 MHz, DMSO–d_6) δ 12.35 (1H, br s, NH), 8.18 (1H, s, CH), 7.68 (1H, d, *J* = 2.3 Hz, CH), 7.52 (1H, d, *J* = 8.7 Hz, CH), 7.18 (1H, dd, *J* = 9.2 and 2.3 Hz, CH), 3.86 (3H, s, OCH_3), 3.85 (3H, s, OCH_3), 3.06 (3H, s, CH_3); ^{13}C NMR (100 MHz, DMSO–d_6) δ 166.5, 154.0, 141.7, 141.2, 131.8, 128.1, 127.3, 122.8, 120.0, 116.6, 115.6, 112.6, 106.1, 90.5, 55.6, 52.0, 17.8. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{17}H_{15}N_2O_3]$ 295.1083, found 295.1078.

Methyl 6-chloro-1-cyano-4-methyl-9H-carbazole-3-carboxylate **(5e).**

In a oven-dried round bottom flask, a solution of (*E*)-methyl 3-(5-chloro-1*H*-indol-3-yl)but-2-enoate **3h** (124.5 mg, 0.5 mmol) in toluene; 2 mL), $Pd(OAc)_2$ (11.2 mg, 10 mol %), $Cu(OAc)_2$ (2.0 equiv) and acrylonitrile **4a** (1.0 mmol) were added. The resulting reaction mixture was heated at 100 °C for 24 h. Progression of the reaction was monitored by TLC while noticing complete consumption of (*E*)-methyl 3-(5-chloro-1*H*-indol-3-yl)but-2-enoate, the reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 95/05) to give the title compound **3a** (122.2 mg, 80%) as a pale yellow needles, mp: 291–293 ^{o}C; FTIR (Zn−Se ATR, cm−1) 3310, 2955, 2853, 1653, 1452, 1202, 1050, 1000, 760; ^{1}H NMR (400 MHz, DMSO–d_6) δ 12.67 (1H, br s, NH), 8.24 (1H, s, CH), 8.20 (1H, d, *J* = 2.3 Hz, CH), 7.62 (1H, d, *J* = 9.2 Hz, CH), 7.55 (1H, dd, *J* = 8.4 and 2.5 Hz, CH), 3.87 (3H, s, OCH_3), 3.04 (3H, s, CH_3); ^{13}C NMR (100 MHz, DMSO–d_6) δ 166.4, 141.4, 139.0, 132.7, 128.2, 127.5, 127.3, 125.0, 123.6, 122.4, 122.2, 121.2, 116.4, 91.1, 52.3, 17.8. HRMS (ESI) $[M-H]^+$ Calcd for $[C_{16}H_{10}ClN_2O_2]$ 297.0431, found 297.0425.

Ethyl 6-chloro-1-cyano-4-methyl-9H-carbazole-3-carboxylate **(5f).**

In a oven-dried round bottom flask, a solution of (*E*)-ethyl 3-(5-chloro-1*H*-indol-3-yl)but-2-enoate **3c** (131.5 mg, 0.5 mmol) in toluene; 2 mL), $Pd(OAc)_2$ (12.4 mg, 10 mol %), $Cu(OAc)_2$ (2.0 equiv) and acrylonitrile **4a** (1.0 mmol) were added. The resulting reaction mixture was heated at 100 °C for 22 h. Progression of the reaction was monitored by TLC while noticing complete consumption of (*E*)-ethyl 3-(5-chloro-1*H*-indol-3-yl)but-2-enoate, the reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 95/05) to give the title compound **3a** (116.9 mg, 75%) as a off white needles, mp: 288–290 ^{o}C; FTIR (Zn−Se ATR, cm−1) 3291, 2920, 2852, 2228, 1714, 1593, 1446, 1285, 1242, 800; ^{1}H NMR (400 MHz, DMSO–d_6) δ 12.62 (1H, br s, NH), 8. 20 (1H, s, CH), 8.16 (1H, d, *J* = 1.5 Hz, CH), 7.59 (1H, d, *J* = 8.4 Hz, CH), 7.53 (1H, dd, *J* = 9.1 and 2.3 Hz, CH), 4.33 (2H, q, *J* = 6.9 Hz, OCH_2), 3.32 (3H, s, CH_3), 1.36 (3H, t, *J* = 6.8 Hz, CH_3); ^{13}C NMR (100 MHz, DMSO–d_6) δ 166.0, 141.9, 141.3, 139.0, 132.5, 126.8, 125.0, 123.5, 122.3, 122.2, 121.4, 116.4, 113.4, 91.0, 60.9, 17.8, 14.1. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{17}H_{14}ClN_2O_2]$ 313.0744, found 313.0738.

Ethyl 6-bromo-1-cyano-4-methyl-9H-carbazole-3-carboxylate **(5g)**.

In a oven-dried round bottom flask, a solution of (*E*)-ethyl 3-(5-bromo-1*H*-indol-3-yl)but-2-enoate **3d** (153.5 mg, 0.5 mmol) in toluene; 2 mL), $Pd(OAc))_2$ (11.20 mg, 10 mol %), $Cu(OAc)_2$ (2.0 equiv) and acrylonitrile **4a** (1.0 mmol) were added. The

resulting reaction mixture was heated at 100 °C for 24 h. Progression of the reaction was monitored by TLC while noticing complete consumption of (*E*)-ethyl 3-(5-bromo-1*H*-indol-3-yl)but-2-enoate, the reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 95/05) to give the title compound **3a** (137.8 mg, 77%) as pale yellow needles, mp: 272–275 ^oC; FTIR (Zn−Se ATR, cm−1) 3281, 2925, 2857, 2238, 1723, 1578, 1465, 1287, 1245, 789; ^1H NMR (400 MHz, DMSO–d_6) δ 12.44 (1H, br s, NH), 8.11–8.06 (1H, m, CH), 8.03 (1H, s, CH), 7.55–7.53 (1H, m, CH), 7.42 (1H, d, J = 8.4 Hz, CH), 4.29 (2H, q, J = 6.9 Hz, OCH_2), 2.84 (3H, s, CH_3), 1.36–1.33 (3H, m, CH_3); ^{13}C NMR (100 MHz, DMSO–d_6) δ 165.7, 141.7, 140.9, 139.1, 132.3, 129.1, 124.9, 123.8, 121.8, 120.9, 116.3, 113.6, 112.7, 90.7, 60.8, 17.6, 14.1. HRMS (ESI) $[M]^+$ Calcd for $[C_{17}H_{13}BrN_2O_2]$ 356.0160, found 356.0155.

Ethyl 1-cyano-6-fluoro-4-methyl-9H-carbazole-3-carboxylate **(5h)**.

In a oven-dried round bottom flask, a solution of (*E*)-ethyl 3-(5-fluoro-1*H*-indol-3-yl)but-2-enoate **3e** (123.6 mg, 0.5 mmol) in toluene; 2 mL), $Pd(OAc)_2$ (11.20 mg, 10 mol %), $Cu(OAc)_2$ (2.0 equiv) and acrylonitrile **4a** (1.0 mmol) were added. The resulting reaction mixture was heated at 100 °C for 24 h. Progression of the reaction was monitored by TLC, while noticing complete consumption of (*E*)-ethyl 3-(5-fluoro-1*H*-indol-3-yl)but-2-enoate, reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. Organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 95/05) to give the title compound **5h**(108.0 mg, 73%) as a yellow needles, mp: 141–143 ^oC; FTIR (Zn−Se ATR, cm−1) 3300, 2984, 2926, 2866, 2231, 1706, 1604, 1464, 1371, 1247, 760; ^1H NMR (400 MHz, DMSO–d_6) δ 12.51 (1H, br s, NH), 8.17 (1H, s, CH), 7.93 (1H, dd, J = 10.1 and 2.7 Hz,CH), 7.59–7.56 (1H, m, CH), 7.40–7.34 (1H, m, CH), 4.31 (2H, q, J = 7.3 Hz, OCH_2), 2.99 (3H, s, CH_3), 1.34 (3H, t, J = 6.9 Hz, CH_3); ^{13}C NMR (100 MHz, DMSO–d_6) δ 165.9, 157.2 (d, J = 236.7 Hz, 1C), 141.9, 141.6, 137.0, 132.4, 128.2, 127.3, 122.6 (d, J = 9.6 Hz, 1C), 120.9, 114.6 (d, J = 24.0 Hz, 1C), 112.9 (d, J = 10.5 Hz, 1C), 108.8 (d, J = 25.9 Hz, 1C), 90.8, 60.8, 17.7, 14.1. HRMS (ESI) $[M-H]^+$ Calcd for $[C_{17}H_{12}FN_2O_2]$ 295.0883, found 295.0877.

Methyl 1-cyano-9H-carbazole-3-carboxylate **(6a).**

In a oven-dried round bottom flask, a solution of (*E*)-methyl 3-(1H-indol-3-yl)acrylate **3l** (100.6 mg, 0.5 mmol) in toluene; 2 mL), $Pd(OAc))_2$ (11.2 mg, 10 mol %), $Cu(OAc)_2$ (2.0 equiv) and acrylonitrile **4a** (1.0 mmol) were added. The resulting reaction mixture was heated at 100 °C for 18 h. Progression of the reaction was monitored by TLC while noticing complete consumption of (*E*)-methyl 3-(1H-indol-3-yl)acrylate, the reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 95/05) to give the title compound **6a** (103.6 mg, 83%) as a off-white needles, mp: 256–258 ^oC (103.6 mg, 83%); FTIR (Zn−Se ATR, cm−1) 3294, 2923, 2852, 2231, 1725, 1579, 1512, 1458, 1429, 1333, 1262, 1098, 989, 762, 736; ^1H NMR (400 MHz, DMSO–d_6) δ 12.61 (1H, br s, NH), 9.03 (1H, d, J = 1.1 Hz, CH), 8.36–8.33 (2H, m, 2CH), 7.61 (1H, d, J = 8.4 Hz, CH), 7.54 (1H, t, J = 8.4 Hz, CH), 7.31 (1H, t, J = 7.6 Hz, CH), 3.90 (3H, s, OMe); ^{13}C NMR (100 MHz, DMSO–d_6) δ 165.5, 142.3, 140.8, 130.7, 127.7, 126.6, 123.9, 121.9, 121.4, 120.9, 120.3, 116.5, 112.1, 93.2, 52.2. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{15}H_{11}N_2O_2]$ 251.0821, found 251.0790.

Ethyl 1-cyano-9H-carbazole-3-carboxylate **(6b).**

In a oven-dried round bottom flask, a solution of (*E*)-ethyl 3-(1H-indol-3-yl)acrylate **3m** (134.0 mg, 0.5 mmol) in toluene; 2 mL), $Pd(OAc))_2$ (11.2 mg, 10 mol %), $Cu(OAc)_2$ (2.0 equiv) and acrylonitrile **4a** (1.0 mmol) were added. The resulting reaction mixture was heated at 100 °C for 18 h. Progression of the reaction was monitored by TLC, while noticing complete consumption of (*E*)-ethyl 3-(1H-indol-3-yl)acrylate, reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 95/05) to give the title compound **6b** (108.1 mg, 82%) as a colourless needles, mp: 210–213 ^oC; FTIR (Zn−Se ATR, cm−1) 3284, 2920, 2859, 2233, 1720, 1570, 1517, 1453, 1433, 1356, 1234, 1055, 990, 782, 732;; ^1H NMR (400 MHz, DMSO-d_6) δ 12.62 (1H, br s, NH), 9.03 (1H, s, CH), 8.37–8.34 (2H, m, 2CH), 7.61 (1H, d, J = 7.6 Hz, CH), 7.54 (1H, t, J = 6.8 Hz, CH), 7.31 (1H, t, J = 7.6 Hz, CH), 4.39 (2H, q, J = 6.8 Hz, OCH_2), 1.36 (3H, t, J = 7.6 Hz, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.0, 142.3, 140.8, 130.7, 127.8, 126.7, 124.0, 121.9, 121.4, 120.9, 120.6, 116.5, 112.1, 93.1, 61.0, 14.3 HRMS (ESI) $[M+H]^+$ Calcd for $[C_{16}H_{13}N_2O_2]$ 265.0977, found 265.0958.

Butyl 1-cyano-9H-carbazole-3-carboxylate **(6c).**

In a oven-dried round bottom flask, a solution of (*E*)-butyl 3-(1*H*-indol-3-yl)acrylate **3n** (121.5 mg, 0.5 mmol) in toluene; 2 mL), $Pd(OAc))_2$ (11.2 mg, 10 mol %), $Cu(OAc)_2$ (2.0 equiv) and acrylonitrile **4a** (1.0 mmol) were added. The resulting reaction mixture was heated at 100 °C for 18 h. Progression of the reaction was monitored by TLC, while noticing complete consumption of (*E*)-butyl 3-(1*H*-indol-3-yl)acrylate, reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. Organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 95/05) to give the title compound **6c** (116.7 mg, 80%) as a brown needles, mp: 192–194 ^oC; FTIR (Zn−Se ATR, cm−1) 3264, 2912, 2833, 2237, 1715, 1578, 1509, 1456, 1467, 1313, 1243, 1089, 978, 764, 744; ^1H NMR (400

MHz, DMSO–d_6) δ 12.59 (1H, br s, NH), 8.99 (1H, s, CH), 8.33 (2H, t, J = 8.4 Hz, 2CH), 7.60 (1H, d, J = 7.6 Hz, CH), 7.53 (1H, t, J = 7.6 Hz, CH), 7.30 (1H, t, J = 7.6 Hz, CH), 4.30 (2H, t, J = 6.9 Hz, OCH_2), 1.75–1.68 (2H, m, CH_2), 1.47–1.41 (2H, m, CH_2), 0.94 (3H, t, J = 7.2 Hz, CH_3); ^{13}C NMR (100 MHz, DMSO–d_6) δ 165.0, 142.3, 140.8, 130.6, 127.7, 126.6, 123.9, 121.9, 121.3, 120.8, 120.6, 116.5, 112.1, 93.0, 64.6, 30.3, 18.8, 13.7 HRMS (ESI) $[M+H]^+$ Calcd for $[C_{18}H_{17}N_2O_2]$ 293.1290, found 293.1285.

tert-Butyl 1-cyano-9H-carbazole-3-carboxylate (**6d**)

In a oven-dried round bottom flask, a solution of (*E*)-*tert*-butyl 3-(1*H*-indol-3-yl)acrylate **3o** (121.5 mg, 0.5 mmol) in toluene; 2 mL), $Pd(OAc))_2$ (11.2 mg, 10 mol %), $Cu(OAc)_2$ (2.0 equiv) and acrylonitrile **4a** (1.0 mmol) were added. The resulting reaction mixture was heated at 100 °C for 18 h. Progression of the reaction was monitored by TLC, while noticing complete consumption of (*E*)-*tert*-butyl 3-(1*H*-indol-3-yl)acrylate, reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. Organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 95/05) to give the title compound **6d** (112.3 mg, 77%) as a brown needles, mp: 228–230 ^oC; FTIR (Zn−Se ATR, cm−1) 3396, 2978, 2925, 2850, 2224, 1705, 1578, 1500, 1474, 1455, 1392, 1367, 1329, 1309, 1249, 1221, 1161, 1129,, 1024, 999, 825; ^{1}H NMR (400 MHz, DMSO–d_6) δ 12.55 (1H, br s, NH), 8.93 (1H, d, J = 1.5 Hz, CH), 8.30 (1H, d, J = 7.6 Hz, CH), 8.26 (1H, d, J = 1.5 Hz, CH), 7.59 (1H, d, J = 8.0 Hz, CH), 7.52 (1H, t, J = 6.9 Hz, CH), 7.30 (1H, t, J = 6.9 Hz, CH), 1.58 (9H, s, tBu); ^{13}C NMR (100 MHz, DMSO–d_6) δ 164.2, 142.1, 140.8, 130.6, 127.6, 126.4, 123.8, 122.1, 121.9, 121.2, 120.8, 116.6, 112.1, 92.8, 81.0, 27.8. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{18}H_{17}N_2O_2]$ 293.1290, found 293.1297.

1-Cyano-N,N-dimethyl-9H-carbazole-3-carboxamide **(6e).**

In a oven-dried round bottom flask, a solution of (*E*)-3-(1*H*-indol-3-yl)-*N*,*N*-dimethyl acrylamide **3p** (107.0 mg, 0.5 mmol) in toluene; 2 mL), $Pd(OAc))_2$ (11.2 mg, 10 mol %), $Cu(OAc)_2$ (2.0 equiv) and acrylonitrile **4a** (1.0 mmol) were added. The resulting reaction mixture was heated at 100 °C for 18 h. Progression of the reaction was monitored by TLC while noticing complete consumption of (*E*)-3-(1*H*-indol-3-yl)-*N*,*N*-dimethyl acrylamide, the reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 95/05) to give the title compound **6e** (95.9 mg, 73%) as a dark brown needles, mp: 199–201 ^oC; FTIR (Zn−Se ATR, cm−1) 3232, 2955, 2852, 2225, 1606, 1496, 1396, 1090, 749; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.10 (1H, br s, NH), 8.32 (1H, s, CH), 7.96 (1H, d, J = 7.6 Hz, CH), 7.74 (1H, s, CH), 7.53–7.44 (2H, m, 2CH), 7.25 (1H, t, J = 7.6 Hz, CH), 3.14 (6H, s, $2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 141.0, 140.3, 128.3, 127.6, 126.7, 124.4, 124.2, 122.1, 120.8, 120.6, 116.7, 111.7, 93.1, 42.6. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{16}H_{14}N_3O]$ 264.1137, found 264.1131.

Methyl 1-cyano-6-methoxy-9H-carbazole-3-carboxylate **(6f).** In a oven-dried round bottom flask, a solution of (*E*)-methyl 3-(5-methoxy-1*H*-indol-3-yl)acrylate **3q** (115.5 mg, 0.5 mmol) in toluene; 2 mL), $Pd(OAc))_2$ (11.2 mg, 10 mol %), $Cu(OAc)_2$ (2.0 equiv) and acrylonitrile **4a** (1.0 mmol) were added. The resulting reaction mixture was heated at 100 °C for 18 h. Progression of the reaction was monitored by TLC, while noticing complete consumption of (*E*)-methyl 3-(5-methoxy-1*H*-indol-3-yl)acrylate, reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 95/05) to give the title compound **6f** (116.2 mg, 83%) as a off-white needles, mp: 155–157 ^oC; FTIR (Zn−Se ATR, cm−1) FTIR (Zn−Se ATR, cm−1) 3214, 2933, 2845, 2257, 1713, 1665, 1436, 1347, 1233, 1166, 1037, 955, 815, 758; ^{1}H NMR (400 MHz, DMSO–d_6) δ 12.41 (1H, br s, NH), 9.01 (1H, s, CH), 8.27 (1H, d, J = 1.52 Hz, CH), 7.94 (1H, d, J = 2.3 Hz, CH) 7.47 (1H, d, J = 9.2 Hz, CH), 7.13 (1H, dd, J = 8.4 and 2.3 Hz, CH), 3.88 (3H, s, OCH_3), 3.84 (3H, s, OCH_3); ^{13}C NMR (100 MHz, DMSO–d_6) δ 165,6, 154.5, 142.5, 135.3, 130.5, 126.9, 124.0, 122.6, 119.7, 117.3 116.6, 112.8, 103.7, 93.0, 55.6, 52.2 HRMS (ESI) $[M+H]^+$ Calcd for $[C_{16}H_{13}N_2O_3]$ 281.0926, found 281.0946.

Butyl 1-cyano-6-methoxy-9H-carbazole-3-carboxylate **(6g).**

In a oven-dried round bottom flask, a solution of (*E*)-butyl 3-(5-methoxy-1*H*-indol-3-yl)acrylate **3r** (136.5 mg, 0.5 mmol) in toluene; 2 mL), $Pd(OAc))_2$ (11.2 mg, 10 mol %), $Cu(OAc)_2$ (2.0 equiv) and acrylonitrile **4a** (1.0 mmol) were added. The resulting reaction mixture was heated at 100 °C for 18 h. Progression of the reaction was monitored by TLC, while noticing complete consumption of (*E*)-butyl 3-(5-methoxy-1*H*-indol-3-yl)acrylate, the reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 95/05) to give the title compound **6g** (130.3 mg, 81%) as a off-white needles, mp: 205–208 ^oC; FTIR (Zn−Se ATR, cm−1) 3318, 2913, 2850, 2230, 1720, 1656, 1475, 1332, 1241, 1143, 988, 835, 755; ^{1}H NMR (400 MHz, DMSO–d_6) δ 12.39 (1H, br s, NH), 8.97 (1H, d, J = 1.5 Hz, CH), 8.25 (1H, d, J = 1.5 Hz, CH), 7.92 (1H, d, J = 2.2 Hz, CH), 7.47 (1H, d, J = 8.4 Hz, CH), 7.13 (1H, dd, J = 9.2 and 3.0 Hz, CH), 4.28 (2H, q, J = 6.9 Hz, OCH_2), 3.85 (3H, s, OCH_3), 1.75–1.68 (2H, m, CH_2), 1.48–1.39 (2H, m, CH_2), 0.93(3H, t, J = 7.6 Hz, CH_3); ^{13}C NMR (100 MHz, DMSO–d_6) δ 165.1, 154.5, 142.5, 135.3, 130.4, 126.8, 123.9, 122.5, 119.9, 117.2, 116.6, 112.8, 103.6, 92.9, 64.5, 55.6, 30.4, 18.8, 13.7. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{19}H_{19}N_2O_3]$ 323.1396, found 323.1416.

Methyl 8-(benzyloxy)-1-cyano-9H-carbazole-3-carboxylate **(6h).**

In a oven-dried round bottom flask, a solution of (*E*)-methyl 3-(7-(benzyloxy)-1*H*-indol-3-yl)acrylate **3s** (153.5 mg, 0.5 mmol) in toluene; 2 mL), $Pd(OAc))_2$ (11.2 mg, 10 mol %), $Cu(OAc)_2$ (2.0 equiv) and acrylonitrile **4a** (1.0 mmol) were

added. The resulting reaction mixture was heated at 100 °C for 20 h. Progression of the reaction was monitored by TLC, while noticing complete consumption of (*E*)-methyl 3-(7-(benzyloxy)-1*H*-indol-3-yl)acrylate, reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. Organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 95/05) to give the title compound **6h** (129.9 mg, 73%) as a brown needles, mp: 152–154 ^oC; FTIR (Zn−Se ATR, cm−1) FTIR (Zn−Se ATR, cm−1) 3228, 2938, 2845, 2268, 1717, 1634, 1456, 1356, 1146, 1057, 959, 845, 758; ^1H NMR (400 MHz, DMSO–d_6) δ 12.74 (1H, br s, NH), 9.03–9.02 (1H, m, CH), 8.33 (1H, t, *J* = 1.5 Hz, CH), 7.94–7.92 (1H, m,CH), 7.61 (2H, d, *J* = 7.6 Hz, 2CH), 7.41 (2H, t, *J* = 2.6 Hz, 2CH), 7.35–7.31 (1H, m, CH), 7.22–7.21 (2H, m, 2CH), 5.36 (2H,m,CH_2), 3.90 (3H, s, OCH_3); ^{13}C NMR (100 MHz, DMSO–d_6) δ 165.5, 145.1, 141.6, 137.0, 131.5, 131.0, 128.4, 127.8, 126.8, 124.6, 123.6, 120.5, 116.5, 113.5, 110.0, 93.9, 69.6, 54.7. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{22}H_{17}N_2O_3]$ 357.1239, found 357.1240.

Methyl 1,6-dicyano-9H-carbazole-3-carboxylate **(6i).**

In a oven-dried round bottom flask, a solution of (*E*)-methyl 3-(5-cyano-1*H*-indol-3-yl)acrylate **3t** (113.0 mg, 0.5 mmol) in toluene; 2 mL), $Pd(OAc))_2$ (10 mol %), $Cu(OAc)_2$ (2.0 equiv) and acrylonitrile **4a** (1.0 mmol) were added. The resulting reaction mixture was heated at 100 °C for 24 h. Progression of the reaction was monitored by TLC while noticing complete consumption of (*E*)-methyl 3-(5-cyano-1*H*-indol-3-yl)acrylate, the reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 95/05) to give the title compound **6i** (98.9 mg, 72%) as a off-white needles, mp: 298–300 ^oC; FTIR (Zn−Se ATR, cm−1) 3418, 2923, 2855, 2250, 1709, 1644, 1462, 1366, 1254, 1186, 1027, 999, 825, 768; ^1H NMR (400 MHz, DMSO–d_6) δ 12.22 (1H, br s, NH), 9.15 (1H, d, *J* = 1.6 Hz, CH), 8.94 (1H, s, CH), 8.63 (1H, d, *J* = 16.0 Hz, CH), 7.87 (2H, s, 2CH), 4.01 (3H, s, OCH_3); ^{13}C NMR (100 MHz, DMSO–d_6) δ 165.9, 147.1, 130.2, 129.4, 127.6, 126.5, 124.3, 124.2, 123.1, 120.9, 118.4, 115.5, 113.7, 112.4, 102.4, 52.4. HRMS (ESI) $[M]^+$ Calcd for $[C_{16}H_9N_3O_2]$ 275.0695, found 275.0689.

Methyl 1-Cyano-6-nitro-9H-carbazole-3-carboxylate **(6j).**

In a oven-dried round bottom flask, a solution of (*E*)-methyl 3-(5-nitro-1*H*-indol-3-yl)acrylate **3u** (123.1 mg, 0.5 mmol) in toluene; 2 mL), $Pd(OAc))_2$ (10 mol %), $Cu(OAc)_2$ (2.0 equiv) and acrylonitrile **4a** (1.0 mmol) were added. The resulting reaction mixture was heated at 100 °C for 24 h. Progression of the reaction was monitored by TLC while noticing complete consumption of (*E*)-methyl 3-(5-nitro-1*H*-indol-3-yl)acrylate, the reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 95/05) to give the title compound **6j** (107.6 mg, 73%) as a yellow needles, mp: 231–233 ^oC; FTIR (Zn−Se ATR, cm−1) FTIR (Zn−Se ATR, cm−1) 3378, 2913, 2825, 2230, 1719, 1664, 1469, 1368, 1253, 1190, 1031, 969, 845, 778; ^1H NMR (400 MHz, DMSO–d_6) δ 13.17 (1H, br s, NH), 9.37 (1H, s, CH), 9.25 (1H, s, CH), 8.38–8.35 (2H, m, 2CH), 7.68 (1H, d, *J* = 9.2 Hz, CH), 3.91 (3H, s, OCH_3); ^{13}C NMR (100 MHz, DMSO–d_6) δ 165.2, 153.3, 144.3, 143.6, 132.2, 128.3, 123.9, 123.1, 123.0, 121.9, 118.8, 112.5, 94.4, 52.4 HRMS (ESI) $[M+Na]^+$ Calcd for $[C_{15}H_9N_3O_4Na]$ 318.0491, found 318.0485.

Methyl 6-chloro-1-cyano-9H-carbazole-3-carboxylate **(6k)**.

In a oven-dried round bottom flask, a solution of (*E*)-methyl 3-(5-chloro-1*H*-indol-3-yl)acrylate **3v** (117.5 mg, 0.5 mmol) in toluene; 2 mL), $Pd(OAc))_2$ (11.2 mg, 10 mol %), $Cu(OAc)_2$ (2.0 equiv) and acrylonitrile **4a** (1.0 mmol) were added. The resulting reaction mixture was heated at 100 °C for 21 h. Progression of the reaction was monitored by TLC while noticing complete consumption of (*E*)-methyl 3-(5-chloro-1*H*-indol-3-yl)acrylate, the reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 95/05) to give the title compound **6k** (80.1 mg, 77%) as a off-white needles, mp: 297–299 ^oC; FTIR (Zn−Se ATR, cm−1) 3285, 2917, 2854, 2228, 1717, 1247, 1032, 765; ^1H NMR (400 MHz, DMSO–d_6) δ 12.69 (1H, br s, NH), 9.03 (1H, d, *J* = 1.5 Hz, CH), 8.44 (1H, d, *J* = 1.5 Hz, CH), 8.30 (1H, d, *J* = 2.2 Hz, CH), 7.57–7.49 (2H, m, 2CH), 3.89 (3H, s, OCH_3); ^{13}C NMR (100 MHz, DMSO–d_6) δ 165.3, 142.6, 139.2, 131.3, 127.6, 127.4, 125.3, 123.3, 123.0, 121.1, 120.6, 116.3, 113.6, 93.4, 52.3. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{15}H_{10}ClN_2O_2]$ 285.0431, found 285.0425.

3-phenyl-9H-carbazole-1-carbonitrile **(6l).**

In a oven-dried round bottom flask, a solution of (*E*)-3-styryl-1*H*-indole **3w** (109.5 mg, 0.5 mmol) in toluene; 2 mL), $Pd(OAc))_2$ (11.2 mg, 10 mol %), $Cu(OAc)_2$ (2.0 equiv) and acrylonitrile **4a** (1.0 mmol) were added. The resulting reaction mixture was heated at 100 °C for 18 h. Progression of the reaction was monitored by TLC while noticing complete consumption of (*E*)-3-styryl-1*H*-indole, the reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 95/05) to give the title compound **6l** (91.1 mg, 68%) as a brown, mp: 138–140 ^oC; FTIR (Zn−Se ATR, cm−1) 3219, 2958, 2828, 2233, 1715, 1642, 1434, 1332, 1267, 1144, 1022, 945, 856, 754;^1H NMR (400 MHz, DMSO–d_6) δ 12.20 (1H, br s, NH), 8.82 (1H, d, *J* = 1.5 Hz, CH), 8.30 (1H, d, *J* = 7.6 Hz, CH), 8.15 (1H, d, *J* = 2.3 Hz, CH), 7.82 (2H. d, *J* = 7.6 Hz, 2CH), 7.57 (1H, d, *J* = 7.6 Hz, CH), 7.49 (3H, t, *J* = 6.9 Hz, 3CH), 7.35 (1H, t, *J* = 8.4 Hz, CH), 7.27 (1H, t, *J* = 7.6 Hz, CH); ^{13}C NMR (100

MHz, DMSO–d_6) δ 140.7, 139.6, 139.3, 131.4, 129.0, 128.1, 127.2, 126.8, 124.7, 123.8, 122.1, 121.1, 120.0, 117.4, 111.8, 93.4. HRMS (APCI) $[M+H]^+$ Calcd for $[C_{19}H_{13}N_2]$ 269.1079, found 269.1073.

General Procedure analytical data for the of C-H activation:

Dimethyl 4-methyl-9H-carbazole-1,3-dicarboxylate **(7a).**

In a oven-dried round bottom flask, a solution of (*E*)-methyl 3-(1*H*-indol-3-yl)but-2-enoate **3f** (107.5 mg, 0.5 mmol) in toluene 2 mL, $Pd(OAc))_2$ (11.2 mg, 10 mol %), $Cu(OAc)_2$ (2.0 equiv) and methyl acrylate **1e** (1.0 mmol) were added. The resulting reaction mixture was heated at 100 °C for 18 h. Progression of the reaction was monitored by TLC while noticing complete consumption of (*E*)-methyl 3-(1*H*-indol-3-yl)but-2-enoate, reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. Organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 90/10) to give the title compound **3a** (120.2 mg, 81%) as a pale yellow needles, mp: 226–228 ^oC; FTIR (Zn−Se ATR, cm−1) 3377, 2955, 2924, 2855, 1694, 1595, 1443, 1371, 1325, 1245, 1099, 1029, 825, 758; ^1H NMR (400 MHz, DMSO–d_6) δ 11.72 (1H, br s, NH), 8.50 (1H, s, CH), 8.25 (1H, d, *J* = 8.4 Hz, CH), 7.81 (1H, d, *J* = 8.4 Hz, CH), 7.49 (1H, t, *J* = 8.4 Hz, CH), 7.28 (1H, t, *J* = 7.6 Hz, CH), 3.97 (3H, s, OCH_3), 3.86 (3H, s, OCH3), 3.11 (3H, s, CH_3); ^{13}C NMR (100 MHz, DMSO–d_6) δ 167.2, 165.8, 141.5, 139.9, 129.7, 128.1, 127.3, 126.3, 125.6, 122.7, 120.3, 119.8, 112.5, 108.9, 52.0, 51.9, 17.9. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{17}H_{16}NO_4]$ 298.1079, found 298.1079.

1-Ethyl 3-methyl 4-methyl-9H-carbazole-1,3-dicarboxylate **(7b).**

In a oven-dried round bottom flask, a solution of (*E*)-methyl 3-(1*H*-indol-3-yl)but-2-enoate **3f** (107.5 mg, 0.5 mmol) in toluene 2 mL, $Pd(OAc))_2$ (11.2 mg, 10 mol %), $Cu(OAc)_2$ (2.0 equiv) and ethyl acrylate **1f** (1.0 mmol) were added. The resulting reaction mixture was heated at 100 °C for 18 h. Progression of the reaction was monitored by TLC while noticing complete consumption of (E)-methyl 3-(1H-indol-3-yl)but-2-enoate, reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 90/10) to give the title compound **7b** (122.8 mg, 79%) as a yellow needles, mp: 238–240 ^oC; FTIR (Zn−Se ATR, cm−1) 3384, 2955, 2950, 1691, 1596, 1325, 1248, 1069, 761; ^1H NMR (400 MHz, DMSO–d_6) δ 11.74 (1H, br s, NH), 8.49 (1H, s, CH), 8.24 (1H, d, *J* = 7.6 Hz, CH), 7.82 (1H, d, *J* = 8.4 Hz, CH), 7.49 (1H, t, *J* = 7.6 Hz, CH), 7.28 (1H, t, *J* = 7.6 Hz, CH), 4.46 (2H, q, *J* = 7.6 Hz, OCH_2), 3.86 (3H, s, OCH_3), 3.10 (3H, s, CH_3), 1.40 (3H, t, *J* = 6.9 Hz, CH_3); ^{13}C NMR (100 MHz, DMSO–d_6) δ 167.4, 165.5, 140.8, 140.1, 129.6, 128.2, 127.5, 126.4, 122.9, 122.3, 120.5, 120.0, 112.6, 109.2, 60.9, 52.0, 18.1, 14.4. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{18}H_{18}NO_4]$ 312.1236, found 312.1228.

Dimethyl 6-methoxy-4-methyl-9H-carbazole-1,3-dicarboxylate **(7c).**

In a oven-dried round bottom flask, a solution of (*E*)-methyl 3-(5-methoxy-1*H*-indol-3-yl)but-2-enoate **3g** (122.5 mg, 0.5 mmol) in toluene 2 mL, $Pd(OAc))_2$ (11.2 mg, 10 mol %), $Cu(OAc)_2$ (2.0 equiv) and methyl acrylate **1e** (1.0 mmol) were added. The resulting reaction mixture was heated at 100 °C for 18 h. Progression of the reaction was monitored by TLC, while noticing complete consumption of (*E*)-methyl 3-(5-methoxy-1*H*-indol-3-yl)but-2-enoate, the reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 90/10) to give the title compound **7c** (125.9 mg, 77%) as a yellow needles, mp: 123–125 ^oC; FTIR (Zn−Se ATR, cm−1) 3402, 2954, 2853, 1698, 1594, 1309, 1200, 1098, 1026, 755; ^1H NMR (400 MHz, DMSO–d_6) δ 11.54 (1H, br s, NH), 8.45 (1H, s, CH), 7.69 (1H, d, *J* = 9.2 Hz, CH), 7.66 (1H, d, *J* = 1.1 Hz, CH), 7.24 (1H, t, *J* = 6.9 Hz, CH), 3.96 (3H, s, OCH_3), 3.85 (6H, s, $2OCH_3$), 3.07 (3H, s, CH_3); ^{13}C NMR (100 MHz, DMSO–d_6) δ 167.2, 165.8, 153.9, 141.8, 140.3, 129.8, 128.1, 127.4, 125.7, 123.6, 122.7, 119.2, 114.9, 113.0, 106.1, 55.6, 52.0, 51.8, 17.8. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{18}H_{18}NO_5]$ 328.1185, found 328.1177.

1-Ethyl 3-methyl 6-methoxy-4-methyl-9H-carbazole-1,3-dicarboxylate **(7d)**.

In an oven-dried round bottom flask, a solution of (*E*)-methyl 3-(5-methoxy-1*H*-indol-3-yl)but-2-enoate **3g** (122.5 mg, 0.5 mmol) in toluene 2 mL, $Pd(OAc))_2$ (11.2 mg, 10 mol %), $Cu(OAc)_2$ (2.0 equiv) and ethyl acrylate **1f** (1.0 mmol) were added. The resulting reaction mixture was heated at 100 °C for 18 h. Progression of the reaction was monitored by TLC while noticing complete consumption of (*E*)-methyl 3-(5-methoxy-1*H*-indol-3-yl)but-2-enoate, the reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 90/10) to give the title compound **7d** (126.1 mg, 74%) as a yellow needles, mp: 110–113 ^oC; FTIR (Zn−Se ATR, cm−1) 3301, 2988, 2939, 2831, 1684, 1597, 1515, 1485, 1437, 1330, 1284, 1218, 1039, 764; ^1H NMR (400 MHz, DMSO–d_6) δ 11.60 (1H, br s, NH), 8.48 (1H, s, CH), 7.72 (1H, d, *J* = 3.8 Hz, CH), 7.24 (1H, d, *J* = 2.3 Hz, CH), 7.17 (1H, dd, *J* = 8.4 and 2.3 Hz, CH), 4.47 (2H, q, *J* = 6.9 Hz, OCH_2), 3.88 (6H, s, $2OCH_3$) 3.12 (3H, s, CH_3), 1.41 (3H, t, *J* = 6.9 Hz, CH_3); ^{13}C NMR (100 MHz, DMSO–d_6) δ 167.3, 166.7, 156.1, 141.7, 140.4, 123.7, 122.7, 122.3, 115.0, 114.1, 113.2, 113.0, 102.4, 60.8, 55.6, 55.5, 17.9, 14.4. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{19}H_{20}NO_5]$ 342.1341, found 342.1332.

Dimethyl 6-chloro-4-methyl-9H-carbazole-1,3-dicarboxylate **(7e).**

In a oven-dried round bottom flask, a solution of (*E*)-methyl 3-(5-chloro-1*H*-indol-3-yl)but-2-enoate **3h** (0.5 mmol) in toluene

2 mL, $Pd(OAc))_2$ (10 mol %), $Cu(OAc)_2$ (2.0 equiv) and methyl acrylate **1e** (1.0 mmol) were added. The resulting reaction mixture was heated at 100 °C for 22 h. Progression of the reaction was monitored by TLC while noticing complete consumption of (*E*)-methyl 3-(5-chloro-1*H*-indol-3-yl)but-2-enoate, the reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 90/10) to give the title compound **7e** (120.8 mg, 73%) as a off-white needles, mp: 282–284 ^oC; FTIR (Zn−Se ATR, cm−1) 3412, 2923, 2854, 1710, 1639, 1217, 950, 838, 794, 756; ^1H NMR (400 MHz, DMSO–d_6) δ 11.84 (1H, br s, NH), 8.30 (1H, s, CH), 8.23 (1H, s, CH), 8.19 (1H, d, J = 1.3 Hz, CH), 7.52 (1H, dd, J = 2.3 and 1.5 Hz, CH), 3.97 (3H, s, OCH_3), 3.86 (3H, s, OCH_3), 3.06 (3H, s, CH_3); ^{13}C NMR (100 MHz, DMSO–d_6) δ 167.0, 165.7, 145.9, 136.9, 136.5, 135.4, 134.3, 128.4, 127.6, 126.9, 123.8, 121.1, 118.3, 102.3, 51.6, 51.1. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{17}H_{15}ClNO_4]$ 332.0690, found 332.0694.

1-Ethyl 3-methyl 6-chloro-4-methyl-9H-carbazole-1,3-dicarboxylate **(7f)**.

In a oven-dried round bottom flask, a solution of (*E*)-methyl 3-(5-chloro-1*H*-indol-3-yl)but-2-enoate **3h** (124.5 mg, 0.5 mmol) in toluene 2 mL, $Pd(OAc))_2$ (11.2 mg, 10 mol %), $Cu(OAc)_2$ (2.0 equiv) and ethyl acrylate **1f** (1.0 mmol) were added. The resulting reaction mixture was heated at 100 °C for 22 h. Progression of the reaction was monitored by TLC while noticing complete consumption of (*E*)-methyl 3-(5-chloro-1*H*-indol-3-yl)but-2-enoate, the reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 90/10) to give the title compound **7f** (122.4 mg, 71%) as a pale yellow needles, mp: 273–275 ^oC; FTIR (Zn−Se ATR, cm−1) 3367, 2956, 2870, 1688, 1508, 1305, 1246, 1025, 760; ^1H NMR (400 MHz, DMSO–d_6) δ 11.86 (1H, br s, NH), 8.47 (1H, s, CH), 8.18 (1H, d, J = 1.3 Hz, CH), 7.79 (1H, d, J = 9.2 Hz, CH), 7.51 (1H, dd, J = 8.4 and 1.5 Hz, CH), 4.45 (2H, q, J = 6.9 Hz, CH_2), 3.86 (3H, s, OCH_3), 3.05 (3H, s, CH_3), 1.39 (3H, t, J = 6.8 Hz, CH_3); ^{13}C NMR (100 MHz, DMSO–d_6) δ 167.1, 165.2, 141.9, 139.2, 130.1, 128.2, 127.4, 125.7, 124.6, 122.8, 122.0, 120.2, 114.0, 109.4, 60.9, 52.0, 17.9, 14.3. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{18}H_{17}ClNO_4]$ 346.0846, found 346.0841.

Dimethyl 6-bromo-4-methyl-9H-carbazole-1,3-dicarboxylate **(7g)**

In a oven-dried round bottom flask, a solution of (*E*)-methyl 3-(5-bromo-1H-indol-3-yl)but-2-enoate **3i** (146.5 mg, 0.5 mmol) in toluene 2 mL, $Pd(OAc))_2$ (10 mol %), $Cu(OAc)_2$ (2.0 equiv) and methyl acrylate **1e** (1.0 mmol) were added. The resulting reaction mixture was heated at 100 °C for 24 h. Progression of the reaction was monitored by TLC while noticing complete consumption of (*E*)-methyl 3-(5-bromo-1*H*-indol-3-yl)but-2-enoate, the reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 90/10) to give the title compound **7g** (137.2 mg, 73%) as a pale yellow needles, mp: 190–192 ^oC; FTIR (Zn−Se ATR, cm−1) 3422, 2956, 2854, 2253, 1697, 1605, 1137, 1024, 760; ^1H NMR (400 MHz, DMSO–d_6) δ 11.90 (1H, br s, NH), 8.52 (1H, s, CH), 8.35 (1H, d, J = 1.3 Hz, CH), 7.76 (1H, d, J = 9.2 Hz, CH), 7.65–7.62 (1H, m, CH), 3.97 (3H, s, OCH_3), 3.87 (3H, s, OCH_3), 3.09 (3H, s, CH_3); ^{13}C NMR (100 MHz, DMSO–d_6) δ 167.1, 164.5, 147.3, 145.7, 140.1, 139.5, 133.4, 131.0, 130.3, 128.9, 124.9, 124.1, 114.4, 109.3, 52.8, 52.2, 17.9. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{17}H_{15}BrNO_4]$ 376.0184, found 376.0184.

1-Ethyl 3-methyl 6-bromo-4-methyl-9H-carbazole-1,3-dicarboxylate **(7h)**

In a oven-dried round bottom flask, a solution of *E*)-methyl 3-(5-bromo-1H-indol-3-yl)but-2-enoate **3i** (146.5 mg, 0.5 mmol) in toluene 2 mL, $Pd(OAc))_2$ (11.2 mg, 10 mol %), $Cu(OAc)_2$ (2.0 equiv) and ethyl acrylate **1f** (1.0 mmol) were added. The resulting reaction mixture was heated at 100 °C for 24 h. Progression of the reaction was monitored by TLC while noticing complete consumption of *E*)-methyl 3-(5-bromo-1H-indol-3-yl)but-2-enoate, the reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 90/10) to give the title compound **7h** (140.4 mg, 72%) as a pale yellow needles, mp: 167–169 ^oC; FTIR (Zn−Se ATR, cm−1) 3240, 2955, 2853, 1718, 1683, 1493, 1453, 1216, 756; ^1H NMR (400 MHz, DMSO–d_6) δ 11.92 (1H, br s, NH), 8.61 (1H, s, CH), 8.50 (1H, s, CH), 7.77 (1H, d, J = 9.2 Hz, CH), 7.64 (1H, dd, J = 8.4 and 2.3 Hz, CH), 4.37 (2H, q, J = 7.6 Hz, OCH_2), 3.87 (3H, s, OCH_3), 3.08 (3H, s, CH_3), 1.39–1.34 (3H, m, CH_3); ^{13}C NMR (100 MHz, DMSO–d_6) δ 165.2, 164.1, 145.7, 139.6, 133.3, 130.1, 128.2, 127.4, 126.8, 124.9, 124.1, 122.8, 114.5, 109.4, 60.9, 52.0, 17.9, 14.4. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{18}H_{17}BrNO_4]$ 390.0341, found 390.0344.

3-Ethyl 1-methyl 4-methyl-9H-carbazole-1,3-dicarboxylate **(7i)**

In a oven-dried round bottom flask, a solution of (*E*)-ethyl 3-(1*H*-indol-3-yl)but-2-enoate **3a** (114.5 mg, 0.5 mmol) in toluene 2 mL, $Pd(OAc))_2$ (10 mol %), $Cu(OAc)_2$ (2.0 equiv) and methyl acrylate **1e** (1.0 mmol) were added. The resulting reaction mixture was heated at 100 °C for 18 h. Progression of the reaction was monitored by TLC while noticing complete consumption of (*E*)-ethyl 3-(1*H*-indol-3-yl)but-2-enoate, the reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 90/10) to

give the title compound **7i** (124.4 mg, 80%) as a yellow needles, mp: 143–145 °C; FTIR (Zn−Se ATR, cm−1) 3394, 2985, 2952, 2839, 1700, 1596, 1485, 1309, 1223, 1167, 1037, 763; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.15 (1H, br s, NH), 8.60 (1H, s, CH), 8.25–8.23 (1H, m, CH), 7.57–7.53 (1H, m, CH), 7.50–7.48 (1H, m, CH), 7.33–7.29 (1H, m, CH), 4.42 (2H, q, J = 6.9 Hz, OCH_2), 4.01 (3H, s, OCH_3), 3.16 (3H, s, CH_3), 1.45 (3H, t, J = 6.9 Hz, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 167.4, 142.5, 136.3, 130.2, 126.3, 124.6, 124.0, 123.1, 121.4, 121.3, 120.6, 116.3, 60.8, 52.0, 18.3, 14.4. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{18}H_{18}NO_4]$ 312.1236, found 312.1232.

3-Ethyl 1-methyl 6-methoxy-4-methyl-9H-carbazole-1,3-dicarboxylate **(7j)**

In a oven-dried round bottom flask, a solution of (E)-ethyl 3-(5-methoxy-1H-indol-3-yl)but-2-enoate **3b** (129.5 mg, 0.5 mmol) in toluene 2 mL, $Pd(OAc))_2$ (10 mol %), $Cu(OAc)_2$ (2.0 equiv) and methyl acrylate **1e** (1.0 mmol) were added. The resulting reaction mixture was heated at 100 °C for 18 h. Progression of the reaction was monitored by TLC while noticing complete consumption of (*E*)-ethyl 3-(5-methoxy-1*H*-indol-3-yl)but-2-enoate, the reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 90/10) to give the title compound **7j** (131.2 mg, 77%) as a yellow needles, mp: 151–153 °C; FTIR (Zn−Se ATR, cm−1) 3246, 2984, 2830, 1674, 1592, 1478, 1284, 1134, 853, 786; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.05 (1H, br s, NH), 8.62 (1H, s, CH), 7.77 (1H, d, J = 2.3 Hz, CH), 7.44 (1H, d, J = 8.7 Hz, CH), 7.15 (1H, dd, J = 9.2 and 2.7 Hz,CH), 4.42 (2H, q, J = 7.3 Hz, OCH_2), 4.02 (3H, s, OCH_3), 3.94 (3H, s, OCH_3), 3.19 (3H, s, CH_3), 1.45 (3H, t, J = 7.3 Hz, CH_3); ^{13}C NMR (100 MHz, , $CDCl_3$) δ 167.8, 167.4, 154.4, 142.6, 141.8, 134.8, 130.4, 124.0, 123.9, 120.9, 114.6, 111.7, 108.6, 107.2, 60.9, 56.2, 52.0, 18.3, 14.4. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{19}H_{20}NO_5]$ 342.1341, found 342.1336.

Diethyl 6-bromo-4-methyl-9H-carbazole-1,3-dicarboxylate **(7k)**.

In a oven-dried round bottom flask, a solution of (*E*)-ethyl 3-(5-bromo-1*H*-indol-3-yl)but-2-enoate **3d** (153.5 mg, 0.5 mmol) in toluene 2 mL, $Pd(OAc))_2$ (10 mol %), $Cu(OAc)_2$ (2.0 equiv) and ethyl acrylate **1e** (1.0 mmol) were added. The resulting reaction mixture was heated at 100 °C for 24 h. Progression of the reaction was monitored by TLC, while noticing complete consumption of (*E*)-ethyl 3-(5-bromo-1*H*-indol-3-yl)but-2-enoate, reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. Organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 90/10) to give the title compound **7k** (141.4 mg, 70%) as a yellow needles, mp: 258–260 °C; FTIR (Zn−Se ATR, cm−1) 3420, 2979, 1709, 1640, 1540, 1463, 1381, 1178, 1094, 1039, 1002, 955, 834, 768; ^{1}H NMR (400 MHz, DMSO–d_6) δ 11.84 (1H, br s,NH), 8.46 (1H, s, CH) 8.31 (1H, d, J = 2.3 Hz, CH), 7.75 (1H, d, J = 8.4 Hz, CH), 7.61 (1H, dd, J = 8.4 and 1.5 Hz, CH), 4.46 (2H, q, J = 6.9 Hz, CH_2), 4.35 (2H, q, J = 7.6 Hz, OCH_2), 3.05 (3H, s, CH_3), 1.40 (3H, t, J = 7.6 Hz, CH_3), 1.36 (3H, t, J = 6.9 Hz, CH_3); ^{13}C NMR (100 MHz, DMSO–d_6) δ 166.7, 165.2, 141.7, 140.2, 139.5, 130.0, 128.8, 124.9, 124.0, 122.7, 120.7, 114.4, 112.5, 109.4, 60.9, 60.6, 17.9, 14.3, 14.2. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{19}H_{19}BrNO_4]$ 404.0497, found 404.0492.

Ethyl 1-propionyl-9H-carbazole-3-carboxylate **(8a)**.

In a oven-dried round bottom flask, a solution of (*E*)-ethyl 3-(1*H*-indol-3-yl)acrylate **3m** (107.5 mg, 0.5 mmol) in toluene 2 mL, $Pd(OAc)_2$ (10 mol %), $Cu(OAc)_2$ (2.0 equiv) and pent-1-en-3-one **4b** (1.0 mmol) were added. The resulting reaction mixture was heated at 100 °C for 18 h. Progression of the reaction was monitored by TLC while noticing complete consumption of (*E*)-ethyl 3-(1*H*-indol-3-yl)acrylate, the reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 90/10) to give the title compound **8a** (118.0 mg, 80%) as a off-white needles, mp: 168–170 °C ; FTIR (Zn−Se ATR, cm−1) 3410, 2969, 1715, 1635, 1532, 1445, 1387, 1167, 1088, 1045, 1012, 933, 812, 758; ^{1}H NMR (400 MHz, DMSO–d_6) δ 12.12 (1H, br s, NH), 9.00 (1H, s, CH), 8.64 (1H, d, J = 1.5 Hz, CH), 8.30 (1H, d, J = 8.4 Hz, CH), 7.78 (1H, d, J = 7.6 Hz, CH), 7.47 (1H, t, J = 6.9 Hz, CH), 7.29–7.24 (1H, m, CH), 4.40(2H, q, J = 7.6 Hz, OCH_2), 3.25 (2H, q, J = 6.9 Hz, CH_2), 1.39 (6H, t, J = 6.9 Hz, $3CH_3$); ^{13}C NMR (100 MHz, DMSO–d_6) δ 201.0, 165.9, 140.1, 128.2, 127.0, 126.6, 124.6, 121.5, 120.7, 120.5, 119.6, 118.7, 112.8, 60.7, 31.5, 14.4, 8.1. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{18}H_{18}NO_3]$ 296.1287, found 296.1281.

Methyl 1-propionyl-9H-carbazole-3-carboxylate **(8b).**

In a oven-dried round bottom flask, a solution of (*E*)-methyl 3-(1*H*-indol-3-yl)acrylate **3l** (100.5 mg, 0.5 mmol) in toluene 2 mL, $Pd(OAc)_2$ (10 mol %), $Cu(OAc)_2$ (2.0 equiv) and pent-1-en-3-one **4b** (1.0 mmol) were added. The resulting reaction mixture was heated at 100 °C for 18 h. Progression of the reaction was monitored by TLC while noticing complete consumption of (*E*)-methyl 3-(1*H*-indol-3-yl)acrylate, the reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 90/10) to give the title compound **8b** (109.5 mg, 78%) as a off-white needles, mp: 196–198 °C; FTIR (Zn−Se ATR, cm−1) 3390, 2985, 1715, 1650, 1544, 1444, 1367, 1185, 1090, 1045, 1012, 956, 812, 758; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.79 (1H, br s, NH), 8.95 (1H, s, CH), 8.72 (1H, d, J = 1.5 Hz, CH), 8.13 (1H, d, J = 7.6 Hz, CH), 7.54–7.48 (2H, m, 2CH), 7.35–7.29 (1H, m, CH), 4.01 (3H, s, OCH_3), 3.24 (2H, q, J = 7.6 Hz, CH_2), 1.34–1.30 (3H, m, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.8, 167.2, 140.4, 128.7, 127.2, 127.18, 125.0, 122.2, 121.0, 120.6, 120.2, 118.2, 111.6, 52.2, 31.7, 8.3. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{17}H_{16}NO_3]$ 282.1130, found 282.1125.

Ethyl 6-methoxy-4-methyl-1-propionyl-9H-carbazole-3-carboxylate **(8c)**.

In a oven-dried round bottom flask, a solution of (*E*)-ethyl 3-(5-methoxy-1*H*-indol-3-yl)but-2-enoate **3b** (129.5 mg, 0.5 mmol) in toluene 2 mL, $Pd(OAc))_2$ (10 mol %), $Cu(OAc)_2$ (2.0 equiv) and pent-1-en-3-one **4b** (1.0 mmol) were added. The resulting reaction mixture was heated at 100 °C for 16 h. Progression of the reaction was monitored by TLC, while noticing complete consumption of (*E*)-ethyl 3-(5-methoxy-1*H*-indol-3-yl)but-2-enoate, reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. Organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 90/10) to give the title compound **8c** (132.2 mg, 78%) as a yellow needles, mp: 168–170 ^oC; FTIR (Zn−Se ATR, cm−1) 3412, 2915, 2865, 1712, 1613, 1416, 1290, 1232, 1099, 750, 660; ^1H NMR (400 MHz, DMSO–d_6) δ 11.92 (br s, 1H), 8. 47 (s, 1H), 7.72 (d, J = 9.2 Hz, 1H), 7.67 (d, J = 2.3 Hz, 1H), 7.13 (dd, J = 9.2 and 2.3 Hz, 1H), 4.34 (q, J = 6.9 Hz, 2H), 3.85 (s, 3H), 3.33 (s, 3H), 3.16 (q, J = 7.6 Hz, 2H), 1.37 (t, J = 7.6 Hz, 3H), 1.19–1.15 (m, 3H); ^{13}C NMR (100 MHz, DMSO–d_6) δ 200.6, 167.1, 153.9, 141.5, 139.4, 135.6, 129.6, 123.6, 122.4, 119.6, 116.2, 114.8, 113.3, 105.9, 60.5, 55.6, 30.8, 18.0, 14.2, 8.2. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{20}H_{22}NO_4]$ 340.1549, found 340.1543.

Ethyl 6-chloro-4-methyl-1-propionyl-9H-carbazole-3-carboxylate **(8d)**.

In a oven-dried round bottom flask, a solution of (*E*)-ethyl 3-(5-chloro-1*H*-indol-3-yl)but-2-enoate **3c** (131.5 mg, 0.5 mmol) in toluene 2 mL, $Pd(OAc))_2$ (10 mol %), $Cu(OAc)_2$ (2.0 equiv) and pent-1-en-3-one **4b** (1.0 mmol) were added. The resulting reaction mixture was heated at 100 °C for 24 h. Progression of the reaction was monitored by TLC, while noticing complete consumption of (*E*)-ethyl 3-(5-chloro-1*H*-indol-3-yl)but-2-enoate, reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. Organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 90/10) to give the title compound **8d** (130.4 mg, 76%) as a pale yellow needles, mp: 194–196 ^oC; FTIR (Zn−Se ATR, cm−1) 3420, 2925, 2855, 1702, 1691, 1452, 1289, 1212, 1092, 759, 668; ^1H NMR (400 MHz, $CDCl_3$) δ 10.88 (1H, br s, NH), 8.58 (1H, s, CH), 8.20 (1H, s, CH), 7.45 (2H, d, J = 1.4 Hz, 2CH), 4.45 (2H, q, J = 7.3 Hz, OCH_2), 3.22–3.18 (2H, m, CH_2), 3.16 (3H, s, CH_3), 1.47 (3H, t, J = 6.4 Hz, CH_3), 1.31 (3H, t, J = 7.3 Hz, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.4, 167.7, 143.2, 140.9, 138.5, 130.6, 126.4, 126.2, 124.0, 123.6, 122.8, 121.4, 116.5, 112.4, 61.1, 31.5, 18.5, 14.5, 8.3 HRMS (APCI) $[M+H]^+$ Calcd for $[C_{19}H_{19}ClNO_3]$ 344.1053, found 344.1048.

Methyl 8-(benzyloxy)-1-propionyl-9H-carbazole-3-carboxylate **(8e)**.

In a oven-dried round bottom flask, a solution of (E)-methyl 3-(7-(benzyloxy)-1H-indol-3-yl)acrylate **3s** (153.5 mg, 0.5 mmol) in toluene 2 mL, $Pd(OAc))_2$ (10 mol %), $Cu(OAc)_2$ (2.0 equiv) and pent-1-en-3-one **4b** (1.0 mmol) were added. The resulting reaction mixture was heated at 100 °C for 24 h. Progression of the reaction was monitored by TLC while noticing complete consumption of (E)-methyl 3-(7-(benzyloxy)-1H-indol-3-yl)acrylate, the reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 90/10) to give the title compound **8e** (139.3 mg, 72%) as a pale brown needles, mp: 155–157 ^oC; FTIR (Zn−Se ATR, cm−1) 3442, 2924, 2855, 1710, 1461, 1323, 1249, 1121, 992, 762; ^1H NMR (400 MHz, $CDCl_3$) δ 10.79 (1H, br s, NH), 8.91 (1H, s, CH), 8.69 (1H, s, CH), 7.70 (1H, d, J = 7.6 Hz, CH), 7.48 (2H, d, J = 7.6 Hz, 2CH), 7.42–7.38 (2H, m, 2CH), 7.36–7.32 (1H, m, CH), 7.19 (1H, t, J = 7.6 Hz, CH), 7.00 (1H, d, J = 7.6 Hz CH,), 5.26 (2H, s, OCH_2), 3.98 (3H, s, OCH_3), 3.21 (2H, q, J = 7.6 Hz, CH_2), 1.31–1.27 (3H, m, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.5, 167.1, 145.2, 140.9, 136.5, 131.0, 128.7, 128.6, 113.1, 108.7, 70.5, 52.2, 31.6, 8.2. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{24}H_{22}NO_4]$ 388.1549, found 388.1543.

1-(3-Phenyl-9H-carbazol-1-yl)propan-1-one **(8f)**.

In a oven-dried round bottom flask, a solution of (*E*)-3-styryl-1*H*-indole **3w** (109.5 mg, 0.5 mmol) in toluene 2 mL, $Pd(OAc)_2$ (10 mol %), $Cu(OAc)_2$ (2.0 equiv) and pent-1-en-3-one **4b** (1.0 mmol) were added. The resulting reaction mixture was heated at 100 °C for 24 h. Progression of the reaction was monitored by TLC while noticing complete consumption of (*E*)-3-styryl-1*H*-indole, the reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 90/10) to give the title compound **8f** (104.6 mg, 70%) as a yellow needles, mp: 145–147 ^oC; FTIR (Zn−Se ATR, cm−1) 3431, 2926, 2856, 1710, 1658, 1481, 1206, 1023, 759 ^1H NMR (400 MHz, $CDCl_3$) δ 10.58 (1H, br s, NH), 8.48 (1H, s, CH), 8.21 (1H, s, CH), 8.13 (1H, d, J = 7.6 Hz, CH), 7.71 (2H, d, J = 7.6 Hz, CH), 7.54–7.46 (4H, m, 4CH), 7.40–7.37 (1H, m, CH), 7.29 (1H, t, J = 7.6 Hz, CH), 3.24 (2H, q, J = 6.1 Hz, CH_2), 1.36–1.32 (3H, m, CH_3); ^{13}C NMR (100 MHz, DMSO–d_6) δ 201.7, 141.0, 140.5, 137.3, 130.5, 130.0, 129.0, 127.0, 126.8, 126.4, 126.1, 125.2, 123.9, 121.6, 120.5, 119.6, 119.4, 112.5, 31.2, 8.3. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{21}H_{18}NO]$ 300.1388, found 300.1385.

General Procedure and analytical data for the one pot carbazoles synthesis:

9H-Carbazole-1,3-dicarbonitrile **(9a)**.

In a oven-dried round bottom flask, a solution of 1*H*-indole **2a** (58.5 mg, 0.5 mmol) in DMF/DMSO (5:1; 2 mL), $Pd(OAc)_2$ (15 mol %), $Cu(OAc)_2$ (2.0 equiv) and acrylonitrile **4a** (2.0 mmol) were added. The resulting reaction mixture was heated at 70 °C for 24 h. Progression of the reaction was monitored by TLC while noticing complete consumption of indole, the reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were

separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate, 90/10) to give the title compound **9a** (65.1 mg, 60%) as a off-white needles, mp: 119–121 °C (65.1 mg, 60%); FTIR (Zn−Se ATR, cm−1) 3281, 2921, 2853, 2238, 2231, 1570, 1460, 1283, 1242; ^{1}H NMR (400 MHz, DMSO–d_6) δ 12.97 (1H, br s, NH), 9.02 (1H, s, CH), 8.40 (1H, d, J = 1.5 Hz, CH), 8.29 (1H, d, J = 7.6 Hz, CH), 7.67–7.62 (1H, m, CH), 7.57 (1H, t, J = 7.6 Hz, CH), 7.38–7.33 (1H, m, CH); ^{13}C NMR (100 MHz, DMSO–d_6) δ 141.0, 129.8, 128.3, 124.3, 122.6, 121.4, 121.2, 120.6, 118.3, 115.8, 112.3, 100.9, 94.2, 87.1. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{14}H_8N_3]$ 218.0718, found 218.0720.

6-Methyl-9H-carbazole-1,3-dicarbonitrile (**9b**).

In a oven-dried round bottom flask, a solution of 5-methyl-1*H*-indole **2f** (65.5 mg, 0.5 mmol) in DMF/DMSO (5:1; 2 mL), $Pd(OAc)_2$ (15 mol %), $Cu(OAc)_2$ (2.0 equiv) and acrylonitrile **4a** (2.0 mmol) were added. The resulting reaction mixture was heated at 70 °C for 24 h. Progression of the reaction was monitored by TLC while noticing complete consumption of 5-methyl-1*H*-indole, the reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 90/10) to give the title compound **9b** (66.9 mg, 58%) as a yellow needles, mp: 215–217 °C (66.9 mg, 58%); FTIR (Zn−Se ATR, cm−1) 3271, 2901, 2833, 2232, 2214, 1560, 1434, 1242; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.65 (1H, br s, NH), 8.92 (1H, s, CH), 8.34 (1H, s, CH), 8.07 (1H, s, CH), 7.51 (1H, d, J = 8.4Hz, CH), 7.39 (1H, d, J = 8.4 Hz, CH), 2.47 (3H, s, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 141.7, 139.0, 133.0, 130.3, 129.6, 129.5, 124.1, 121.4, 121.0, 118.9, 115.8, 112.0, 100.7, 94.1, 21.1 HRMS (ESI) $[M+Na]^+$ Calcd for $[C_{15}H_9N_3Na]$ 254.0694, found 254.0689.

8-Methyl-9H-carbazole-1,3-dicarbonitrile **(9c).**

In a oven-dried round bottom flask, a solution of 7-methyl-1*H*-indole **2g** (65.5 mg, 0.5 mmol) in DMF/DMSO (5:1; 2 mL), $Pd(OAc)_2$ (15 mol %), $Cu(OAc)_2$ (2.0 equiv) and acrylonitrile **4a** (2.0 mmol) were added. The resulting reaction mixture was heated at 70 °C for 24 h. Progression of the reaction was monitored by TLC, while noticing complete consumption of 7-methyl-1*H*-indole, reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 90/10) to give the title compound **9c** (63.5 mg, 55%) as a brown needles, mp: 221–223 °C (63.5 mg, 55%); FTIR (Zn−Se ATR, cm−1) 3271, 2924, 2843, 2228, 2212, 1460, 1283, 1232, 778; ^{1}H NMR (400 MHz, DMSO–d_6) δ 12.57 (1H, br s, NH), 8.99 (1H, s, CH), 8.37 (1H, s, CH), 8.15–8.10 (1H, m, CH), 7.36 (1H, d, J = 7.6 Hz, CH), 7.24 (1H, d J = 7.6 Hz, CH), 2.61 (3H, s, CH_3); ^{13}C NMR (100 MHz, DMSO–d_6) δ 141.4, 133.6, 129.6, 129.0, 126.4, 124.9, 123.2, 122.5, 121.4, 121.2, 120.7, 118.6, 101.0, 94.4, 17.3. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{15}H_{10}N_3]$ 232.0875, found 232.0875.

Dimethyl 6-chloro-9H-carbazole-1,3-dicarboxylate **(9d)**.

In a oven-dried round bottom flask, a solution of 5-chloro-1*H*-indole **2c** (75.5 mg, 0.5 mmol) in DMF/DMSO (5:1; 2 mL), $Pd(OAc)_2$ (15 mol %), $Cu(OAc)_2$ (2.0 equiv) and methyl acrylate **1e** (2.0 mmol) were added. The resulting reaction mixture was heated at 70 °C for 24 h. Progression of the reaction was monitored by TLC while noticing complete consumption of 5-chloro-1*H*-indole, reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate ; 90/10) to give the title compound **9d** (103.0 mg, 65%) as a yellow needles, mp: 240–242 °C; FTIR (Zn−Se ATR, cm−1) 3381, 2922, 2856, 1713, 1572, 1461, 1282, 1242, 773; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.11 (1H, br s, NH), 8.87 (1H, d, J = 1.4 Hz, CH), 8.76 (1H, d, J = 1.8 Hz, CH), 8.07 (1H, s, CH), 7.45 (2H, d, J = 1.4 Hz, 2CH), 4.04 (3H, s, OCH_3), 3.99 (3H, s, OCH_3); ^{13}C NMR (100 MHz, , $CDCl_3$) δ 167.1, 166.8, 142.7, 138.4, 129.6, 127.4, 127.17, 126.5, 123.8, 123.7, 121.1, 120.5, 112.4, 111.6, 52.3, 52.2. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{16}H_{13}ClNO_4]$ 318.0533, found 318.0528.

Ethyl 1-cyano-9-(2-cyanoethyl)-6-methoxy-4-methyl-9H-carbazole-3-carboxylate **(10a)**

In a oven-dried round bottom flask, a solution of (*E*)-ethyl 3-(5-methoxy-1*H*-indol-3-yl)but-2-enoate **3b** (129.5 mg, 0.5 mmol) in DMF/DMSO (5:1; 2 mL), $Pd(OAc)_2$ (15 mol %), $Cu(OAc)_2$ (2.0 equiv) and acrylonitrile **4a** (2.0 mmol) were added. The resulting reaction mixture was heated at 70 °C for 24 h. Progression of the reaction was monitored by TLC while noticing complete consumption of (*E*)-ethyl 3-(5-methoxy-1*H*-indol-3-yl)but-2-enoate, reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 90/10) to give the title compound **10a** (131.7 mg, 73%) as a pale yellow needles, mp: 183–185 °C; FTIR (Zn−Se ATR, cm−1) 2924, 2850, 2232, 2228, 1465, 1268, 1226, 751; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31(1H, d, J = 2.3 Hz, CH), 7.75 (1H, d, J = 2.3 Hz, CH), 7.51–7.49 (1H, m, CH), 7.28–7.23 (1H, m, CH), 4.99 (2H ,q, J = 6.1 Hz, OCH_3), 4.44–4.39 (2H, m, NCH_2), 3.94 (3H, s, OCH_3), 3.15 (3H, s, CH_3), 3.03–2.99 (2H, m, CH_2), 1.47–1.43 (3H, m, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 155.3, 142.9, 139.6, 135.3, 134.5, 124.5, 123.7, 122.4, 117.9, 116.8, 115.3, 109.6, 107.8, 89.8, 61.3, 56.1, 39.3, 18.8, 18.2, 14.3. HRMS (ESI) $[M+H]^+$ Calcd for $[C_{21}H_{20}N_3O_3]$ 362.1505, found 362.1499.

9-(2-Cyanoetshyl)-6-nitro-9H-carbazole-1,3-dicarbonitrile **(10b)**. In a oven-dried round bottom flask, a solution of 5-nitro-1*H*-indole **2h** (131.0 mg, 0.5 mmol) in DMF/DMSO (5:1; 2 mL), $Pd(OAc)_2$ (15 mol %), $Cu(OAc)_2$ (2.0 equiv) and acrylonitrile **4a** (2.0 mmol) were added. The resulting reaction mixture was heated at 70 °C for 24 h. Progression of the reaction was

monitored by TLC while noticing complete consumption of 5-nitro-1*H*-indole, the reaction was brought to room temperature. The additional amount of acrylate also added if required for complete conversion. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL) and then filtered through a plug of celite. The layers were separated, and the organic layer was washed with aqueous saturated brine solution, dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel (hexane: ethylacetate; 90/10) to give the title compound **10b** (70.8 mg, 45%) as a brown crystal, mp 106−108 °C; (70.8 mg, 45%), FTIR (Zn−Se ATR, cm−1) 2914, 2847, 2223, 2223, 1456, 1245, 1223, 764; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (1H, s, CH), 8.16 (1H, d, J = 9.2 Hz, CH), 7.38−7.33(2H, m, CH), 6.76 (1H, s, CH), 4.53−4.50 (2H, m, NCH_2), 2.90−2.87 (2H, m, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.1, 138.2, 130.6, 130.4, 128.2, 118.6, 118.5, 117.9, 117.8, 116.7, 108.7, 108.6, 105.5, 105.4, 42.4, 19.3; HRMS (ESI) Calcd for $[C_{17}H_9N_5O_2]$ requires $[M]^+$ 315.0756 found 315.0787.

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(16)Crystallographic data of compounds **5c** and **6b** have been deposited at the Cambridge Crystallographic data Centre as a CIF deposit with file number **1498753** and **1498752** respectively. Copies of these data can be obtained free of charge on application to CCDC. Email: deposit@ccdc.cam.ac.uk.

Highlights

1. A regioselective synthesis of highly functionalized carbazoles by using Pd(II)-Cu bimetallic system. The sterically hindered substrate bearing electron-rich and electron-deficient styrylindoles with alkenes, were examined for the synthesises of the tri- and di-substituted carbazoles.
2. The results of the designed protocol suggested that the C-H activation is preferred over [4+2] cycloaddition.
3. The designed one-pot strategy was also successful in providing the tricyclic N-heterocycle.
4. *N*-Protected carbazoles were prepared by double and triple C-H activation followed by concomitant Michael addition.
5. The C-H activation strategy for the synthesis of carbazole has been well supported by the proposed mechanistic pathway via di-Heck intermediate.