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An organocatalytic highly efficient approach to the direct synthesis of substituted carbazoles in water†

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A simple, mild, green, catalytic and general procedure for the direct synthesis of highly functionalized 1-methoxycarbonyl-2-aryl/alkyl-3-nitro-9*H*-carbazoles has been achieved in water medium *via* a one-pot domino Michael–Henry/aromatization reaction of methyl 2-(3-formyl-1*H*-indol-2-yl)acetates with aryl/alky-substituted β-nitroolefins under air using DABCO (30 mol%) as an organocatalyst. In addition, the bench scale synthesis can be performed without using toxic organic solvents and a biologically important new fused carbazole has been prepared.

Introduction

The development of an efficient and sustainable protocol for the construction of a functionalized carbazole framework has been a key research area in recent years because this moiety is found in a variety of active drug candidates and natural products.[1,2] Its several synthetic analogues display remarkable biological activities as described profusely in the literature.[2] Apart from this, they have many useful applications in materials science,[3] *e.g.* in organic light emitting diodes (OLED), photovoltaic cells, field effect transistors, *etc.* Owing to their several applications in various fields, a large number of classical and modern techniques have been developed for their synthesis.[1–3] Among them, the most common routes involve the palladium[4] catalyst, namely, oxidative cyclodehydrogenation of diarylamines, annulations of arynes with 2-haloacetamides, the domino N–H/C–H bond activation reaction of anilines with dihaloarenes, *etc.* Besides, other transition metal (Cu, Pt, Au, Rh, *etc.*)[5] mediated syntheses of carbazole derivatives have been also well documented. However, because of potential environmental concerns about metal catalysts in general, organocatalysis has gained much recognition in the context of green chemistry.

In this connection, a few metal free mediated one-pot syntheses of carbazoles have been successfully developed,[6] which include the hypervalent iodine mediated intramolecular oxidative C–N bond formation of N-substituted amidobiphenyls, iodine mediated cascade cyclization of *N*,*N*-dimethyl-2-[2-(2-ethynylphenyl)-ethynyl]anilines, and HCl salt of arylhydrazine with cyclohexanone at 140 °C. However, these protocols, although metal free, are not much appreciated from an environmental point of view. A primary reason is that they often suffer from one or more disadvantages such as the use of volatile organic solvents, stoichiometric amounts of strong oxidants, longer reaction periods, higher temperatures, unsatisfactory yields, *etc.* To overcome these limitations, the development of a one-pot metal free based catalytic system for the synthesis of substituted carbazoles in water under aerobic conditions is still of great interest for synthetic organic chemists.

In recent years, the organocatalytic domino[7] Michael–Henry[8] reaction has been one of the most straightforward routes for assembling a diverse range of multifaceted architectures in a highly practical manner. Such a process is likely to have notable advantages as compared to a conventional step-by-step operation because of potential structural alterations, reduction in the number of synthetic steps, minimizing the by-products, avoiding the tedious extraction and purification steps, *etc.* As part of our continuing interest in the development of environmentally friendly protocols in organic transformations as well as metal free mediated based catalytic systems for the synthesis of N-heterocycles,[9] we have reported on the one-pot domino Michael–Henry reaction for the synthesis of highly functionalized tetrahydrocarbazoles in THF medium using DABCO as a catalyst.[9d] Against this background, we envisaged that this domino route is expected to be useful for assembling the benzene ring of the carbazole moiety under mild conditions (Scheme 1). Herein, we report a mild, simple, catalytic and robust procedure for the synthesis of highly functionalized carbazoles through a one-pot domino Michael–Henry/aromatization reaction of aryl/alkyl-substituted *trans*-β-nitroolefins with methyl 2-(3-formyl-1*H*-indol-2-yl)acetates in water under air using DABCO as an organocatalyst.

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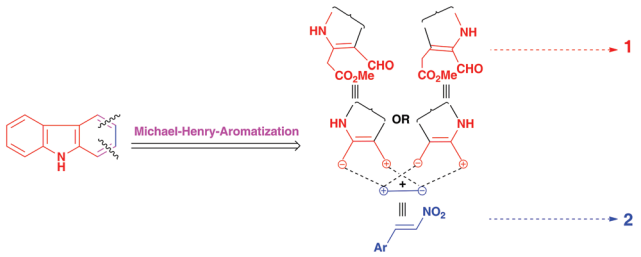


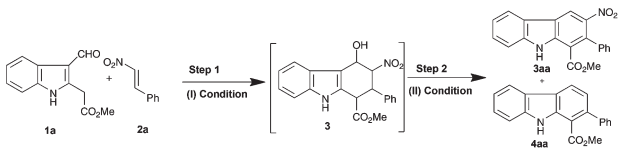
Scheme 1 Retro-synthetic path.

Results and discussion

Initially, to obtain the 1-methoxycarbonyl-2-phenyl-3-nitro-9*H*-carbazole (**3aa**), we carried out the reaction between methyl 2-(3-formyl-1*H*-indol-2-yl)acetate **1a** and *trans*-β-nitrostyrene **2a** at room temperature in THF medium for 7 h using 10 mol% loading of the catalyst DABCO, followed by aromatization using aqueous 8 N HCl (entry 1, Table 1). This two-step sequence provided the desired carbazole **3aa** in moderate 60% yield along with the unexpected denitrated carbazole **4aa** in low 27% yield. The products were fully characterized by their spectroscopic data (^{1}H and ^{13}C NMR, HRMS). In order to improve the yield of the desired compound **3aa** and suppress the formation of **4aa**, we tested common organic solvents such as dioxane, MeOH and EtOH for this two-step process. All these cases led to moderate yields of targeted product **3aa** (55–58%, entries 2–4) and an unavoidable side product **4aa** (25–33%, entries 2–4). Next, our efforts were focused on optimization of the second step by treatment of different organic acids such as TFA and AcOH under various conditions (entries 5–8). In all these cases, the results were unsatisfactory. Moreover, there was no substantial beneficial effect observed when a DDQ in acetic acid was used as an oxidant (entry 9). At this juncture, we realized that denitrated product **4aa** was formed during aromatization (step **2**) in the presence of an acid. As such, we surmised that this problem might be resolved if the aromatization step would be conducted in a basic medium under air. With this understanding, the reaction was performed at 50 °C in THF medium in the presence of DABCO (10 mol%). Surprisingly, after 30 h, we found only the desired carbazole **3aa** in 57% yield (entry 10). From the green chemistry standpoint, the use of water in the reaction medium is an inevitable choice for synthetic organic chemists.[10] In this regard, we performed the reaction in water instead of THF at 50 °C; pleasantly, after 24 h, very good results were observed (63%, **3a**, entry 11). For this catalyst, on further increasing the reaction temperature from 50 °C to 70 °C as well as the catalyst loading from 10 mol% to 30 mol%, the yield improved significantly from 63% to 97% (entries 13) in a shorter time. Next, we investigated the effects of bases on this reaction. The results showed that DABCO was a superior catalyst as compared to Et_3N and DBU (entries 14 and 15) in terms of reactivity under identical conditions. In particular, no significant positive effect was observed when the reaction was carried out in the presence of oxygen instead of air (entry 16).

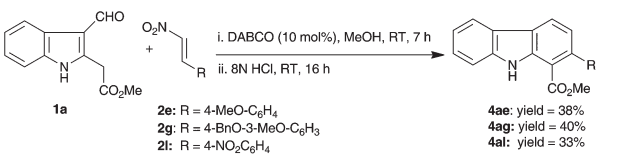
Due to the unexpected formation of denitrated carbazole **4aa**, we were curious to study the general trends of this phenomenon which may further help us in establishing the reaction mechanism. In this line, a series of reactions were carried out between aryl-substituted β-nitrostyrenes (**2e**, **2g** and **2l**) and **1a** in MeOH medium under air at room temperature using a catalytic amount of DABCO (10 mol%) for 7 h followed by 8 N HCl as a two-step sequence. In all these cases, similar kinds of denitrated carbazoles (**4ae–4al**) were obtained in poor yields (33–40%) as shown in Scheme 2.

Table 1 Optimization of the reaction conditions

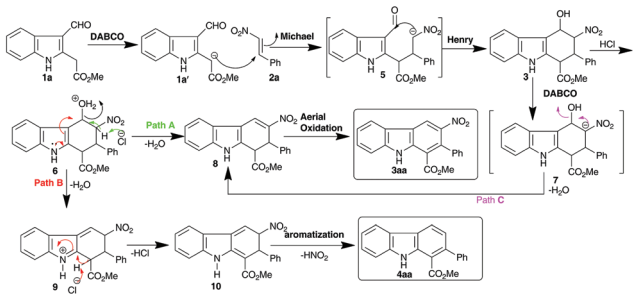


Entry	Step	Conditions	3aa : 4aa	Yield[g] (%) 3aa	4aa
1	I[a] II[b]	THF, DABCO, RT, 7 h 8 N HCl, RT, 16 h	67 : 33	60	27
2	I[a] II[b]	Dioxane, DABCO, RT, 7 h 8 N HCl, RT, 16 h	68 : 28	57	25
3	I[a] II[b]	EtOH, DABCO, 7 h, RT 8 N HCl, RT, 16 h	65 : 35	58	28
4	I[a] II[b]	MeOH, DABCO, RT, 7 h 8 N HCl, RT, 16 h	60 : 40	55	33
5	I[a] II[c]	THF, DABCO, RT, 7 h TFA, RT, 16 h	55 : 45	50	39
6	I[a] II[c]	THF, DABCO, RT, 7 h AcOH, RT, 20 h	—	<7	
7	I[a] II[c]	THF, DABCO, RT, 7 h AcOH, 50 °C, 20 h	63 : 37	33	18
8	I[a] II[c]	DCM, DABCO, RT, 7 h AcOH, 50 °C, 20 h	55 : 35	28	19
9	I[a] II[d]	DCM, DABCO, RT, 7 h AcOH, DDQ, 50 °C, 10 h	68 : 32	60	22
10	I[a]	THF, DABCO, 50 °C, 30 h	100 : 0	57	—
11	I[a]	H_2O, DABCO, 50 °C, 24 h	100 : 0	63	—
12	I[e]	H_2O, DABCO, 70 °C, 14 h	100 : 0	80	—
13	I[f]	H_2O, DABCO, 70 °C, 10 h	100 : 0	97	—
14	I[f]	H_2O, Et_3N, 70 °C, 10 h	100 : 0	41	—
15	I[f]	H_2O, DBU, 70 °C, 10 h	100 : 0	88	—
16	I[h]	H_2O, DABCO, 70 °C, 10 h	100 : 0	96	—

[a] Unless otherwise mentioned, all the reactions were performed with compound **1a** (0.25 mmol), **2a** (0.3 mmol) and catalyst (10 mol%) in specified solvents (1.0 mL) and temperatures under air. [b] 8 N HCl (4.0 mL) was used. [c] Acid (1.0 ml) was used. [d] Glacial AcOH (0.5 mL) and DDQ (1.5 equiv.) were used. [e] 20 mol% DABCO was used. [f] 30 mol% catalyst. [g] The products **3aa** and **4aa** were isolated after column chromatography. [h] The reaction was carried out under an O_2 atmosphere.



Scheme 2 Synthesis of 1-methoxycarbonyl-2-aryl-9*H*-carbazoles (**4ae–4al**).



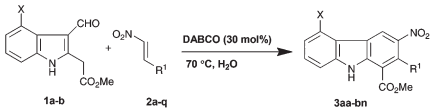
Scheme 3 Proposed mechanism for the formation of compounds **3aa** and **4aa**.

On the basis of the above results, we propose the following probable mechanism for the formation of carbazoles **3aa** and **4aa**. In the first step, the tetrahydrocarbazole **3** is formed *via* a domino Michael–Henry reaction of **1a** with **2a** in the presence of DABCO as reported earlier.[9d] Next, an intermediate **8** is generated by a protonation of the secondary hydroxyl group of **3** by an acid (HCl) followed by dehydration as depicted in path **A** (Scheme 3). Finally, the desired carbazole **3aa** is formed *via* an aerial oxidation of compound **8**. Alternatively, the nitrogen lone pair pushes out the protonated hydroxyl group to form an intermediate **9** as follows in path **B**. The latter undergoes imine–enamine tautomerization to give **10** and subsequently eliminates nitrous acid to form **4aa**. On the other hand, the intermediate **8** can be generated from an anionic intermediate **7** *via* elimination of water in path **C** which upon aerial oxidation leads to **3aa**.

To understand the scope and limitations of this one-pot domino Michael–Henry/aromatization reaction, we studied a group of structurally varied *trans*-aryl/alkyl-substituted β-nitroolefins (**2a–q**) with methyl 2-(3-formyl-1*H*-indol-2-yl)-acetates **1a–b** using 30 mol% loading of DABCO as a catalyst under our standard conditions. The desired carbazoles were isolated by either the column chromatography method or the direct filtration technique (details in the Experimental section). The results are compiled in Table 2. As is evident from Table 2, both electron-donating (Me, OMe and OBn, entries 2–7) and electron-withdrawing (Cl, Br, NO_2 and CN, entries 8–13) substituents on the aromatic nucleus of aryl-substituted β-nitroolefins reacted smoothly with substrate **1a**, leading to the formation of 1-methoxycarbonyl-2-aryl-3-nitro-9*H*-carbazoles (entries 2–13) in good to excellent yields (88–97%, **3ab–3am**, method **B**). During our investigations, we had noticed that electron withdrawing groups on aromatic rings reacted slightly faster than electron donating ones (10 h *vs*. 20 h). Hetero-aryl substituted-β-nitroolefins (**2n** and **2o**, entries 14 and 15) were also good Michael-acceptors for these reactions, resulting in excellent 88% and 91% yields of the corresponding products **3an** and **3ao** respectively. The alkyl substituted β-nitroolefins are well known to be poor Michael acceptors. Gratifyingly, under our conditions, **2p** and **2q** ran smoothly with substrate **1a**, providing the anticipated carbazoles (**3ap** and **3aq**) in high yields (82–83%, method **B**, entries 16 and 17). Similarly, a sterically challenging methyl 2-(3-formyl-4-iodo-1*H*-indol-2yl)acetate (**1b**) underwent clean and complete conversions of several aryl and hetero-aryl substituted *trans*-β-nitroolefins by this protocol to provide the corresponding anticipated products in excellent yields (92–95%, method **B**, entries 18–21). It is noteworthy that even though direct filtration (method **A**) resulted in slightly (5–12%) lower chemical yields of final products (81–89% *vs*. 88–97%, entries 1–7, Table 2) as compared to the column chromatography method, the former method offers superior eco-sustainability. A wide range of sensitive functional groups, namely OMe, OBn, Cl, Br, I, CN, NO_2, furyl, and thiophenyl, are well tolerable under these reaction conditions. Thus, a possibility of a suitable therapeutic target may be achieved by synthetic modifications of the above functional groups depending on the requirements.

Besides, the bench-scale preparation of 1-methoxycarbonyl-2-phenyl-3-nitro-9*H*-carbazole (**3aa**) was performed under our best conditions. To a stirred heterogeneous reaction mixture of starting material **1a** (10.0 mmol) and *trans*-β-nitrostyrene (**2a**, 11.0 mmol) in water (30.0 mL) was added DABCO (3.0 mmol) at 70 °C for 14 h (monitored by TLC). After that, the solid carbazole **3aa** was precipitated out which was easily isolated in 92% yield by simple filtration followed by washing with a small amount of EtOH. This exciting result reveals that our

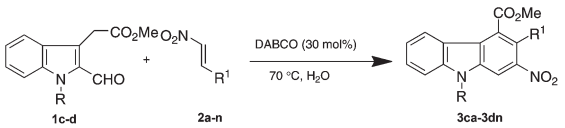
Table 2 DABCO catalyzed one-pot synthesis of 1-methoxycarbonyl-2-aryl/alkyl-3-nitro-9*H*-carbazoles (**3aa–3bn**)[a]



Entry	R^1	X	*T* (h)	Product	Yield[b] (%)
1	C_6H_5	H	10	**3aa**	97 (89)[c]
2	3-Me-C_6H_4	H	12	**3ab**	93 (81)[c]
3	4-Me-C_6H_4	H	12	**3ac**	90 (82)[c]
4	2-MeO-C_6H_4	H	20	**3ad**	92 (85)[c]
5	4-MeO-C_6H_4	H	20	**3ae**	89 (79)[c]
6	2,5-$(OMe)_2$-C_6H_3	H	20	**3af**	88 (83)[c]
7	4-BnO-3-MeO-C_6H_3	H	20	**3ag**	93 (81)[c]
8	2-Cl-C_6H_4	H	10	**3ah**	91
9	4-Cl-C_6H_4	H	10	**3ai**	96
10	4-Br-C_6H_4	H	10	**3aj**	97 (87)[c]
11	2-NO_2-C_6H_4	H	10	**3ak**	96 (86)[c]
12	4-NO_2-C_6H_4	H	10	**3al**	93 (88)[c]
13	4-CN-C_6H_4	H	13	**3am**	96 (84)[c]
14	2-Furyl	H	16	**3an**	88
15	2-Thiophenyl	H	16	**3ao**	91
16	$PhCH_2CH_2$	H	16	**3ap**	83
17	$MeCH_2CH_2$	H	16	**3aq**	82
18	C_6H_5	I	12	**3ba**	93 (82)[c]
19	4-Cl-C_6H_4	I	12	**3bi**	95 (86)[c]
20	4-BnO-3-MeO-C_6H_3	I	12	**3bg**	92
21	2-Furyl	I	15	**3bn**	93

[a] Unless otherwise specified, all the reactions were carried out with **1a–b** (0.25 mmol), substituted *trans*-β-nitroolefins (**2a–q**, 0.3 mmol) and DABCO (30 mol%) at 70 °C in water (1.0 mL). [b] Isolated yield after column chromatography (method **B**). [c] In parentheses, isolated yield after filtration (method **A**).

Table 3 DABCO catalyzed one-pot synthesis of 3-aryl-4-methoxycarbonyl-2-nitro-9*H*-carbazole derivatives (**3ca–3dn**)[a]



Entry	R^1	R	*T* (h)	Product	Yield[b] (%)
1	C_6H_5	H	11	**3ca**	87 (81)[c]
2	C_6H_5	Bn	24	**3da**	92
3	4-Me-C_6H_4	Bn	24	**3dc**	90
4	4-MeO-C_6H_4	Bn	36	**3de**	87
5	4-BnO-3-OMe-C_6H_3	Bn	36	**3dg**	89
6	2-Cl-C_6H_4	Bn	22	**3dh**	91
7	4-Br-C_6H_4	Bn	22	**3dj**	90
8	2-$NO_2C_6H_4$	Bn	24	**3dk**	87
9	2-Furyl	Bn	26	**3dn**	86

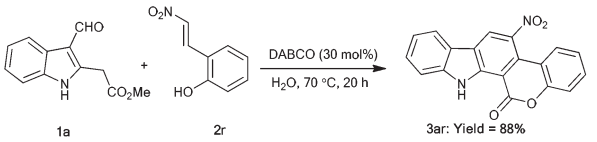
[a] Unless otherwise specified, all reactions were carried out with **1c–d** (0.25 mmol), substituted *trans*-β-nitroolefins (**2a–n**, 0.3 mmol) and DABCO (30 mol%) at 70 °C in water (1.0 mL). [b] Yield of the pure product after column chromatography (method **B**). [c] In parentheses, isolated yield after filtration (method **A**).

present conditions can be applied to milligram to gram scale synthesis. We believe that this method provides a practical alternative to existing methods.

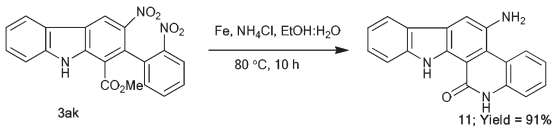
Next we performed the reaction between methyl 2-(2-formyl-1*H*-indol-3-yl)acetate **1c** (reverse regioisomer of **1a**) and **2a** under our optimal conditions. Gratifyingly, after 11 h, a high yield (87%, method **B**) of the desired 3-phenyl-4-methoxycarbonyl-2-nitro-9*H*-carbazole (**3ca**) was isolated (entry 1, Table 3). Even though the substrate **1c** was witnessed to be a good Michael donor, its synthesis is rather difficult. Therefore, we studied further *N*-benzyl protected methyl 2-(2-formyl-1*H*-indol-3-yl)acetate **1d** with various aryl/hetero-substituted β-nitroolefins (**2a–2n**). In all these cases, the corresponding anticipated carbazoles (**3da–3dn**) were obtained in high to excellent yields (86–92%, entries 2–9, Table 3). It is noteworthy that *N*-benzyl protected indole derivative **1d** is less reactive than its unprotected version **1c** towards *trans*-β-nitrostyrene under identical conditions (24 h *vs*. 11 h, entries 1 and 2). Similarly, various sensitive functional groups such as OMe, Cl, Br, furyl, NO_2, Bn, *etc*. are compatible under the present conditions.

The development of a simple route for the synthesis of a fused carbazole scaffold remains a challenging task for synthetic organic chemists. In this context, the current protocol can be applied to one-pot synthesis of 7-nitrochromeno-[3,4-*a*]carbazol-1(13*H*)-one (**3ar**) in 88% yield *via* a Michael–Henry/aromatization reaction of **1a** with **2r** under our standard reaction conditions (Scheme 4).

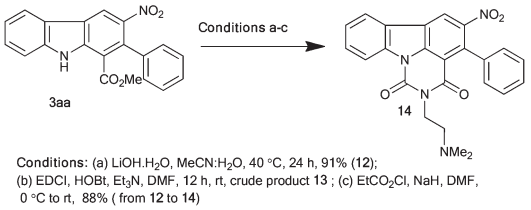
Next, we extended compound **3ak** into a biologically important[11] quinolinone fused carbazole derivative **11** *via* a reduction of nitro to amine using Fe–NH_4Cl in aqueous ethanol under refluxing conditions for 10 h followed by intramolecular cyclization as shown in Scheme 5.



Scheme 4 Synthesis of pentacyclic coumarin fused carbazole derivative (**3ar**).



Scheme 5 Synthesis of quinolinone fused carbazole derivative.



Scheme 6 Synthesis of pyrimidocarbazole derivative **14**.

Finally, we used compound **3aa** for the synthesis of biologically significant (topoisomerase II inhibitors[12]) pyrimidocarbazole derivative **14** which was obtained in excellent 88% yield from **12** (two steps) as shown in Scheme 6.

Experimental

All reactions were carried out under air and monitored by TLC using Merck 60 F_{254} precoated silica gel plates (0.25 mm thickness) and the products were visualized by UV detection. Flash chromatography was carried out with silica gel (200–300 mesh). ^1H and ^{13}C NMR spectra were recorded using a Bruker Avance (III) 400 MHz spectrometer. High resolution mass spectral analyses (HRMS) were carried out using ESI-TOF-MS. All the starting materials and catalysts were either synthesized by literature known procedures or purchased from commercial sources.

Representative experimental procedure for the synthesis of 1-methoxycarbonyl-2-phenyl-3-nitro-9*H*-carbazole (3aa)

Method A: A heterogeneous mixture of methyl 2-(3-formyl-1*H*-indol-2-yl)acetate (**1a**, 54.3 mg, 0.25 mmol), *trans*-β-nitrostyrene (**2a**, 44.7 mg, 0.3 mmol) and DABCO (8.5 mg, 0.075 mmol) in water (1.0 mL) was heated at 70 °C under air for 10 h. The progress of the reaction mixture was monitored by TLC. After completion of the reaction, the solid product was isolated by filtration, washed with water, cold ethanol and dried under reduced pressure to provide the desired carbazole **3aa** (89%). The product was characterized by its spectroscopic data (^1H and ^{13}C NMR, HRMS).

Method B: A heterogeneous mixture of methyl 2-(3-formyl-1*H*-indol-2-yl)acetates (54.3 mg, 0.25 mmol), *trans*-β-nitrostyrene (44.7 mg, 0.3 mmol) and DABCO (8.5 mg, 0.075 mmol) in water (1.0 mL) was heated at 70 °C under air for 10 h (monitored by TLC). After completion of the reaction, the water was removed by decantation. The crude product was purified by column chromatography over silica gel to yield the desired carbazole **3aa** (97%).

All known and unknown compounds in Tables 2 and 3 were fully characterized by their spectroscopic data (^{1}H and ^{13}C NMR, HMRS).

1-Methoxycarbonyl-2-phenyl-3-nitro-9*H*-carbazole (3aa). Yellowish solid; mp 214–216 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.94 (s, 1H), 8.65 (s, 1H), 8.05 (d, J = 7.76 Hz, 1H), 7.50–7.48 (m, 2H), 7.35–7.28 (m, 4H), 7.22–7.19 (m, 2H), 3.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 143.7, 141.4, 140.6, 137.0, 135.4, 128.5, 128.2, 128.0, 127.8, 123.3, 122.2, 121.4, 121.0, 120.1, 112.7, 111.8, 52.2; HRMS (ESI) m/z calcd for $C_{20}H_{14}N_2O_4[M + Na]^+$ 369.0851; Found 369.0846.

1-Methoxycarbonyl-2-phenyl-9*H*-carbazole (4aa). Yellowish solid; mp 96–98 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.75 (br s, 1H), 8.12 (dd, J = 0.8, 8.0 Hz, 1H), 8.01 (dd, J = 0.8, 8.0 Hz, 1H), 7.44–7.27 (m, 7H), 7.21–7.16 (m, 1H), 7.11 (d, J = 8.0 Hz, 1H), 3.55 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.9, 141.4, 141.0, 139.6, 138.9, 127.8, 126.6, 125.8, 125.5, 122.7, 122.6, 121.4, 119.3, 118.9, 110.1, 109.9, 50.5; HRMS (ESI) m/z calcd for $C_{20}H_{15}NO_2[M + Na]^+$ 324.0095; Found 324.1026.

1-Methoxycarbonyl-2-(4-methoxyphenyl)-9*H*-carbazole (4ae). Yellow solid; mp 122 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 8.19 (d, J = 8.0 Hz, 1H), 8.09 (d, J = 8.0 Hz, 1H), 7.45–7.54 (m, 2H), 7.28–7.32 (m, 3H), 7.18–7.19 (m, 1H), 6.95–6.97 (m, 2H), 3.88 (s, 3H), 3.68 9 s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.0, 158.7, 149.7, 141.7, 140.6, 139.9, 135.3, 129.9, 126.4, 125.4, 123.7, 123.3, 122.6, 122.5, 120.3, 119.9, 113.2, 111.0, 55.3, 51.6; HRMS (ESI) m/z calcd for $C_{21}H_{17}NO_3[M + Na]^+$ 354.1101; Found 354.1103.

1-Methoxycarbonyl-2-(4-benzyloxy-3-methoxyphenyl)-9*H*-carbazole (4ag). Yellow solid; mp 128 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.78 (s, 1H), 8.18 (d, J = 8.0 Hz, 1H), 8.09 (d, J = 7.6 Hz, 1H), 7.45–7.52 (m, 3H), 7.37–7.41 (m, 2H), 7.28–7.33 (m, 2H), 7.20 (d, J = 8.0 Hz, 1H), 6.93–6.94 (m, 2H), 6.74–6.87 (m, 1H), 5.23 (s, 2H), 3.92 (s, 3H), 3.64 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 149.0, 147.3, 141.6, 140.6, 139.9, 137.2, 136.3, 128.5, 127.9, 127.4, 126.5, 123.6, 123.5, 122.5, 122.4, 121.2, 120.3, 120.0, 113.6, 113.1, 111.1, 111.0, 71.2, 56.1, 51.6; HRMS (ESI) m/z calcd for $C_{28}H_{23}NO_4[M + Na]^+$ 460.1519; Found 460.1514.

1-Methoxycarbonyl-2-(4-nitrophenyl)-9*H*-carbazole (4al). Yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.94 (s, 1H), 8.25–8.29 (m, 3H), 8.12 (d, J = 8.0 Hz, 1H), 7.50–7.56 (m, 4H), 7.30–7.33 (m, 1H), 7.12 (d, J = 7.6 Hz, 1H), 3.67 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.9, 150.2, 146.8, 140.7, 140.1, 139.5, 129.7, 127.1, 124.8, 124.1, 122.9, 122.2, 121.8, 120.6, 120.4, 111.2, 110.3, 51.8; HRMS (ESI) m/z calcd for $C_{20}H_{14}N_2O_4$-$[M + Na]^+$ 369.0846; Found 369.0875.

1-Methoxycarbonyl-2-(3-methylphenyl)-3-nitro-9*H*-carbazole (3ab). White powder; mp 196–198 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.96 (s, 1H, 8.71 (s, 1H), 8.13 (d, J = 8.0 Hz, 1H), 7.56–7.57 (m, 2H), 7.35–7.39 (m, 1H), 7.27–7.31 (m, 1H), 7.19–7.21 (m, 1H), 7.08–7.10 (m, 2H), 3.57 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 143.8, 141.3, 140.6, 137.3, 136.8, 135.5, 129.0, 128.6, 128.1, 127.6, 125.7, 123.1, 122.2, 121.4, 121.0, 120.0, 112.8, 111.7, 52.1, 21.4; HRMS (ESI) m/z calcd for $C_{21}H_{16}N_2O_4[M + Na]^+$ 383.1008; Found 383.1002.

1-Methoxycarbonyl-2-(4-methylphenyl)-3-nitro-9*H*-carbazole (3ac). White solid; mp 219–221 °C; ^{1}H NMR (400 MHz, $CDCl_3$) 9.95 (s, 1H), 8.68 (s, 1H), 8.13–8.11 (m, 1H), 7.57–7.54 (m, 2H), 7.39–7.35 (m, 1H), 7.23–7.16 (m, 4H), 3.59 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 144.0, 141.3, 140.6, 137.5, 135.4, 133.9, 128.6, 128.4, 128.1, 123.1, 122.2, 121.3, 121.0, 119.9, 112.8, 111.7, 52.2, 21.4; HRMS (ESI) m/z calcd for $C_{21}H_{16}N_2O_4[M + Na]^+$ 383.1008; Found 383.1002.

1-Methoxycarbonyl-2-(2-methoxyphenyl)-3-nitro-9*H*-carbazole (3ad). Light yellowish solid; mp 203–205 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.96 (s, 1H), 8.78 (s, 1H), 8.12 (d, J = 7.6 Hz, 1H), 7.52–7.55 (m, 2H), 7.33–7.40 (m, 2H), 7.08–7.11 (m, 1H), 6.96–7.03 (m, 2H), 3.75 (s, 3H), 3.58 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 156.6, 143.5, 141.7, 140.5, 132.3, 129.5, 129.4, 128.0, 126.5, 123.2, 122.3, 121.3, 120.9, 120.6, 120.4, 113.2, 111.7, 110.4, 55.7, 52.1; HRMS (ESI) m/z calcd for $C_{21}H_{16}N_2O_5[M + Na]^+$ 399.0957; Found 399.0951.

1-Methoxycarbonyl-2-(4-methoxyphenyl)-3-nitro-9*H*-carbazole (3ae). Light yellowish solid; mp 198–200 °C; ^{1}H NMR (400 MHz, $CDCl_3$) 9.97 (s, 1H), 8.67 (s, 1H), 8.12 (d, J = 8.04 Hz, 1H), 7.59–7.56 (m, 2H), 7.39–7.35 (m, 1H), 7.20 (d, J = 8.52 Hz, 2H), 6.94 (d, J = 8.52 Hz, 2H), 3.87 (s, 3H), 3.61 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 159.3, 144.2, 141.3, 140.6, 135.0, 129.7, 129.0, 128.1, 123.1, 122.2, 121.3, 120.1, 119.9, 113.4, 112.9, 111.7, 55.3, 52.3; HRMS (ESI) m/z calcd for $C_{21}H_{16}N_2O_5[M + Na]^+$ 399.0957; Found 399.0951.

1-Methoxycarbonyl-2-(2,5-dimethoxyphenyl)-3-nitro-9*H*-carbazole (3af). Yellowish solid; mp 209–211 °C; IR; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.83 (s, 1H), 9.08 (s, 1H), 8.37 (d, J = 8.0 Hz, 1H), 7.70–7.72 (m, 1H), 7.54–7.58 (m, 1H), 7.31–7.35 (m, 1H), 6.93–7.00 (m, 2H), 6.70–6.71 (m, 1H), 3.72 (s, 3H), 3.67 (s, 3H), 3.60 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.8, 153.0, 150.3, 142.2, 141.3, 139.1, 129.3, 127.7, 126.4, 122.4, 121.7, 121.3, 120.6, 119.6, 115.7, 115.4, 113.6, 112.3, 111.8, 55.8, 55.4, 52.3; HRMS (ESI) m/z calcd for $C_{22}H_{18}N_2O_6[M + Na]^+$ 429.1063; Found 429.1057.

1-Methoxycarbonyl-2-(4-benzyloxy-3-methoxyphenyl)-3-nitro-9*H*-carbazole (3ag). Light yellowish solid; mp 199–201 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.94 (s, 1H), 8.66 (s, 1H), 8.11 (dd, J = 0.8, 8.0 Hz, 1H), 7.53–7.58 (m, 2H), 7.47–7.49 (m, 2H), 7.29–7.40 (m, 4H), 6.92 (d, J = 8.4 Hz, 1H), 6.84–6.85 (m, 1H), 6.74–6.76 (m, 1H), 5.20–5.22 (m, 2H), 3.87 (s, 3H), 3.54 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 149.2, 147.9, 144.0, 141.3, 140.6, 137.1, 134.7, 129.9, 128.6, 128.1, 127.9, 127.4, 123.1, 122.2, 121.4, 121.1, 121.0, 119.7, 113.5, 113.0, 112.7, 111.7, 71.1, 56.2, 52.2; HRMS (ESI) m/z calcd for $C_{28}H_{22}N_2O_6[M + Na]^+$ 505.1376; Found 505.1370.

1-Methoxycarbonyl-2-(2-chlorophenyl)-3-nitro-9*H*-carbazole (3ah). White solid; mp 217–219 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.21 (s, 1H), 8.90 (d, J = 0.4 Hz, 1H), 8.15 (dd, J = 0.4, 8.0 Hz, 1H), 7.56–7.61 (m, 2H), 7.47–7.50 (m, 1H), 7.29–7.41 (m, 3H), 7.19–7.21 (m, 1H), 3.61 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 142.7, 141.9, 140.7, 136.6, 133.5, 132.9, 129.5, 129.1, 128.8, 128.4, 126.4, 124.0, 122.1, 121.6, 121.1, 121.0, 112.3, 111.8, 52.5; HRMS (ESI) m/z calcd for $C_{20}H_{13}ClN_2O_4$[M + Na]$^+$ 403.0462; Found 403.0456.

1-Methoxycarbonyl-2-(4-chlorophenyl)-3-nitro-9*H*-carbazole (3ai). Light yellowish solid; mp 216–218 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.07 (s, 1H), 8.75 (s, 1H), 8.14 (d, J = 8.0 Hz, 1H), 7.56–7.61 (m, 2H), 7.37–7.41 (m, 3H), 7.21–7.24 (m, 2H), 3.61 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3, 143.5, 141.5, 140.7, 135.6, 134.1, 133.9, 129.9, 128.4, 128.0, 123.6, 122.1, 121.5, 121.1, 120.3, 112.4, 111.8, 52.3; HRMS (ESI) m/z calcd for $C_{20}H_{13}ClN_2O_4$[M + Na]$^+$ 403.0462; Found 403.0456.

1-Methoxycarbonyl-2-(4-bromophenyl)-3-nitro-9*H*-carbazole (3aj). Light yellowish solid; mp 235–237 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.07 (s, 1H), 8.74 (d, J = 0.76 Hz, 1H), 8.13 (dd, J = 0.8, 7.76 Hz, 1H), 7.59–7.53 (m, 4H), 7.41–7.37 (m, 1H), 7.17–7.15 (m, 2H), 3.61 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3, 143.4, 141.5, 140.7, 136.1, 134.1, 130.9, 130.2, 128.4, 123.6, 122.1, 122.0, 121.5, 121.0, 120.3, 112.3, 111.8, 52.3; HRMS (ESI) m/z calcd for $C_{20}H_{13}BrN_2O_4$[M + Na]$^+$ 446.9956; Found 446.9951 and [M + Na + **2**] 448.9931.

1-Methoxycarbonyl-2-(2-nitrophenyl)-3-nitro-9*H*-carbazole (3ak). Brown solid; mp 218–220 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.19 (s, 1H), 8.93 (d, J = 0.8 Hz, 1H), 8.34–8.36 (m, 1H), 8.12–8.14 (m, 1H), 7.52–7.66 (m, 4H), 7.38–7.42 (m, 1H), 7.14–7.17 (m, 1H), 3.60 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 148.4, 142.1, 141.2, 140.6, 134.3, 133.9, 133.3, 129.7, 128.7, 128.4, 124.4, 123.9, 122.1, 121.7, 121.6, 121.0, 111.9, 110.6, 52.6; HRMS (ESI) m/z calcd for $C_{20}H_{13}N_3O_6$[M + Na]$^+$ 414.0702; Found 414.0697.

1-Methoxycarbonyl-2-(4-nitrophenyl)-3-nitro-9*H*-carbazole (3al). Brown solid; mp 223–225 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.19 (s, 1H), 8.89 (d, J = 0.48 Hz, 1H), 8.32–8.28 (m, 2H), 8.19–8.16 (m, 1H), 7.62–7.61 (m, 2H), 7.48–7.46 (m, 2H), 7.44–7.40 (m, 1H), 3.60 (s, 3H); ^{13}CNMR (100 MHz, $CDCl_3$) δ 166.7, 147.4, 144.7, 142.6, 141.7, 140.8, 133.3, 129.6, 128.8, 124.3, 123.0, 122.0, 121.8, 121.2, 120.9, 112.0, 111.8, 52.4; HRMS (ESI) m/z calcd for $C_{20}H_{13}N_3O_6$[M + Na]$^+$ 414.0702; Found 414.0697.

1-Methoxycarbonyl-2-(4-cyanophenyl)-3-nitro-9*H*-carbazole (3am). White solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.17 (s, 1H), 8.86 (s, 1H), 8.17 (d, J = 8.0 Hz, 1H), 7.72 (d, J = 8.0 Hz, 2H), 7.59–7.63 (m, 2H), 7.39–7.43 (m, 3H), 3.59 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.5, 147.6, 146.7, 146.5, 144.5, 137.0, 136.9, 134.9, 133.4, 128.4, 126.8, 126.7, 126.2, 125.7, 124.0, 119.7, 117.8, 115.6, 57.7; HRMS (ESI) m/z calcd for $C_{21}H_{13}N_3O_4$[M + **1**]$^+$ 372.0906; Found 372.0979.

1-Methoxycarbonyl-2-(2-furyl)-3-nitro-9*H*-carbazole (3an). Brown solid; mp 175–177 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.99 (s, 1H), 8.70 (s, 1H), 8.09 (d, J = 8.0 Hz, 1H), 7.53–7.61 (m, 3H), 7.35–7.38 (m, 1H), 6.52–6.53 (m, 1H), 6.42–6.44 (m, 1H), 3.78 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 146.9, 143.4, 143.0, 141.1, 140.8, 128.6, 124.3, 123.8, 122.0, 121.5, 121.1, 120.1, 113.4, 111.8, 111.4, 110.1, 52.9; HRMS (ESI) m/z calcd for $C_{18}H_{12}N_2O_5$[M + Na]$^+$ 359.0644; Found 359.0638.

1-Methoxycarbonyl-2-(2-thiophenyl)-3-nitro-9*H*-carbazole (3ao). Yellowish solid; mp 180–182 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.96 (s, 1H), 8.65 (s, 1H), 8.11 (d, J = 7.2 Hz, 1H), 7.62–7.52 (m, 2H), 7.46 (dd, J = 0.16 Hz, 5.2 Hz, 1H), 7.39–7.35 (m, 1H), 7.09–7.07 (m, 1H), 7.02–7.01 (m, 1H), 3.69 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3, 144.6, 141.0, 140.7, 136.4, 128.5, 128.1, 127.1, 127.0, 126.7, 124.0, 122.1, 121.5, 121.1, 119.6, 114.1, 111.8, 52.6; HRMS (ESI) m/z calcd for $C_{18}H_{12}N_2O_4S$[M + Na]$^+$ 375.0415; Found 375.0410.

1-Methoxycarbonyl-2-(2-ethylphenyl)-3-nitro-9*H*-carbazole (3ap). Yellow solid; mp 137–139 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.03 (s, 1H), 8.70 (d, J = 0.48 Hz, 1H), 8.08 (dd, J = 0.80 Hz, 7.6 Hz, 1H), 7.53–7.55 (m, 2H), 7.31–7.37 (m, 5H), 7.22–7.27 (m, 1H), 4.11 (s, 3H), 3.54–3.59 (m, 2H), 3.06–3.11 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 144.7, 142.3, 141.7, 140.3, 136.1, 128.5 (2C), 127.9, 126.2, 122.5, 122.2, 121.3, 121.2, 120.8, 112.2, 111.6, 52.7, 37.7, 32.7; HRMS (ESI) m/z calcd for $C_{22}H_{18}N_2O_4$[M + Na]$^+$ 397.1164; Found 397.1159.

1-Methoxycarbonyl-2-propyl-3-nitro-9*H*-carbazole (3aq). Yellowish solid; mp 146–148 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.96 (s, 1H), 8.61 (s, 1H), 8.05 (d, J = 7.78 Hz, 1H), 7.48–7.53 (m, 2H), 7.30–7.34 (m, 1H), 4.09 (s, 3H), 3.20–3.24 (m, 2H), 1.70–1.80 (m, 2H), 1.05 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 144.8, 142.2, 140.2, 137.2, 127.8, 122.2 (2C), 121.2, 120.9, 120.7, 112.1, 111.5, 52.6, 32.2, 25.3, 14.5; HRMS (ESI) m/z calcd for $C_{17}H_{16}N_2O_4$[M + Na]$^+$ 335.1002; Found 335.1021.

1-Methoxycarbonyl-5-iodo-2-phenyl-3-nitro-9*H*-carbazole (3ba). Light yellowish solid; mp 198–200 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.18 (s, 1H), 9.60 (s, 1H), 7.81 (d, J = 7.6 Hz, 1H), 7.57 (d, J = 8.0 Hz, 1H), 7.41–7.42 (m, 3H), 7.24–7.26 (m, 3H), 3.55 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 139.1, 137.3, 136.9, 132.4, 131.6, 128.0, 124.5, 124.1, 123.6, 123.5, 119.5, 119.4, 116.3, 108.1, 107.2, 83.5, 47.9; HRMS (ESI) m/z calcd for $C_{20}H_{13}IN_2O_4$[M + Na]$^+$ 494.9818; Found 494.9812.

1-Methoxycarbonyl-5-iodo-2-(4-chlorophenyl)-3-nitro-9*H*-carbazole (3bi). White solid; mp 233–235 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.23 (s, 1H), 9.63 (s, 1H), 7.82 (dd, J = 0.8, 7.6 Hz, 1H), 7.59 (dd, J = 0.8, 7.6 Hz, 1H), 7.38–7.42 (m, 2H), 7.29–7.21 (m, 3H), 3.60 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3, 143.2, 141.7, 141.3, 135.3, 134.7, 134.0, 132.5, 129.8, 128.9, 128.1, 124.1, 123.8, 120.8, 112.2, 111.6, 87.9, 52.4; HRMS (ESI) m/z calcd for $C_{20}H_{12}ClIN_2O_4$[M + Na]$^+$ 528.9428; Found 528.9422.

1-Methoxycarbonyl-5-iodo-2-(4-benzyloxy-3-methoxyphenyl)-3-nitro-9*H*-carbazole (3bg). Brown solid; mp 180–182 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.09 (s, 1H), 9.51 (s, 1H), 7.67 (d, J = 7.6 Hz, 1H), 7.46–7.54 (m, 3H), 7.21–7.40 (m, 4H), 6.93 (d, J = 8.0 Hz, 1H), 6.64–6.85 (m, 1H), 6.74–6.77 (m, 1H), 5.19–5.20 (m, 2H), 3.87 (s, 3H) 3.53 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 149.2, 148.0, 143.6, 141.4, 141.2,

137.0, 135.3, 132.3, 129.6, 128.7, 128.6, 127.9, 127.5, 123.8, 123.5, 121.1, 120.2, 113.5, 112.7, 112.6, 111.5, 87.6, 71.1, 56.2, 52.2; HRMS (ESI) *m*/*z* calcd for $C_{28}H_{21}IN_2O_6[M + Na]^+$ 631.0342; Found 631.0337.

1-Methoxycarbonyl-5-iodo-2-(2-furyl)-3-nitro-9*H*-carbazole (3bn). Pale yellow solid; mp 190–192 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.15 (s, 1H), 9.62 (s, 1H), 7.81 (dd, J = 0.8, 8.0 Hz, 1H), 7.55–7.61 (m, 2H), 7.24–7.28 (m, 1H), 6.53–6.54 (m, 1H), 6.46–6.47 (m, 1H), 3.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 146.7, 143.2, 143.0, 141.4, 141.3, 132.5, 129.1, 124.7, 124.4, 123.7, 120.6, 113.0, 111.6, 111.5, 110.4, 88.0, 53.0; HRMS (ESI) *m*/*z* calcd for $C_{18}H_{11}IN_2O_5[M + Na]^+$ 484.9610; Found 484.9605.

4-Methoxycarbonyl-3-phenyl-2-nitro-9*H*-carbazole (3ca). Yellowish solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (s, 1H), 8.07 (s, 1H), 7.94 (d, J = 8.0 Hz, 1H), 7.51–7.57 (m, 2H), 7.39–7.44 (m, 3H), 7.32–7.35 (m, 2H), 7.27–7.31 (m, 1H), 3.67 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 141.7, 137.4, 135.6, 129.9, 129.7, 129.1, 128.8, 128.6, 128.2, 128.0, 122.6, 122.4, 121.1, 120.4, 111.3, 108.0, 52.5; HRMS (ESI) *m*/*z* calcd for $C_{20}H_{14}N_2O_4[M + Na]^+$ 369.0851; Found 369.0846.

9-Benzyl-4-methoxycarbonyl-3-phenyl-2-nitro-9*H*-carbazole (3da). Light yellowish solid; mp 209–211 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.97–8.00 (m, 1H), 7.54–7.58 (m, 1H), 7.46–7.48 (m, 1H), 7.39–7.44 (m, 3H), 7.28–7.36 (m, 6H), 7.13–7.15 (m, 2H), 5.61 (s, 2H), 3.68 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 147.1, 143.0, 138.7, 135.7, 135.6, 129.1, 129.0, 128.9, 128.6, 128.2, 128.1, 128.0, 126.3, 125.5, 122.6, 122.2, 121.0, 120.2, 109.8, 106.3, 52.5, 47.0; HRMS (ESI) *m*/*z* calcd for $C_{27}H_{20}N_2O_4[M + Na]^+$ 459.1321; Found 459.1315.

9-Benzyl-4-methoxycarbonyl-3-(4-methylphenyl)-2-nitro-9*H*-carbazole (3dc). Yellowish solid; mp 223–225 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97–7.99 (m, 2H), 7.54–7.58 (m, 1H), 7.45 (d, J = 8.0 Hz, 1H), 7.29–7.33 (m, 4H), 7.20–7.25 (m, 4H), 7.12–7.14 (m, 2H), 5.60 (s, 2H), 3.73 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 147.3, 142.9, 138.6, 137.6, 135.6, 132.5, 129.1, 129.0, 128.9, 128.8, 128.5, 128.1, 126.3, 125.4, 122.3, 122.0, 120.9, 120.2, 109.7, 106.2, 52.5, 46.9, 21.3; HRMS (ESI) *m*/*z* calcd for $C_{28}H_{22}N_2O_4[M + Na]^+$ 473.1477; Found 473.1472.

9-Benzyl-4-methoxycarbonyl-3-(4-methoxyphenyl)-2-nitro-9*H*-carbazole (3de). White solid; mp 206–208 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96–7.99 (m, 2H), 7.54–7.58 (m, 2H), 7.45 (d, J = 8.0 Hz, 1H), 7.28–7.33 (m, 4H), 7.24–7.26 (m, 1H), 7.12–7.15 (m, 2H), 6.93–6.97 (m, 2H), 5.60 (s, 2H), 3.86 (s, 3H), 3.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 159.4, 147.4, 142.9, 138.5, 135.6, 130.5, 130.3, 129.1, 128.5, 128.1, 127.6, 126.3, 125.0, 122.4, 121.9, 120.9, 120.1, 113.8, 109.8, 106.1, 55.3, 52.6, 46.9; HRMS (ESI) *m*/*z* calcd for $C_{28}H_{22}N_2O_5[M + Na]^+$ 489.1426; Found 489.1421.

9-Benzyl-4-methoxycarbonyl-3-(4-benzyloxy-3-methoxy-phenyl)-2-nitro-9*H*-carbazole (3dg). Light yellowish; mp 179–181 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, J = 7.6 Hz, 1H), 7.94 (s, 1H), 7.53–7.58 (s, 1H), 7.44–7.48 (m, 3H), 7.37–7.41 (m, 2H), 7.27–7.34 (m, 5H), 7.11–7.13 (m, 2H), 6.90–6.95 (m, 2H), 6.82–6.85 (m, 1H), 5.59 (s, 2H), 5.20 (s, 2H), 3.87 (s, 3H), 3.70 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 149.3, 148.0, 147.4, 142.9, 138.6, 137.0, 135.6, 129.1, 129.0, 128.6, 128.5, 128.4, 128.1, 127.9, 127.5, 126.3, 125.0, 122.5, 122.0, 121.6, 121.0, 120.2, 113.7, 113.0, 109.8, 106.1, 71.0, 56.1, 52.7, 46.9; HRMS (ESI) *m*/*z* calcd for $C_{35}H_{28}N_2O_6[M + Na]^+$ 595.1840; Found 595.1840.

9-Benzyl-4-methoxycarbonyl-3-(2-chlorophenyl)-2-nitro-9*H*-carbazole (3dh). Yellowish solid; mp 178–180 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (s, 1H), 7.99–8.01 (m, 1H), 7.55–7.59 (m, 2H), 7.46–7.49 (m, 2H), 7.29–7.37 (m, 6H), 7.16–7.18 (m, 2H), 5.64 (s, 2H), 3.67 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 145.9, 143.2, 139.2, 135.5, 135.3, 134.3, 132.1, 130.9, 129.4, 129.2, 129.1, 128.9, 128.1, 126.5, 126.3, 123.2, 122.9, 122.8, 121.1, 120.2, 109.9, 106.9, 52.5, 47.1; HRMS (ESI) *m*/*z* calcd for $C_{27}H_{19}ClN_2O_4[M + Na]^+$ 493.0931; Found 493.0926.

9-Benzyl-4-methoxycarbonyl-3-(4-bromophenyl)-2-nitro-9*H*-carbazole (3dj). Light orange solid; mp 230–232 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.96 (d, J = 8.0 Hz, 1H), 7.53–7.59 (m, 3H), 7.47 (d, J = 8.4 Hz, 1H), 7.28–7.33 (m, 4H), 7.20–7.23 (m, 2H), 7.13–7.15 (m, 2H), 5.61 (s, 2H), 3.73 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 146.7, 143.1, 138.8, 135.5, 134.7, 131.4, 130.8, 129.1, 128.8, 128.7, 128.2, 126.3, 124.2, 122.5, 122.4, 122.3, 121.1, 120.1, 109.8, 106.5, 52.6, 47.0; HRMS (ESI) *m*/*z* calcd for $C_{27}H_{19}BrN_2O_4[M + Na]^+$ 537.0426; Found 537.0395 and $[M + Na + 2]^+$ 539.0540.

9-Benzyl-4-methoxycarbonyl-3-(2-nitrophenyl)-4-nitro-9*H*-carbazole (3dk). Orange solid; mp 213–215 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (s, 1H), 8.25–8.27 (m, 1H), 7.96 (d, J = 8.0 Hz, 1H), 7.66–7.69 (m, 1H), 7.55–7.63 (m, 2H), 7.46–7.48 (m, 1H), 7.28–7.36 (m, 5H), 7.16–7.18 (m, 2H), 5.65 (s, 2H), 3.61 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 148.3, 144.9, 143.3, 139.9, 135.5, 133.1, 132.4, 131.6, 129.2, 129.1, 129.0, 128.2, 127.2, 126.4, 124.6, 123.2, 123.0, 122.9, 121.2, 120.0, 109.9, 107.6, 52.5; 47.0; HRMS (ESI) *m*/*z* calcd for $C_{27}H_{19}N_3O_6[M + Na]^+$ 504.1172; Found 504.1166.

9-Benzyl-4-methoxycarbonyl-3-(2-furyl)-2-nitro-9*H*-carbazole (3dn). Light brownish solid; mp 173–175 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99–8.02 (m, 2H), 7.54–7.59 (m, 2H), 7.44 (d, J = 8.8 Hz, 1H), 7.26–7.35 (m, 4H), 7.08–7.10 (m, 2H), 6.51–6.55 (m, 2H), 5.57 (s, 2H), 3.93 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 147.1, 146.4, 143.5, 142.8, 139.1, 135.4, 129.1, 128.8, 128.7, 128.1, 126.2, 122.5, 122.0, 121.2, 120.1, 114.6, 111.4, 110.1, 109.9, 106.8, 53.0, 46.8; HRMS (ESI) *m*/*z* calcd for $C_{25}H_{18}N_2O_5[M + Na]^+$ 449.1113; Found 449.1108.

7-Nitrochromeno[3,4-*a*]carbazol-1(13*H*)-one (3ar). Brown solid, mp 260 °C (decompose); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.43 (s, 1H), 9.26 (s, 1H), 8.36 (d, J = 8.0 Hz, 1H), 7.90 (d, J = 8.0 Hz, 1H), 7.56–7.66 (m, 4H); 7.35–7.42 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.2, 150.6, 141.7, 139.2, 138.8, 131.5, 128.0, 125.0, 124.8, 124.2, 123.9, 122.3, 121.4, 121.3, 121.2, 118.0, 114.5, 113.4, 105.1; HRMS (ESI) *m*/*z* calcd for $C_{19}H_{10}N_2O_4[M + Na]^+$ 353.0538; Found 353.0533.

7-Amino-2,13-dihydro-1*H*-idolo[2,3-*i*]phenanthridin-1-one (11). A mixture of compound **3ak** (196.0 mg, 0.5 mmol), Fe powder (280 mg, 5.0 mmol) and NH_4Cl (321 mg, 6.0 mmol) in EtOH–H_2O (20 mL, 4 : 1) was heated at 80 °C for 10 h.

Afterwards the reaction mixture was concentrated under reduced pressure. The crude residue was extracted with ethyl acetate. The combined organic solvent evaporated under reduced pressure followed by purification through a pad of silica-gel (eluent: hexane–EtOAc = 3 : 1) afforded the pure product **11** (136 mg, 91%).

Brown solid; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.77 (br s, 1H), 11.52 (br s, 1H), 9.27 (d, J = 8.0 Hz, 1H), 8.04–8.07 (m, 2H), 7.78–7.80 (m, 1H), 7.41–7.46 (m, 3H), 7.17–7.26 (m, 2H), 5.19 (br s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.3, 140.5, 138.7, 135.9, 132.9, 127.6, 126.3, 125.7, 122.1, 121.5, 121.4, 120.6, 119.7, 119.5, 118.6, 115.7, 114.2, 112.2, 110.3; HRMS (ESI) m/z calcd for $C_{19}H_{14}N_3O$ $[M + H]^+$ 300.1137; Found 300.1160.

1-Carboxylic acid-2-phenyl-3-nitro-9*H*-carbazole (12). To a stirred solution of compound **3aa** (346 mg, 1.0 mmol) in a mixture of MeCN–H_2O (5 mL, 7 : 3) was added LiOH·H_2O (84 mg, 2.0 mmol) at room temperature. After that the reaction mixture was heated at 40 °C for 24 h (monitored by TLC). Next, the reaction mixture was extracted with ethyl acetate before being acidified with HCl. The evaporation of the solvent left the crude product which was purified by column chromatography over silica-gel (eluent: hexane–ethyl acetate = 3 : 7) to furnish the pure product **12** (309.0 mg, 93%). The product was characterized by spectroscopic data (^{1}H and ^{13}C NMR and HRMS).

White solid; ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.4 (br s, 1H), 11.8 (s, 1H), 9.03 (s, 1H), 8.36 (d, J = 7.6 Hz, 1H), 7.72 (d, J = 8.0 Hz, 1H), 7.52–7.57 (m, 1H), 7.29–7.44 (m, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 167.00, 142.4, 141.5, 138.9, 136.6, 132.0, 128.6, 127.8, 127.6, 127.5, 122.2, 121.7, 121.2, 120.5, 118.5, 117.1, 112.5; HRMS (ESI) m/z calcd for $C_{19}H_{12}N_2O_4[M - 1]^-$ 331.0719; Found 331.0713.

2-[2-(Dimethylamino)ethyl]-5-nitro-1*H*-pyrimido[5,6,1-*jk*]carbazole-1,3(2*H*)-dione (14). To a mixture of compound **12** (166 mg, 0.5 mmol), EDC·HCl (135 mg, 0.7 mmol), HOBt (95.0 mg, 0.7 mmol) and Et_3N (0.42 mL, 3.0 mmol) in DMF (5.0 mL) was added *N*,*N*-dimethylethylenediamine (66.0 mg, 0.75 mmol) at room temperature. The reaction mixture was stirred for 8 h (monitored by TLC). After that the reaction mixture was quenched with water before being removed DMF under reduced pressure. Then the reaction mixture was extracted with EtOAc (3 × 10 mL), washed with water, brine and dried with Na_2SO_4. The combined organic solvent was evaporated under reduced pressure to afford crude product **13** which was sufficiently pure and directly used for the next step.

To a stirred solution of the above compound **13** in dry DMF (5.0 mL) under an argon atmosphere was added NaH (50–55% dispersion in mineral oil; 72 mg) at 0 °C. After being stirred for 1 h at the same temperature, EtO_2Cl (1.0 mmol) was added into the above reaction mixture and stirring was continued for 12 h at room temperature. Then the reaction mixture was quenched with water, extracted with ethyl acetate (3 × 10 mL), washed with water and brine, and dried with Na_2SO_4. The combined organic solvent was concentrated in a vacuum under reduced pressure to give the crude residue which was purified by column chromatography over silica-gel (eluent: DCM–MeOH = 19 : 1) to afford the pure product **14** in 88% yield.

Yellowish solid; 196–198 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52–8.54 (m, 2H), 8.04–8.05 (m, 1H), 7.65–7.69 (m, 1H), 7.48–7.56 (m, 4H), 7.34–7.35 (m, 2H), 4.22 (t, J = 6.4 Hz, 2H), 2.66 (br s, 2H), 2.33 (br s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 148.2, 147.5, 138.8, 138.2, 136.1, 130.0, 128.7, 128.3, 128.1, 125.6, 123.9, 123.7, 121.5, 120.0, 116.3, 111.1, 55.5, 45.5, 39.2; HRMS (ESI) m/z calcd for $C_{24}H_{22}N_4O_4[M + 1]^+$ 429.1563; Found 429.1557.

Conclusions

In the current paper, we have developed a clean, expedient, mild and general method for the synthesis of functionalized carbazole derivatives in water medium *via* a one-pot domino Michael–Henry/aromatization reaction under aerobic conditions. Our current method avoids the use of acids, metals, toxic organic solvents, stoichiometric amounts of strong oxidants, any need for an inert atmosphere, multiple steps, *etc.* In addition, a marketable organocatalyst, operational simplicity, excellent yields (≤97%), a broad substrate scope, suitability for bench scale synthesis, and environmentally friendly reaction conditions make this procedure more convenient as compared to the existing ones. Furthermore, biologically attractive pyrimido, quinolinone and coumarin fused carbazole derivatives have been prepared. Investigations into the application of these molecules are in progress.

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