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Anionic [4+2] cycloaddition strategy in the regiospecific synthesis of carbazoles: formal synthesis of ellipticine and murrayaquinone A

Dipakranjan Mal,* Bidyut Kumar Senapati and Pallab Pahari

Department of Chemistry, Indian Institute of Technology, Kharagpur 721 302, West Bengal, India

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Abstract—Anionic [4+2] cycloaddition of furoindolones (e.g., **7** and **10**) has been developed as an effective means to the synthesis of carbazoles. This reaction has been shown to be feasible with a wide variety of Michael acceptors to give carbazoles and fused carbazoles in good yields. The scope and limitations of the reaction have been briefly studied. The nature of N-protection of the furoindolones (cf. **7**) plays a major role in the success of annulation.

1. Introduction

The substituted carbazoles are embodied in many naturally occurring compounds as well as synthetic materials. During the past four decades, a wide variety of biologically active carbazole alkaloids (Fig. 1) have been isolated from plant sources. Many of these natural products possess interesting biological properties, which include antitumor, psychotropic, anti-inflammatory, and antihistaminic, antibiotic, and antioxidative activities.[1] The publication of Knollker's recent review[2] is a testament of the intense activity in the field. Polymeric carbazole derivatives are used as organic materials due to their photoreactive, photoconductive, and light emitting properties.[3] Recently, functionalized carbazoles have also been recognized as a useful scaffold in anion binding studies.[4] Consequently, the synthesis of carbazoles continues to be a vigorously active research area.[5a,b] Moreover, problems related to regiochemistry, efficacy, and generality are often encountered in a carbazole synthesis.

The conventional methodologies for the synthesis of carbazoles center around utilization of three classes of starting

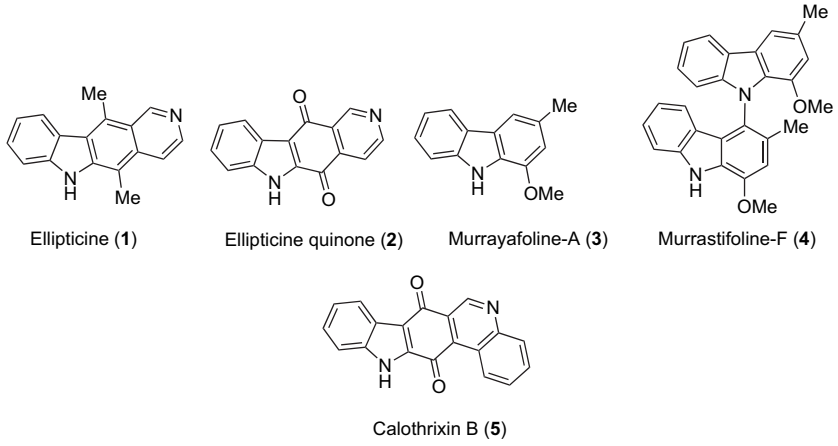

Figure 1. Structures of few representative naturally occurring carbazoles.

Keywords: Carbazole quinone; Anionic cycloaddition; Furoindolone.
* Corresponding author. Tel.: +91 3222 283318; fax: +91 3222 282252; e-mail: dmal@chem.iitkgp.ernet.in

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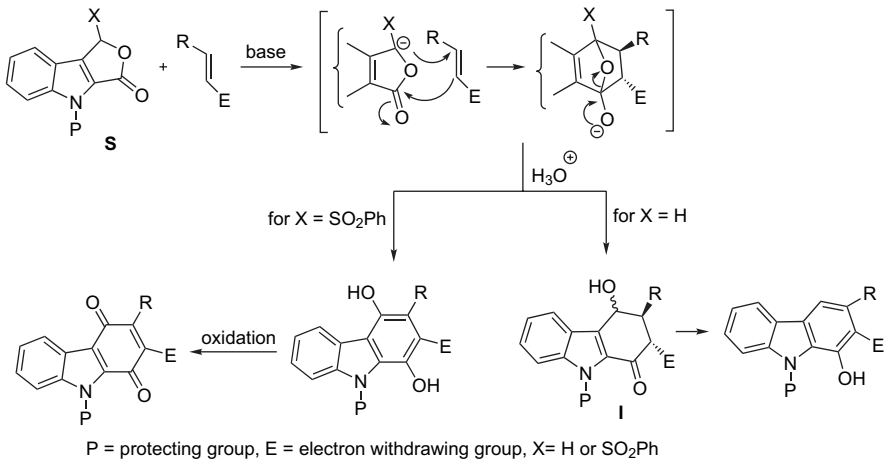


Scheme 1. Proposed methodology for the synthesis of carbazole quinones and carbazoles.

materials such as 2′-nitrogen substituted biaryls,[6a–k] diarylamines,[6l,m] and substituted indole derivatives.[6n–r] We now wish to report a new synthesis of carbazole quinones and 1-oxygenated carbazoles by benzannulation (anionic [4+2] cycloaddition) of furoindolones[10] (e.g., **7** and **10**) with various Michael acceptors. This methodology provides a very simple and straightforward regiospecific route to carbazole quinones and 1-oxygenated multi-substituted carbazoles. We also report the formal synthesis of ellipticine (**1**) and murrayaquinone A (**21**).

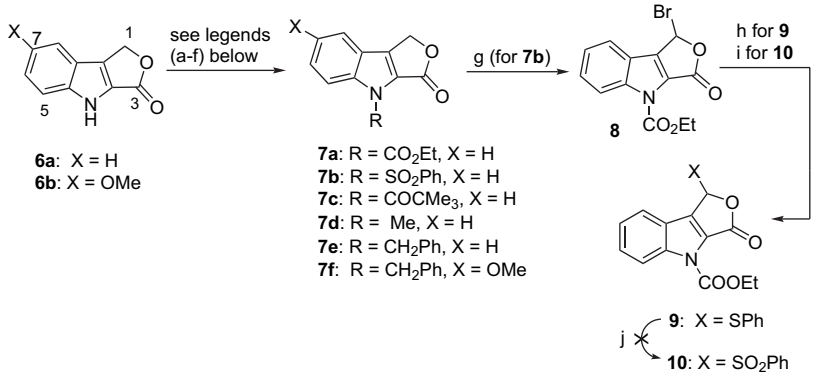
The anionic [4+2] cycloaddition of isobenzofuranones is a well-known reaction for the synthesis of condensed aromatics and hydroaromatics[7,9] but to date it has not been extended to the synthesis of a heterocyclic quinone compound.[8] Therefore, we became interested in the synthesis of ellipticine[11a–d] (**1**) and calothrixin[11e–g] (**5**) by application of the Hauser annulation,[12] a widely studied anionic cycloaddition. The formulated strategy (Scheme 1) was based on lateral lithiation of a suitably *N*-protected furoindolone (cf. S) followed by Michael initiated ring closure. In two recent communications,[13] we reported the successful application of this methodology in the synthesis of carbazole quinones and 1-hydroxycarbazoles. Herein we report a full account of a study in this area.

2. Results and discussion

2.1. Synthesis of ellipticine quinone

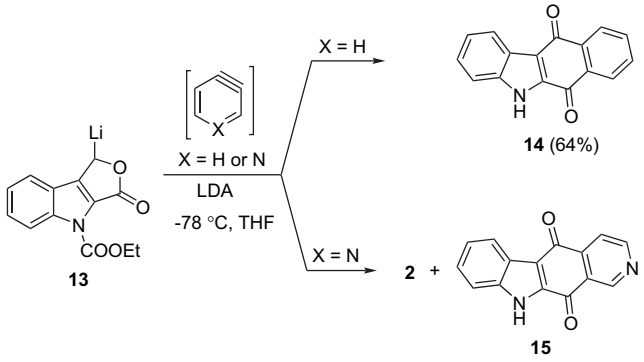
In view of importance of ellipticine quinone (**2**)[14] as a cytotoxic compound against HeLa cell lines as well as a late-stage intermediate in the synthesis of ellipticine (**1**), we examined the proposed strategy for its synthesis. The starting furoindolone **6a** was prepared in 40% yield by Fischer indolization of 3-(2-phenylhydrazono)dihydrofuran-2(3*H*)-one in the presence of HCl.[10] Compound **6a** was then transformed into *N*-ethoxycarbonyl derivative **7** (92%, Scheme 2) by treatment with triethylamine and ethyl chloroformate. Similarly, *N*-phenylsulfonyl derivative **7b** was prepared in 68% yield from compound **6a**, using benzenesulfonyl chloride, K_2CO_3, and benzyltriethylammonium chloride.

Furoindolone **7a** was further functionalized at C-1 with a phenylsulfonyl group (Scheme 3) in line with the original work[12b] of Hauser and Rhee on benzoisofuranones. Bromination of compound **7a** with *N*-bromosuccinimide in the presence of benzoyl peroxide gave 1-bromo derivative **8** in 70% yield. Treatment of compound **8** with thiophenol in the presence of triethylamine gave phenylsulfanyl derivative **9** in 77% yield. Exposure of compound **9** to *m*-CPBA did not



Scheme 2. Preparation of furoindolones. Reagents and conditions: (a) $ClCO_2Et$, Et_3N, CH_2Cl_2, 0 °C to rt, 12 h, 92% for **7a**; (b) $PhSO_2Cl$, K_2CO_3, TEBAC, rt, 6 h, 68% for **7b**; (c) ^nBuLi, Me_3COCl, THF, 71% for **7c**; (d) LDA, MeI, THF, 84% for **7d**; (e) K_2CO_3, $PhCH_2Cl$, NaI, Me_2CO, 62% for **7e**; (f) K_2CO_3, $PhCH_2Cl$, NaI, Me_2CO, 69% for **7f**; (g) NBS, Bz_2O_2, 70%; (h) PhSH, Et_3N, $CHCl_3$, 77% for **9**; (i) $PhSO_2Na$, DMF, 85% for **10**; (j) *m*-CPBA.

give the desired sulfone **10**, which was, alternatively prepared in 85% yield by direct displacement of the bromine of **8** with sodium benzenesulfinate ion in DMF. We briefly attempted to prepare the 1-cyano derivative of **7a** by treating **8** with KCN in the presence of 18-crown-6 ether without success.



Scheme 3. Base-promoted cyclization of furoindolone (**7a**) with aryne and heteroaryne.

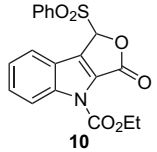
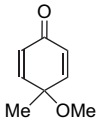
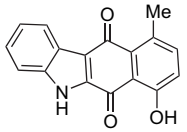
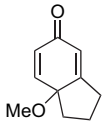
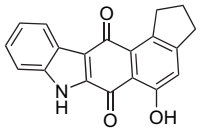
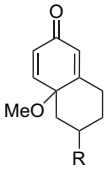
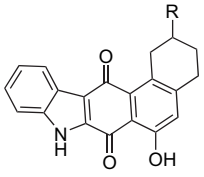
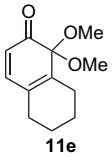
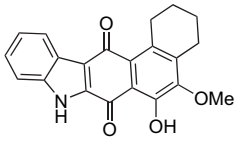
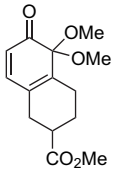
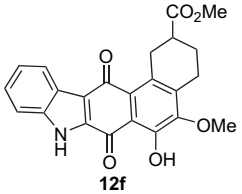
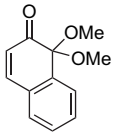
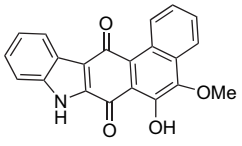
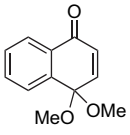
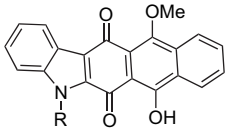
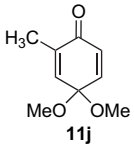
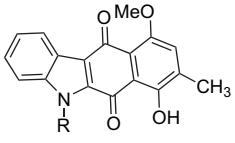
After successful preparation of compound **10**, we investigated its cycloaddition reactivity as proposed in Scheme 1. When it was treated with LDA (3.0 equiv), followed by 2-cyclohexenone (2 equiv) at −78 °C, and the resulting mixture warmed to room temperature, the expected quinol or respective quinone was not obtained. Nor were the starting materials recovered. Both the substrates had been destroyed. The failure of the reaction was attributed to extensive base catalyzed self-condensation[15] of 2-cyclohexenone. Consequently, we chose to work with quinol ether **11a**,[16] which is known to be stable to LDA in THF even at room temperature. When the light yellow anion of the sulfone **10**, generated by treating with LDA at −78 °C, was reacted with **11a**, the color of the reaction mixture changed to deep red. The reaction mixture was allowed to stir for 3 h at ambient temperature and worked up to afford expected compound **12a** in 70% yield (Table 1). The yield of carbazole quinone **12a** improved to 85% when the base was changed to lithium-*tert*-butoxide. It is interesting to note that under the reaction conditions (LDA or *t*-BuOLi) *N*-ethoxycarbonyl group was removed. Upon brief experimentation, it was found that the cleavage took place at room temperature. Likewise, the reaction between **10** and **11b**[17] gave ring-fused carbazole **12b** in 62% and 75% yield in the presence of LDA and *t*-BuOLi, respectively. Compound **12b** was fully characterized by analysis of its IR, ^{1}H NMR, and mass spectral data. Unfortunately, a ^{13}C NMR spectrum of **12b** could not be recorded due to its poor solubility in common deuterated solvents. We generalized the annulation reaction with few more quinol ethers, prepared by phenyliodine(III) diacetate (PIDA) oxidation of the corresponding phenols. Oxidation of 5,6,7,8-tetrahydro-2-naphthol with $PhI(OAc)_2$ yielded a 7:3 mixture of two inseparable compounds **11c** and **11e**.[17] Annulation of this mixture (**11c** and **11e**) with **10** produced pentacyclic carbazole quinone **12e** in 72% (method B) yield corresponding to compound **11e**, and compound **11c** was recovered in 95% yield after usual work-up of the reaction mixture. The quinol ether **11e** was annulated, and **11c** remained inert to annulation with compound **10**. The expected compound **12c** was not obtained. The failure may be attributed due to the presence of greater steric crowding at the ring junction of **11c** than that in **11e**. Again, the ^{13}C NMR spectrum of **12e** could not be recorded due to its poor solubility in common deuterated solvents. The similar loss of a methoxy group from a ketal was earlier noted in our laboratory.[17] Similarly, $PhI(OAc)_2$ oxidation of methyl 6-hydroxy-1,2,3,4-tetrahydro-2-naphthalene-2-carboxylate yielded an inseparable 4:1 mixture of quinol ethers **11d** and **11f**. Interestingly, when the mixture of quinol ethers (**11d** and **11f**) was reacted with **10**, only **11f** underwent annulation with **10**, to give carbazole quinone **12f** in 70% yield (with respect to **11f**) and **11d** was recovered in 98% yield. The corresponding annulation product **12d** was not formed.

Next, we focused our attempts to extend the work to naphthoquinol ether. Accordingly, aromatic quinol ether **11g**[17] was prepared from β-naphthol by usual $PhI(OAc)_2$ oxidation and reacted with **10** in the presence of *t*-BuOLi at −60 °C to give carbazole quinone **12g** in 67% yield. Similarly, the reaction of aromatic quinol ether **11h**[18] with furoindolone **10** afforded carbazole quinone **12h** in 76% yield. The same reaction gave a different product, for example, *N*-protected quinone **12i**, when the work-up was carried out at 0 °C instead of room temperature. ^{1}H NMR signals at δ 4.62 (q, 2H, J=8.0 Hz) and δ 1.54 (t, 3H, J=8.0 Hz) indicated the presence of *N*-ethoxycarbonyl protection. Likewise, quinol ether **11j**[16] (prepared from *o*-cresol by $PhI(OAc)_2$ oxidation) reacted successfully with furoindolone **10** to afford carbazole quinone **12j** in 78% yield. The same reaction furnished N-protected quinone **12k** in 75% yield, when the work-up was carried out at 0 °C instead of room temperature. Due to the poor solubility in common deuterated solvents, ^{13}C NMR spectrum of **12j** could not be recorded.

Although a good number of Michael acceptors were reactive toward furoindolone **10**, simple acceptors like cyclohexenone, methyl crotonate, ethyl cinnamate, coumarin, and ethyl 2-oxo-1(2*H*)-quinolinecarboxylate were not. While the failure with former two acceptors could be explained in terms of their instability toward strong bases, that with the latter three was inexplicable. In view of the recent finding[19] that a phenylsulfanyl in the place of a phenylsulfonyl group would suffice in the Hauser annulation, we experimented with compound **9** that contains a 3-phenylsulfanyl group. When it was treated with lithium diisopropylamide (3.0 equiv), followed by methyl crotonate at −78 °C, and the resulting mixture processed in the usual manner, the expected carbazole quinol was not obtained. Nor were the starting materials recovered, meaning that both substrates had been destroyed. Therefore, we performed the above cycloaddition reaction of **9** with base-stable acceptor **11a** and again we failed to obtain the expected quinone **12a** derivative.

Following the results in Table 1, we were interested in examining the reactivity of **10** to arynes. We first carried out the cycloaddition reaction between compound **10** and bromobenzene under the benzyne-generating conditions reported[20] by Sammes et al. and found that the expected product **14** was not obtained. The same result was found when the above reaction was performed with compound **9**. On the other hand, the reaction of **7b** with bromobenzene in the presence of LDA provided the quinone **14** in only 10% yield. The corresponding product with *N*-SO_2Ph was not obtained, meaning

Table 1. Preparation of carbazole quinones from furoindolone **10** and Michael acceptors

Entry	Michael donor	Michael acceptors	Product (s)	% Yield
1	 **10**	 **11a**	 **12a**	70[a], 85[b]
2	**10**	 **11b**	 **12b**	62[a], 75[b]
3	**10**	 **11c** R = H **11d** R = CO_2Me	 **12c** R = H **12d** R = CO_2Me	0
4	**10**	 **11e**	 **12e**	72[b]
5	**10**	 **11f**	 **12f**	70[b]
6	**10**	 **11g**	 **12g**	67[b]
7	**10**	 **11h**	 **12h** R = H,**12i** R = CO_2Et	76[b] (**12h**), 72[b] (**12i**)
8	**10**	 **11j**	 **12j** R = H,**12k** R = CO_2Et	78[b] (**12j**), 75[b] (**12k**)

[a] Method A: LDA, −78 °C, THF, 3 h.
[b] Method B: *t*-BuOLi, −60 °C, THF, 3 h.

that the phenylsulfonyl group was cleaved under the reaction conditions or during work-up. Reaction between **7a** and bromobenzene in the presence of LDA furnished quinone **14** in 64% yield (Scheme 3), and the corresponding product with the *N*-CO_2Et protecting group was not obtained. In order to establish that deprotection took place with LDA, compound **7a** was treated with LDA at room temperature to give respective deprotected compound **6a**.

The study was then extended to a heteroaryne for the synthesis of ellipticine quinone **2** (Scheme 3). Annulation of furoindolone **7a** with 3-pyridyne[21] prepared in situ from 3-bromopyridine under the previously described conditions yielded an inseparable mixture of two compounds. Detailed comparison of the NMR data[14,22] with those reported for ellipticine quinone **2** and isoellipticine quinone **15** (45% combined yield) confirmed their formation. Although there were no significant differences in the pattern of their NMR data, the two singlets at δ 9.19 and 9.21 were indicative of 2:1 formation of the two isomers, ellipticine quinone **2** being the major product. Since both ellipticine quinone (**2**) and isoellipticine quinone (**15**) have been previously transformed to ellipticine (**1**) and isoellipticine,[23] respectively, this study constitutes the formal syntheses of these alkaloids.

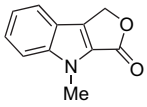
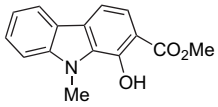
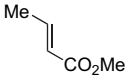
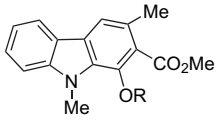
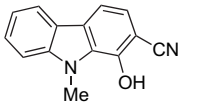
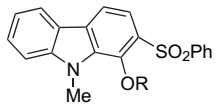
2.2. Synthesis of 1-hydroxycarbazoles

Following the above successes, we extended the study to the preparation of the title compounds. Attempted annulation reaction between compound **7a** and methyl crotonate in the presence of LDA for the construction of substituted carbazole derivatives did not lead to any condensed product but provided compound **6a**. This observation clearly indicated that *N*-ethoxycarbonyl protection of **7a** cleaved under the influence of LDA before the expected annulation with methyl crotonate. Due to the formation of amide anion upon the cleavage, the formation of C-1 carbanion, which would result in a dianion, was difficult and the anticipated cyclocondensation was precluded. However, these results provided an important clue for further investigations.

We decided to examine protecting group stable to LDA (Scheme 2) and their reactivity toward simple Michael acceptors as proposed in Scheme 1 to access substituted carbazoles. Since *N*-pivaloyl group of an indole has been reported[24] to be stable to LDA up to 40–45 °C, we examined reactivity of compound **7c** (Scheme 2). This was readily prepared in 71% yield from parent furoindolone **6a** by pivaloylation with *n*-BuLi and pivaloyl chloride at −78 °C. When compound **7c** was treated with LDA (3.0 equiv), followed by methyl acrylate at −78 °C, and the resulting mixture processed in the usual manner, the expected carbazole was not obtained. Compound **6a** was recovered in a substantial amount, meaning that the pivaloyl group of **7c** was cleaved in the presence of LDA before it could undergo annulation.

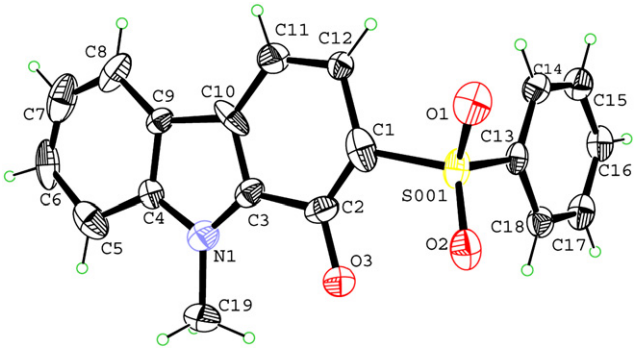
The instability of **7c** to LDA led to the choice of more robust *N*-methylfuroindolone **7d** as a synthon. This was prepared in 84% yield from compound **6a** by methylation with LDA and iodomethane. N-Methylation of **6a** involving NaH/CH_3I in DMF or K_2CO_3/CH_3I-phase transfer catalyst was not at all satisfactory with respect to the yields obtained. Treatment of **7d** with LDA, followed by methyl acrylate gave the desired annulated product **16a** in 72% yield. It was clearly evident from this result that stability of N-protection to LDA was crucial to the success of the proposed annulation. Although the annulation of phthalides (isobenzofuranones) has been established to involve intermediacy of a hydroxytetrahydronaphthalene,[25] no such intermediate (cf. **I**, Scheme 1) could be isolated in the reaction with **7d**. The results of similar annulations of **7d** with various Michael acceptors are summarized in Table 2. When methyl crotonate was

Table 2. Preparation of N-protected carbazoles using *N*-methylfuroindolone **7d** and Michael acceptors

Entry	Furoindolone	Michael acceptor	Carbazole	% Yield[a] (products)
1	 **7d**		 **16a**	72
2	**7d**		 **16b**: R = H; **16c**: R = Me (b, 76%)	78
3	**7d**		 **16d**	81
4	**7d**		 **16e**: R = H; **16f**: R = Me (b, 73%)	65

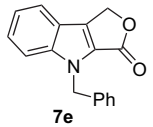
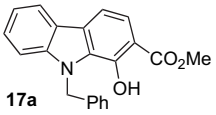
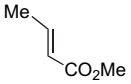
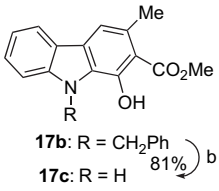
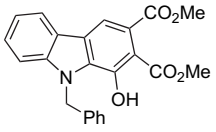
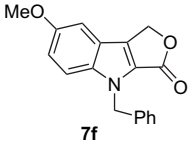
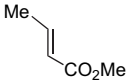
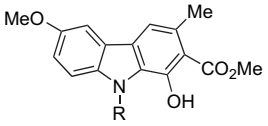
[a] Method A: LDA, −78 °C, THF, 3 h.
[b] Me_2SO_4, K_2CO_3, Me_2CO.

reacted with **7d** in the presence of LDA at −78 °C and the desired 1,2,3-trisubstituted carbazoles **16b** was obtained in 78% yield. To confirm its structure, it was converted to *O*-methyl derivative **16c**. In striking contrast to the above, ethyl cinnamate did not undergo annulation with **7d** under similar conditions. Both *N*-methylfuroindolone **7d** and ethyl cinnamate were recovered, after usual work-up of the reaction. Similarly, methyl vinyl ketone and mesityl oxide were not compatible for the reaction with **7d**, both these ketones were destroyed during the reaction. On the other hand, cyano-containing and sulfone-containing Michael acceptors (entries 3 and 4) underwent smooth annulations with compound **7d** to give **16d** (81%) and **16e** (65%), respectively. The structure of carbazole **16e** was confirmed by its conversion to *O*-methyl derivative **16f** as well as by an X-ray crystallographic analysis.



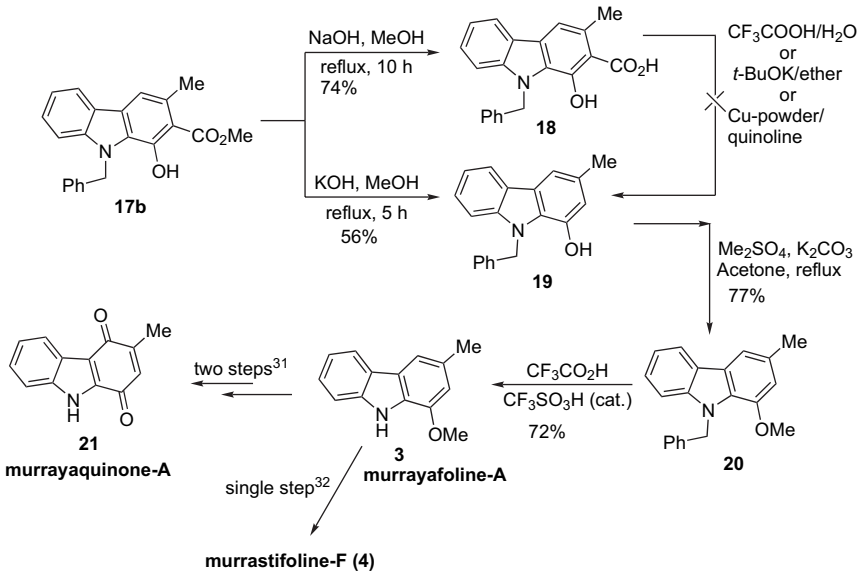
Ortep plot of X-ray structure of **16e**

Table 3. Preparation of N-protected carbazoles from furoindolones (**7e** and **7f**) and Michael acceptors

Entry	Furoindolone	Michael acceptor	Carbazole	% Yield[a]
1	 **7e**		 **17a**	64
2	**7e**		 **17b**: R = CH_2Ph **17c**: R = H (81%, b)	67
3	**7e**		 **17d**	85
4	 **7f**		 **17e**: R = CH_2Ph **17f**: R = H (76%, b)	58

[a] Method A: LDA, −78 °C, THF, 3 h.
[b] $AlCl_3$, CH_2Cl_2.

N-Demethylation of carbazole nitrogen of compound **16b** was examined in order to reveal the utility of the products **16a–16f**. Methods[26] (e.g., $AlCl_3/CH_2Cl_2$, BBr_3/CH_2Cl_2, HBr/AcOH, Bz_2O_2) tested on **16b** resulted in intractable mixtures of products. The difficulty in removing *N*-methyl protection led us to scrutinize benzyl derivative **7e** as an annulating agent. N-Benzylation of **6a** with benzyl chloride in the presence of potassium carbonate and sodium iodide (Scheme 2) furnished **7e**. Annulation of compound **7e** with methyl acrylate in the presence of LDA afforded compound **17a** in 64% yield. Compound **7e** also reacted with methyl crotonate to furnish the annulated product **17b**. In the same manner, annulation between **7e** and dimethyl maleate afforded trisubstituted carbazole **17d** in 85% yield. Compound **7f**, prepared from **6b**[27] also responded to the above annulation reaction with methyl crotonate and produced tetrasubstituted carbazole **17e**. In contrast to demethylation of **16**, which was a difficult task, N-debenzylation of **17b** and **17e** could be readily accomplished with anhydrous $AlCl_3$ in CH_2Cl_2 to give carbazoles **17c** (81%) and **17f** (76%), respectively. For compound **17f**, deprotection proved to be benzyl-selective (Table 3).



Scheme 4. Synthesis of murrayafoline-A (**3**).

2.2.1. Synthesis of murrayafoline-A (3). As a finale, the utility of compound **17b** was established as a key intermediate in the synthesis of natural product murrayafoline-A[28] (**3**).

Although the sequence depicted in Scheme 4 appeared to be trivial, it required rigorous experimentation. For the crucial demethoxycarbonylation of **17b**, few literature methods[29] (e.g., NaOH, MeOH, reflux; DBU, toluene, reflux; HBr, AcOH, reflux; KOH, MeOH, reflux) were attempted. When it was reacted with NaOH and the reaction stopped after stipulated time, the corresponding acid derivative **18** was obtained. Decarboxylation of **18** by methods as CF_3COOH/H_2O, *t*-BuOK/ether, Cu-powder/quinoline was not successful. In all cases, the reaction ended up in an intractable mixture of products. The reaction of **17b** with HBr in AcOH returned the starting material even after long reflux time. Similar was the fate of **17b**, when treated with DBU in toluene at reflux. The differential behavior of sodium and potassium salts of phenol in classic Kolbe–Schmidt synthesis of salicylic acid prompted us to examine KOH in place of NaOH. Indeed, demethoxycarbonylation of **17b** underwent smoothly with concentrated KOH solution in methanol to give **19** in moderate yield (56%). For full characterization, compound **19** was immediately converted to the *O*-methyl derivative **20** (77%) with a mixture of K_2CO_3 and Me_2SO_4 in acetone at reflux. Debenzylation of compound **20** to compound **3** proved problematical. Literature methods[30] (e.g., H_2, Pd/C, MeOH; H_2, Pd/C, MeOH, 1–2 drops of formic acid; $AlCl_3$, CH_2Cl_2; CF_3COOH, reflux) were investigated without success. Finally, it was successfully accomplished by treatment of **20** with refluxing TFA with a catalytic amount of TfOH for 20–25 min. The synthesis of murrayafoline-A (**3**) reported herein constitutes formal synthesis of the fully aromatic alkaloids murrayaquinone-A[31] (**21**) and murrastifoline-F[32] (**4**), since they had been synthesized previously from **3**.

3. Conclusion

In conclusion, the anionic [4+2] cycloaddition of furoindolones has been introduced as a facile method for synthesizing carbazole quinones and 1-oxygenated carbazoles. The method is regiospecific, efficient, and applicable to a range of Michael acceptors. The starting furoindolones are readily accessible. It is to be noted that the choice of N-protection could be crucial, and further work is warranted for finding out a more suitable one.

4. Experimental

4.1. General

Melting points were determined in open capillary tubes and are uncorrected. Among the spectra, ^1H NMR spectra and ^{13}C NMR spectra were recorded on 200, 300 or 500 MHz spectrometer (Brücker) as solution in ^2H-Chloroform with TMS as the internal standard. Chemical shifts are expressed in δ unit and ^1H–^1H coupling constant in hertz. IR spectra were recorded on a Thermo Nicolet Nexus 870 FTIR spectrophotometers using KBr pellet. EIMS (70 eV) spectra were taken using a VG Autospec M mass spectrometer. Elemental analyses were carried out by using an elemental analyzer VARIO EL instrument.

Dry solvents used for reactions were purified, before use, according to the standard protocols. All solvents for chromatography (column and preparative layer chromatography) were distilled prior to use. In most of the column chromatographic separations, ethyl acetate and petroleum ether (60–80 °C) were used as eluents. Columns were prepared with silica gel (60–120 mesh). For preparative thin layer chromatographic (plc) separations, the layer was formed over a glass plate using water gel. The silica gel-GF_{254} was used for the plc plate preparation.

4.2. General procedure for the annulation with LDA (method A)

In a flame-dried flask flushed with nitrogen, LDA (3 mmol) was prepared by adding diisopropylamine (3.6 mmol) to a solution of *n*-BuLi (3 mmol, 1.6 M in hexane) in THF (20 mL) at −78 °C under nitrogen atmosphere. After the solution was stirred for 10 min at −78 °C, an appropriate furoindolone (3 mmol) in THF (10 mL) was added dropwise over 15 min. The reaction mixture was stirred at −78 °C for 15 min and then allowed to warm to −40 °C. A solution of appropriate Michael acceptor (3 mmol) in THF (10 mL) was added dropwise over 15 min at −40 °C (bromobenzene and 3-bromopyridine were dried over calcium hydride and distilled). The reaction mixture was further stirred and allowed to warm slowly to room temperature over 3 h. The dark reddish-brown solution was then quenched with a saturated ammonium chloride solution. The resulting mixture was concentrated under reduced pressure and the residue extracted with ethyl acetate (3×100 mL). The combined extracts were washed with brine (3×1/3 vol), dried (Na_2SO_4), and concentrated to provide crude product, which was purified by column chromatography on silica gel using mixtures of ethyl acetate and petroleum ether as eluents.

4.3. General procedure for the annulation reaction with lithium *tert*-butoxide (method B)

To a stirred solution of lithium *tert*-butoxide (9.84 mmol) in THF (40 mL) at −60 °C (chloroform/liquid N_2 bath) under an inert atmosphere was added a solution of furoindolone (3.28 mmol) in THF (5 mL). The resulting yellowish solution was stirred at −60 °C for 25 min, after which a solution of a Michael acceptor (1 equiv unless otherwise stated) in THF (5 mL) was added to it. The cooling bath was removed after about 1 h at −60 °C and the reaction mixture was brought to room temperature over a period of 1 h and further stirred for 5–6 h. The reaction was then quenched with 10% NH_4Cl (15 mL) and the resulting solution was concentrated under reduced pressure. Generally, a bright yellow solid appeared, which was filtered and washed with 1:1 mixture (20 mL) of diethyl ether and petroleum ether. Otherwise, the residue was diluted with ethyl acetate (50 mL) and the layers were separated. The aqueous layer was extracted with ethyl acetate (3×25 mL). The combined extracts were washed with brine (3×1/3 vol), dried (Na_2SO_4), and concentrated to provide crude product. The crude solid product was purified by column chromatography on silica gel or by recrystallization to get a pure product.

4.4. General procedure of O-methylation of phenolic compounds

A hydroxy compound (3.0 mmol) was dissolved in dry acetone under N_2-atmosphere. To this solution were added dry K_2CO_3 (15 mmol) and Me_2SO_4 (6 mmol; freshly washed with cold water, saturated $NaHCO_3$ solution, and brine and then dried over anhydrous K_2CO_3). After 2 h of reflux, on completion of the reaction, the inorganic salts were removed by filtration and the filtrate concentrated. The residue was diluted with diethyl ether (30 mL), treated with Et_3N (6 mmol) at room temperature, and stirred for 30 min. The reaction mixture was then diluted with ethyl acetate (50 mL), washed with water (40 mL), 5% aqueous HCl solution (15 mL), and brine (3×1/3 vol), dried (Na_2SO_4), and concentrated to get a crude residue, which was further purified by recrystallization or by column chromatography on silica gel to give a pure methoxy compound.

4.4.1. 1-Methoxy-3-methyl-9*H*-carbazole (3). A solution of *N*-benzylmurrayafoline-A **23** (0.04 g, 0.132 mmol) in trifluoroacetic acid (2 mL) and two drops of trifluoromethanesulfonic acid was heated at reflux for 15 min. The solution was then taken up in water (30 mL) and extracted with dichloromethane (3×30 mL). The combined organic extracts were washed with brine (3×20 mL), dried (Na_2SO_4), and concentrated to give crude residue. Purification of the crude residue by chromatography (1:4 ethyl acetate/petroleum ether, R_f=0.67) gave compound **3**[31] (0.02 g, 77%) as an oily material. ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.21 (br s, 1H), 7.96 (d, 1H, J=8.0 Hz), 7.46 (s, 1H), 7.40–7.15 (m, 3H), 6.78 (s, 1H), 4.01 (s, 3H), 2.51 (s, 3H). These data were in agreement with the reported values.[31]

4.4.2. Ethyl 1,3-dihydro-3-oxo-4*H*-furo[3,4-*b*]indole-4-carboxylate (7a). To an ice-cold solution of **6a** (2 g, 11.56 mmol) and triethylamine in dry CH_2Cl_2 (50 mL) was added a solution of ethyl chloroformate (1.12 mL, 11.56 mmol) in dry CH_2Cl_2 (10 mL). The temperature of the mixture was slowly increased to room temperature. After 12 h of stirring, the resulting reaction mixture was poured into 5% aqueous HCl (30 mL) and extracted with CH_2Cl_2 (3×40 mL). The combined organic layers were washed with 5% $NaHCO_3$ solution (20 mL), brine (20 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was chromatographed (1:1 $CHCl_3$/petroleum ether, R_f=0.62) to give **7a** (2.6 g, 92%) as a white crystalline solid. Mp 121–123 °C; FTIR (KBr) cm^{-1} 2923, 2857, 1777 (s), 1742 (s), 1599, 1441, 1381, 1321, 1269, 1235, 1115, 1043, 755; ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.39 (d, 1H, J=8.6 Hz), 7.52–7.65 (m, 2H), 7.38 (t, 1H, J=7.6 Hz), 5.34 (s, 2H), 4.56 (q, 2H, J=5.8 Hz), 1.529 (t, 3H, J=5.8 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 160.4, 149.9, 143.3, 142.6, 128.8, 127.8, 124.0, 121.4, 120.6, 116.8, 65.1, 63.9, 14.0. Anal. Calcd for $C_{13}H_{11}NO_4$: C, 63.67; H, 4.52; N, 5.71. Found: C, 63.83; H, 4.34; N, 5.62.

4.4.3. 1,4-Dihydro-4-(phenylsulfonyl)-3*H*-furo[3,4-*b*]-indol-3-one (7b). To a stirred solution of compound **6a** (1.0 g, 5.78 mmol) in toluene (20 mL) were successively added K_2CO_3 (7.98 g, 57.8 mmol), benzenesulfonyl chloride (5.8 g, 33 mmol), and triethyl benzyl ammonium chloride (0.33 g, 1.44 mmol). The reaction mixture was stirred for 6 h at room temperature. It was then filtered and washed with ethyl acetate (3×40 mL). The combined organic phase was washed with brine (20 mL), dried (Na_2SO_4), and concentrated under reduced pressure to get a crude yellow residue. This was purified by column chromatography (1:5 $CHCl_3$/ethyl acetate, R_f=0.45) to give **7b** (1.23 g, 68%) as a white solid. Mp 215–217 °C; FTIR (KBr) cm^{-1} 3070, 2937, 1774 (s), 1582, 1460, 1378, 1272, 1187, 1120, 1046, 979, 766; ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.38 (d, 1H, J=8.6 Hz), 8.15 (dd, 2H, J_1=1.4 Hz, J_2=7.0 Hz), 7.32–7.65 (m, 6H), 5.29 (s, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 160.3, 144.0, 143.0, 138.01, 134.4, 129.4, 129.1, 127.8, 127.4, 124.5, 121.7, 121.2, 115.7, 65.5; MS ESI [M+Na]$^+$ 336.2. Anal. Calcd for $C_{16}H_{11}NO_4S$: C, 61.33; H, 3.54; N, 4.47. Found: C, 61.82; H, 3.72; N, 4.68.

4.4.4. 1,4-Dihydro-4-(2,2-dimethyl-1-oxopropyl)-3*H*-furo[3,4-*b*]indol-3-one (7c). To a stirred solution of *n*-butyllithium (0.44 mL, 0.7 mmol) in THF (20 mL) at −78 °C temperature (ethyl acetate/liquid N_2 bath) under an inert atmosphere was added a solution of **6a** (0.1 g, 0.578 mmol) in THF (5 mL). The resulting solution was stirred at −78 °C for 15 min, after which a solution of pivaloyl chloride (0.2 mL, 1.73 mmol) in THF (5 mL) was added. The cooling bath was removed after about 1 h at −78 °C temperature and the reaction mixture was brought to room temperature over a period of 1 h and further stirred for 30 min. The reaction was then quenched with 10% NH_4Cl (15 mL) and the resulting solution was concentrated. The aqueous layer was extracted with diethyl ether (3×25 mL). The combined organic phase was washed with brine (20 mL), dried (Na_2SO_4), and concentrated under reduced pressure to get a crude residue. The crude product was purified by column chromatography (3:7 $CHCl_3$/petroleum ether, R_f=0.82) to get **7c** (0.105 g, 71%) as a white solid. Mp 130 °C; FTIR (KBr) cm^{-1} 1742 (s), 1682 (s), 1580, 1530; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.86 (d, 1H, J=8.0 Hz), 7.62 (d, 1H, J=8.0 Hz), 7.51 (t, 1H, J=7.2 Hz), 7.30 (t, 1H, J=7.8 Hz), 5.39 (s, 2H), 1.51 (s, 9H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 177.1, 163.7, 144.1, 134.2, 134.7, 128.7, 127.8, 121.0, 120.3, 111.6, 66.9, 42.5, 29.1. Anal. Calcd for $C_{15}H_{15}NO_3$: C, 70.02; H, 5.88; N, 5.44. Found: C, 69.86; H, 5.84; N, 5.18.

4.4.5. 1,4-Dihydro-4-methyl-3*H*-furo[3,4-*b*]indol-3-one (7d). In a flame-dried flask flushed with nitrogen, LDA (6.36 mmol) was prepared by adding diisopropylamine (7.62 mmol) to a solution of *n*-BuLi (6.36 mmol, 1.6 M in hexane) in THF (40 mL) at −78 °C under nitrogen atmosphere. After the solution was stirred for 10 min at −78 °C, compound **6a** (1.0 g, 5.78 mmol) in THF (10 mL) was added dropwise over 15 min. The reaction mixture was stirred at −78 °C for 15 min and then allowed to warm to −40 °C. Thereafter, a solution of MeI (0.396 mL, 6.36 mmol) in THF (10 mL) was added dropwise over 15 min. The reaction mixture was further stirred and allowed to warm slowly to room temperature over 3 h. The reaction was then quenched with 10% NH_4Cl (25 mL) and the resulting solution was concentrated under reduced pressure. It was extracted with diethyl ether (3×50 mL). The combined organic layers were washed with brine (20 mL), dried (Na_2SO_4), and concentrated under reduced pressure to get a crude residue. The crude product was purified by column chromatography (1:4 ethyl acetate/petroleum ether,

R_f=0.78) to get **7d** (0.908 g, 84%) as a white solid. Mp 147 °C; FTIR (KBr) cm^{-1} 2942, 2362, 1747 (s), 1571, 1456, 1321 (m), 1199, 1047, 979, 740; ^1H NMR (200 MHz, $CDCl_3$): δ 7.64 (d, 1H, J=8.2 Hz), 7.40–7.50 (m, 2H), 7.15–7.30 (m, 1H), 5.39 (s, 2H), 3.95 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 163.8, 144.3, 133.8, 128.6, 126.1, 121.0 (2 'C'); 120.2, 111.3, 66.9, 30.0; HRMS ESI: for $C_{11}H_9NO_2$ $[M+H]^+$ calcd 188.0712, found 188.0709.

4.4.6. 1,4-Dihydro-4-(phenylmethyl)-3*H*-furo[3,4-*b*]-indol-3-one (7e). This compound was prepared as a white solid in 62% yield by reaction of compound **6a** with benzyl chloride following the general procedure for the N-benzylation described for **6b** to **7f**. The crude product was purified by column chromatography (1:5 ethyl acetate/petroleum ether, R_f=0.62). Mp 112 °C; FTIR (KBr) cm^{-1} 2937, 2885, 1741 (s), 1560, 1442 (m), 1325 (m), 1265, 1178, 1058, 983, 737; ^1H NMR (200 MHz, $CDCl_3$): δ 7.64 (d, 1H, J=7.8 Hz), 7.33–7.47 (m, 3H), 7.18–7.29 (m, 5H), 5.54 (s, 2H), 5.41 (s, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 163.7, 143.6, 136.6, 134.6, 128.7 (two 'C'), 128.3, 127.8, 127.3, 126.3, 121.2, 120.5, 112.1, 67.0, 47.5; HRMS ESI: for $C_{17}H_{13}NO_2$ $[M+H]^+$ calcd 264.1025, found 264.1020.

4.4.7. 1,4-Dihydro-7-methoxy-4-(phenylmethyl)-3*H*-furo[3,4-*b*]indol-3-one (7f). To a stirred solution of **6b** (0.2 g, 0.985 mmol) in dry acetone (20 mL) under an inert atmosphere was added K_2CO_3 (0.679 g, 4.92 mmol) and NaI (0.295 g, 1.97 mmol). After 25 min, a solution of benzyl chloride (0.16 mL, 1.97 mmol) in dry acetone (5 mL) was added to this mixture. The resulting mixture was further stirred for 3 h and then extracted with diethyl ether (3×50 mL). The combined organic layers were washed with brine (30 mL), dried (Na_2SO_4), and concentrated under reduced pressure to get a crude residue. The residue on column chromatographic purification (3:7 ethyl acetate/petroleum ether, R_f=0.71) afforded **7f** (0.2 g, 69%) as a light yellowish solid. Mp 135 °C; FTIR (KBr) cm^{-1} 2935, 1740 (s), 1623, 1558, 1504 (m), 1456, 1306, 1242 (m), 1168, 983, 792, 752; ^1H NMR (200 MHz, $CDCl_3$): δ 7.15–7.70 (m, 6H), 7.05–7.13 (m, 1H), 7.0 (s, 1H), 5.56 (s, 2H), 5.36 (s, 2H), 3.83 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 163.6, 154.9, 138.9, 136.6, 133.6, 128.7, 128.5, 127.7, 127.2, 120.6, 117.4, 112.9, 101.6, 66.8, 55.6, 47.5; HRMS ESI: for $C_{18}H_{15}NO_3$ $[M+H]^+$ calcd 294.1130, found 294.1140.

4.4.8. Ethyl 1-bromo-1,3-dihydro-3-oxo-4*H*-furo[3,4-*b*]indole-4-carboxylate (8). A mixture of **7** (2.0 g, 8.16 mmol), NBS (1.6 g, 8.97 mmol), and benzoyl peroxide (70 mg) in CCl_4 (40 mL) was heated at reflux under the exposure of a 100-W bulb for 2 h. The completion of the reaction was ascertained by the disappearance of NBS from the bottom of the flask. The mixture was cooled to 0 °C, filtered, and then concentrated under reduced pressure. The residue was diluted with water (50 mL). The mixture was extracted with ether (3×30 mL). The combined organic extracts were washed with $NaHCO_3$ solution (25 mL), brine, and concentrated. Purification of the crude residue by chromatography (1:4 $CHCl_3$/petroleum ether, R_f=0.38) gave **8** (1.85 g, 70%) as a brownish white solid. Mp 132–134 °C; FTIR (KBr) cm^{-1} 2922, 1799 (s), 1748 (s), 1444, 1383, 1230, 1145, 977, 822, 760; ^1H NMR (200 MHz, $CDCl_3$) δ 8.4 (d, 1H, J=8.2 Hz), 7.72 (d, 1H, J=7.8 Hz), 7.62 (t, 1H, J=8.2 Hz), 7.45 (t, 1H, J=7.8 Hz), 7.35 (s, 1H), 4.55 (q, 2H, J=7.2 Hz), 1.52 (t, 3H, J=7.2 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 156.7, 149.6, 144.9, 142.9, 129.6, 126.9, 124.8, 120.8, 120.3, 116.9, 68.6, 64.5, 14.1. Anal. Calcd for $C_{13}H_{10}BrNO_4$: C, 48.17; H, 3.11; N, 4.32. Found: C, 48.39; H, 2.87; N, 4.36.

4.4.9. Ethyl 1,3-dihydro-3-oxo-1-phenylsulfanyl-4*H*-furo[3,4-*b*]indole-4-carboxylate (9). To a stirred solution of NaSPh (0.815 g, 6.17 mmol) in MeOH (40 mL) at room temperature under an argon atmosphere was added a solution of compound **8** (2.0 g, 6.17 mmol). The reaction mixture was heated at reflux for 3.5 h and then cooled to room temperature. The contents of the flask were diluted with water (50 mL) and then extracted into diethyl ether (3×40 mL). The combined organic layers were washed with brine (30 mL), dried (Na_2SO_4), and concentrated under reduced pressure to get a crude residue. The residue was purified by chromatography (1:5 ethyl acetate/petroleum ether, R_f=0.46) to give **9** (1.68 g, 77%) as a white solid. Mp 155–157 °C; FTIR (KBr) cm^{-1} 2924, 1742 (s), 1680 (s), 1596, 1414, 1378, 1321, 1238, 1109, 1037, 747, 695, 618; ^1H NMR (200 MHz, $CDCl_3$) δ 8.3 (d, 1H, J=7.6 Hz), 8.05 (d, 1H, J=8.8 Hz), 7.20–7.60 (m, 7H), 4.41 (q, 2H, J=6.8 Hz), 1.37 (t, 3H, J=6.8 Hz); ^{13}C NMR (50 MHz, d_6-DMSO) δ 162.0, 150.1, 135.9, 133.6, 131.4, 129.3, 128.1, 127.6, 127.2, 125.5, 123.2, 123.0, 122.5, 114.3, 64.2, 50.6, 13.6. Anal. Calcd for $C_{19}H_{15}NO_4S$: C, 64.58; H, 4.28; N, 3.96. Found: C, 64.96; H, 4.32; N, 4.12.

4.4.10. Ethyl 1,3-dihydro-3-oxo-1-(phenylsulfonyl)-4*H*-furo[3,4-*b*]indole-4-carboxylate (10). To a well-stirred solution of **8** (1.8 g, 5.55 mmol) in dry DMF (20 mL) was added solid sodium benzenesulfinate (0.91 g, 5.55 mmol) in portions. The mixture was stirred overnight at room temperature and the resulting mass was poured into cold water (50 mL). The yellow crystalline material precipitated was filtered and recrystallized (1:5 CH_2Cl_2/hexane, R_f=0.58) to give **10** (1.82 g, 85%) in white crystalline state. Mp 220–222 °C; FTIR (KBr) cm^{-1} 2362, 2356, 1801 (s), 1734 (s), 1560, 1447, 1384, 1350, 1312, 1150, 995, 750; ^1H NMR (200 MHz, $CDCl_3$) δ 8.36 (d, 1H, J=8.6 Hz), 8.05 (d, 1H, J=7.6 Hz), 7.86 (dd, 2H, J_1=8.0 Hz, J_2=8.6 Hz), 7.45–7.8 (m, 5H), 6.25 (s, 1H), 4.51 (q, 2H, J=7.0 Hz), 1.51 (t, 3H, J=7.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 156.9, 149.5, 142.9, 136.6, 135.1, 134.3, 129.9, 129.7, 129.5, 129.3, 125.2, 122.7, 121.3, 116.8, 87.5, 64.5, 14.1; HRMS ESI: for $C_{19}H_{15}NO_6S$ $[M+H]^+$ calcd 386.0728, found 386.0722. Anal. Calcd for $C_{19}H_{15}NO_6S$: C, 59.21; H, 3.92; N, 3.63. Found: C, 59.35; H, 3.84; N, 3.76.

4.4.11. 7-Hydroxy-10-methyl-5*H*-benzo[*b*]carbazole-6,11-dione (12a). This compound was prepared as a red solid in 85% yield (70% by method A) by condensation of **10** and **11a**, according to general procedure for the annulation with lithium *tert*-butoxide (method B). Mp 308–310 °C; FTIR (KBr) cm^{-1} 3305, 2925, 2362, 1630 (s), 1629 (s), 1533, 1460, 1411, 1384, 1205, 1172, 1106, 746; ^1H NMR (200 MHz, $CDCl_3$+2 drops of d_6-DMSO) δ 12.65 (s, 1H), 12.23 (br, 1H), 8.05 (d, 1H, J=7.8 Hz), 7.31 (d, 1H, J=7.8 Hz), 7.0–7.20 (m, 3H), 6.81 (d, 1H, J=8.6 Hz), 2.48 (s, 3H). ^{13}C NMR (50 MHz, d_6-DMSO) δ 182.6,

182.3, 160.7, 141.7, 138.5, 135.2, 133.2, 129.9, 127.0, 123.9, 123.6, 123.2, 122.3, 118.1, 115.7, 113.5, 22.2; MS EI, *m/z*: $[M]^+$, 277 (100%), 248, 220, 204, 191, 165, 129, 112, 89, 78, 69. Anal. Calcd for $C_{17}H_{11}NO_3$: C, 73.64; H, 4.00; N, 5.05. Found: C, 73.96; H, 3.80; N, 4.82.

4.4.12. 1,2,3,7-Tetrahydroindeno[6,7-*b*]carbazol-6,12-dione (12b). This compound was prepared as a red solid in 75% (62% yield by method A) yield by condensation of **10** and **11b**, according to general procedure for the annulation with lithium *tert*-butoxide (method B). Mp 318–20 °C; FTIR (KBr) cm^{-1} 3315 (br), 2362, 1626 (s), 1629 (s), 1529, 1421, 1226 (m), 1143, 1037, 750; ^1H NMR (200 MHz, sparingly soluble in $CDCl_3$) δ 12.62 (s, 1H), 9.33 (br, 1H), 8.39 (d, 1H, J=8.2 Hz), 7.37–7.54 (m, 3H), 7.06 (s, 1H), 3.43 (t, 2H, J=7.4 Hz), 2.92 (t, 2H, J=7.6 Hz), 2.06–2.25 (m, 2H). (Due to poor solubility in common deuterated solvents, ^{13}C NMR could not be recorded.) MS ESI $[M+H]^+$ 304.2. Anal. Calcd for $C_{19}H_{13}NO_3$: C, 75.24; H, 4.32; N, 4.62. Found: C, 75.15; H, 4.57; N, 4.83.

4.4.13. 6-Hydroxy-5-methoxy-1,2,3,4-tetrahydro-8*H*-naphtho[2,1-*b*]carbazol-7,13-dione (12e). This compound was prepared as a red solid in 72% yield by condensation of **10** and a 3:7 mixture of **11c** and **11e**, according to general procedure for the annulation with lithium *tert*-butoxide (method B). Mp 333–35 °C; FTIR (KBr) cm^{-1} 3276 (br), 2362, 1612 (s), 1610 (s), 1400, 1242 (m), 132, 144; ^1H NMR (200 MHz, sparingly soluble in $CDCl_3$) δ 13.05 (s, 1H), 9.32 (br s, 1H), 8.43 (d, 1H, J=7.6 Hz), 7.97 (d, 1H, J=7.6 Hz), 7.35–7.50 (m, 2H), 3.99 (s, 3H), 3.25–3.40 (m, 2H), 2.60–2.90 (m, 6H). (Due to poor solubility in common deuterated solvents, ^{13}C NMR could not be recorded.) MS ESI $[M+H]^+$ 348.2. Anal. Calcd for $C_{21}H_{17}NO_4$: C, 72.61; H, 4.93; N, 4.03. Found: C, 72.73; H, 5.07; N, 4.18.

4.4.14. Methyl 6-hydroxy-5-methoxy-1,2,3,4-tetrahydro-8*H*-naphtho[2,1-*b*]carbazole-2-carboxylate (12f). This compound was prepared as a red solid in 70% yield by condensation between **10** and a 1:4 mixture of **11d** and **11f**, according to the general procedure for the annulation with lithium *tert*-butoxide (method B). Mp 326–28 °C; FTIR (KBr) cm^{-1} 3292 (br s), 1724 (s), 1612 (s), 1609 (s), 1533, 1477, 1405, 1334, 1255 (m), 1172, 1137, 1054, 1018, 754; ^1H NMR (200 MHz, $CDCl_3$) δ 13.04 (s, 1H); 9.32 (br s, 1H), 8.37 (d, 1H, J=8.2 Hz), 7.45 (d, 1H, J=8.2 Hz), 7.26–7.40 (m, 2H), 4.01 (s, 3 H), 3.76 (s, 3H), 3.30–3.50 (m, 1H), 2.90–3.25 (m, 3H), 2.60–2.85 (m, 3H). (Due to poor solubility in common deuterated solvents, ^{13}C NMR could not be recorded.) MS ESI $[M+H]^+$ 406.2. Anal. Calcd for $C_{23}H_{19}NO_6$: C, 68.14; H, 4.72, N, 3.46. Found: C, 68.32; H, 4.83; N, 3.61.

4.4.15. 7-Hydroxy-8-methoxy-5*H*-naphtho[2,1-*b*]carbazol-6,13-dione (12g). This compound was prepared as a pink solid in 67% yield by condensation of **10** and **11g** according to the general procedure of annulation with lithium *tert*-butoxide (method B). Mp 342–44 °C; FTIR (KBr) cm^{-1} 3296 (br), 2925, 1614 (s), 1539, 1394, 1317 (m), 1132, 1060, 710; ^1H NMR (200 MHz, sparingly soluble in d_6-DMSO) δ 13.01 (s, 1H), 12.49 (s, 1H), 9.63 (d, 1H, J=8.5 Hz), 8.23 (d, 1H, J=8.0 Hz); 8.06 (d, 1H, J=8.2 Hz), 7.52–7.63 (m, 3H), 7.43–7.48 (t, 1H, J=7.5 Hz), 7.34–7.38 (t, 1H, J=7.5 Hz), 4.09 (s, 3H). (Due to poor solubility in common deuterated solvents; ^{13}C NMR could not be recorded.) MS ESI $[M+H]^+$ 344.1. Anal. Calcd for $C_{21}H_{13}NO_4$: C, 73.46; H, 3.82, N, 4.08. Found: C, 73.32; H, 3.95; N, 4.21.

4.4.16. 7-Hydroxy-12-methoxy-5*H*-naphtho[2,3-*b*]carbazol-6,13-dione (12h). This compound was prepared as an orange yellow solid in 76% yield by condensation of **10** and **11h**, according to general procedure for the annulation with lithium *tert*-butoxide (method B). Mp>350 °C; FTIR (KBr) cm^{-1}: 3293, 3250, 3059, 1650, 1604 (s), 1602 (s), 1528 (m), 1442, 1400, 1364, 1236, 1145, 1020, 742; ^1H NMR (200 MHz, sparingly soluble in d_6-DMSO) δ 13.04 (br, 1H), 12.24 (s, 1H), 8.42 (d, 1H, J=6.0 Hz), 8.31 (d, 1H, J=6.0 Hz), 7.90–7.72 (m, 2H), 7.70–7.26 (m, 4H), 3.98 (s, 3H). (Due to poor solubility in common deuterated solvents; ^{13}C NMR could not be recorded.) MS ESI $[M+H]^+$ 344.1. Anal. Calcd for $C_{21}H_{13}NO_4$: C, 73.46; H, 3.82; N, 4.08. Found: C, 73.67; H, 3.75; N, 4.01.

4.4.17. Ethyl 6,13-dioxo-7-hydroxy-12-methoxynaphtho[2,3-*b*]carbazole-5-carboxylate (12i). The preparative procedure is essentially same as that for **12h**, except that the reaction mixture was quenched at 0 °C with ice-cold 10% NH_4Cl. Compound **12h** (0.062 g, 72%) was obtained as a deep red solid. Mp 180 °C; FTIR (KBr) cm^{-1} 3432, 2991, 2931, 1755 (s), 1660, 1624 (s), 1622 (s), 1542, 1430, 1366, 1306, 1236, 1148, 1070, 1022, 756; ^1H NMR (200 MHz, $CDCl_3$, poorly soluble) δ 14.64 (s, 1H), 8.70–8.45 (m, 2H), 8.40–8.28 (m, 1H), 8.10–7.92 (d, 1H, J=6.0 Hz), 7.90–7.75 (m, 2H), 7.70–7.45 (m, 2H), 4.62 (q, 2H, J=8.0 Hz), 4.11 (s, 3H), 1.54 (t, 3H, J=8.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 182.2, 180.2, 162.9, 153.4, 150.5, 139.2, 135.9, 133.4, 131.2, 129.6, 129.2, 129.1, 126.4, 125.3, 125.0, 124.9, 124.3, 118.2, 113.7, 109.6, 65.1, 62.4, 13.9; MS ESI $[M+H]^+$ 416.1. Anal. Calcd for $C_{24}H_{17}NO_6$: C, 69.39, H, 4.12; N, 3.37. Found: C, 69.67; H, 3.95; N, 3.52.

4.4.18. 7-Hydroxy-10-methoxy-8-methyl-5*H*-benzo[*b*]-carbazole-6,11-dione (12j). This compound was prepared as an orange yellow solid in 78% yield by condensation of **10** and **11j**, according to the general procedure for the annulation with lithium *tert*-butoxide (method B). Mp 312 °C; FTIR (KBr) cm^{-1} 3290 (br s), 2930, 2360, 1618 (s), 1616 (s), 1530, 1440, 1410, 1366, 1238, 1142, 1020, 756; ^1H NMR (200 MHz, d_6-DMSO, poorly soluble) δ 13.14 (s, 1H), 12.32 (s, 1H), 8.56 (d, 1H, J=6.8 Hz), 8.04 (d, 1H, J=8.0 Hz), 7.38–7.70 (m, 2H), 7.30 (s, 1H), 3.88 (s, 3H), 2.30 (s, 3H). (Due to poor solubility in common deuterated solvents; ^{13}C NMR could not be recorded.) MS ESI $[M+H]^+$ 308.1. Anal. Calcd for $C_{18}H_{13}NO_4$: C, 70.35; H, 4.26; N, 4.56. Found: C, 70.28; H, 4.41; N, 4.49.

4.4.19. Ethyl 7-hydroxy-10-methoxy-8-methyl-6,11-dioxo-benzo[*b*]carbazole-5-carboxylate (12k). Annulation method B when applied to **10** and **11j**, followed by work-up, i.e., quenching with aq NH_4Cl solution (10 mL) at 0 °C, dilution with ethyl acetate (3×30 mL), washing with brine (3×20 mL), drying (Na_2SO_4), concentration under reduced pressure, and purification by column chromatography gave compound **12k** as a red solid in 75% yield.

Mp 153–155 °C; FTIR (KBr) cm^{-1} 3428, 3007, 2936, 1750 (s), 1628 (s), 1624 (s), 1542, 1432, 1360, 1310, 1238, 1140, 1070, 1022, 754; ^1H NMR (200 MHz, $CDCl_3$): δ 12.93 (s, 1H), 8.55 (d, 1H, J=6.8 Hz), 7.97 (d, 1H, J=8.4 Hz), 7.35–7.62 (m, 2H), 7.21 (s, 1H), 4.60 (q, 2H, J=7.2 Hz), 4.03 (s, 3H), 2.38 (s, 3H), 1.50 (t, 3H, J=7.2 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 181.1, 180.7, 156.2, 154.0, 150.5, 139.3, 137.9, 134.6, 129.3, 125.9, 125.4, 124.4, 124.3, 123.5, 116.4, 115.2, 113.8, 65.0, 56.7, 16.6, 13.9; MS ESI $[M+H]^+$ 380.1. Anal. Calcd for $C_{21}H_{17}NO_6$: C, 66.49; H, 4.52; N, 3.69. Found: C, 66.56; H, 4.59; N, 3.76.

4.4.20. 5*H*-Benzo[*b*]carbazole-6,11-dione (14). This compound was prepared as a dark orange solid in 64% yield by condensation of **7a** and bromobenzene following general procedure for the LDA mediated annulation (method A). Mp 306–308 °C (lit.[14] 307–310 °C); FTIR (KBr) cm^{-1} 3261, 2362, 1644, 1648, 1527, 1525, 1390, 1398, 1232, 1213, 1014, 709; ^1H NMR (200 MHz, d_6-DMSO): δ 13.07 (br, 1H), 8.19 (d, 1H, J=7.7 Hz), 8.0–8.15 (m, 2H), 7.75–7.89 (m, 2H), 7.58 (d, 1H, J=7.7 Hz), 7.32–7.50 (m, 2H); ^{13}C NMR (50 MHz, d_6-DMSO) δ 181.2, 178.3, 139.1, 138.0, 135.0, 134.9, 133.9, 133.5, 127.7, 126.9, 126.8, 124.8, 124.7, 123.2, 118.3, 114.7. All these data were in agreement with the reported values.[14]

4.4.21. Methyl 1-hydroxy-9-methyl-9*H*-carbazole-2-carboxylate (16a). This compound was prepared as a white solid in 72% yield by condensation between **7d** and methyl acrylate, following general procedure for the LDA promoted annulation (method A). Mp 98–100 °C; FTIR (KBr) cm^{-1} 3066, 2977, 2362, 1674 (s), 1640, 1585, 1446 (m), 1315 (s), 1147, 1085, 993, 873, 754; ^1H NMR (200 MHz, $CDCl_3$): δ 11.68 (s, 1H), 8.04 (d, 1H, J=7.8 Hz), 7.50–7.66 (m, 3H), 7.40 (d, 1H, J=8.1 Hz), 7.21–7.24 (m, 1H), 4.23 (s, 3H), 3.97 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 171.9, 150.8, 142.3, 128.6, 128.5, 126.4, 122.1, 120.8, 119.5, 119.2, 110.9, 109.1, 107.7, 52.1, 31.9; MS EI $[M+H]^+$ 256.1. Anal. Calcd for $C_{15}H_{13}NO_3$: C, 70.58; H, 5.13; N, 5.49. Found: C, 70.30; H, 5.02; N, 5.27.

4.4.22. Methyl 1-hydroxy-3,9-dimethyl-9*H*-carbazole-2-carboxylate (16b). This compound was prepared as a yellow solid in 78% yield by condensation between **7d** and methyl crotonate, following general procedure for the LDA promoted annulation (method A). Mp 170 °C; FTIR (KBr) cm^{-1} 3402 (br s), 2929, 2362, 1735, 1655 (s), 1546, 1442 (m), 1376, 1319 (s), 1265, 1159; ^1H NMR (200 MHz, $CDCl_3$): δ 12.32 (s, 1H), 7.99 (d, 1H, J=7.6 Hz), 7.25–7.50 (m, 2H), 7.10–7.23 (m, 1H), 4.19 (s, 3H), 3.97 (s, 3H), 2.65 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 173.5, 152.1, 142.5, 130.1, 127.1, 126.7, 121.7, 120.7, 118.8, 113.6, 108.9, 107.7, 51.8, 31.8, 24.4; MS ESI $[M+H]^+$ 270.1. Anal. Calcd for $C_{16}H_{15}NO_3$: C, 71.36; H, 5.61; N, 5.20. Found: C, 71.62; H, 5.42; N, 5.37.

4.4.23. Methyl 1-methoxy-3,9-dimethyl-9*H*-carbazole-2-carboxylate (16c). This compound was prepared as a white solid in 76% yield from **16b**, following the general procedure of O-methylation for the phenolic compounds described above. Mp 90–92 °C; FTIR (KBr) 3408 (br s), 2934, 2352, 1730, 1660 (s), 1543, 1438 (m), 1310 (s), 1158 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 8.03 (d, 1H, J=7.8 Hz), 7.67 (s, 1H), 7.45–7.56 (m, 1H), 7.39 (d, 1H, J=8.0 Hz), 7.15–7.27 (m, 2H), 4.09 (s, 3H), 4.05 (s, 3H), 3.95 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 169.2, 143.1, 142.1, 142.2, 130.7, 126.3, 126.1, 125.6, 122.3, 120.3, 119.1, 117.2, 108.6, 63.7, 52.2, 30.9, 19.3. Anal. Calcd for $C_{17}H_{17}NO_3$: C, 72.07; H, 6.05; N, 4.94. Found: C, 72.16; H, 5.96; N, 4.66.

4.4.24. 1-Hydroxy-9-methyl-9*H*-carbazole-2-carbonitrile (16d). This compound was prepared as an off-white solid in 81% by condensation between **7d** and acrylonitrile, following general procedure for the LDA promoted annulation (method A). Mp 120–22 °C; FTIR (KBr) 3432, 3262, 2977, 2362, 2232, 1640, 1527, 1438, 1242, 1085, 754 cm^{-1}; ^1H NMR (200 MHz, d_6-DMSO): δ 10.86 (s, 1H), 8.21 (d, 1H, J=8.0 Hz), 7.82 (d, 1H, J=8.2 Hz), 7.62–7.48 (m, 2H), 7.35–7.26 (m, 2H), 4.15 (s, 3H); ^{13}C NMR (50 MHz, d_6-DMSO): δ 147.0, 141.9, 130.3, 127.0, 127.5, 122.7, 121.5, 121.8, 119.3, 118.3, 113.7, 109.8, 97.3, 31.9; HRMS ESI: for $C_{14}H_{10}N_2O$ $[M+H]^+$ calcd 264.1025, found 264.1020.

4.4.25. 9-Methyl-2-phenylsulfonyl-9*H*-carbazole-1-ol (16e). This compound was prepared as a brown crystalline needle form in 65% yield by reaction between **7d** and vinyl sulfone, according to general procedure for the LDA promoted annulation (method A). Mp 160–162 °C; FTIR (KBr) 3062, 2975, 2355, 1602, 1482, 1455, 1320, 1147, 1088, 754 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 9.91 (s, 1H), 8.03–7.85 (m, 2H), 7.66–7.35 (m, 7H), 7.30–7.20 (m, 2H), 4.22 (s, 3H); MS ESI $[M+H]^+$ 338.1. Anal. Calcd for $C_{19}H_{15}NO_4S$: C, 67.64; H, 4.48; N, 4.15. Found: C, 67.92; H, 4.64; N, 4.25.

4.4.26. 1-Methoxy-9-methyl-2-phenylsulfonyl-9*H*-carbazole (16f). This compound was prepared from **16f** as a light brown solid in 73% yield, following the general procedure for the O-methylation of phenolic compounds using Me_2SO_4. Mp 165 °C; ^1H NMR (200 MHz, $CDCl_3$): δ 8.10–7.95 (m, 5H), 7.56–7.30 (m, 6H), 4.06 (s, 3H), 4.05 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 143.2, 142.7, 132.7, 130.7, 128.6, 127.8, 122.0, 121.0, 120.1, 119.7, 116.0, 109.2, 64.8, 31; MS ESI $[M+H]^+$ 352.1. Anal. Calcd for $C_{20}H_{17}NO_3S$: C, 68.36; H, 4.88; N, 3.99. Found: C, 68.64; H, 4.75; N, 4.12.

4.4.27. Methyl 1-hydroxy-9-(phenylmethyl)-9*H*-carbazole-2-carboxylate (17a). This compound was prepared as a white solid in 64% yield by condensation between **7e** and methyl acrylate, following general procedure for the LDA promoted annulation (method A). Mp 118 °C; FTIR (KBr) cm^{-1} 3031, 2926, 1712, 1666 (s), 1445 (m), 1319 (s), 1261 (m), 1187, 1151, 1025, 744; ^1H NMR (200 MHz, $CDCl_3$): δ 11.72 (s, 1H), 8.08 (d, 1H, J=8.0 Hz), 7.72–7.55 (m, 2H), 7.47–7.39 (m, 2H), 7.30–7.12 (m, 6H), 5.97 (s, 2H), 3.97 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 171.9, 150.6, 141.9, 138.7, 129.0, 128.5, 128.2, 127.2, 127.1, 126.5, 122.6, 121.0, 119.9, 119.6, 111.0, 109.9, 108.1, 52.2, 48.6; HRMS ESI: for $C_{21}H_{17}NO_3$ $[M+H]^+$ calcd 332.1287, found 332.1276.

4.4.28. Methyl 1-hydroxy-3-methyl-9-(phenylmethyl)-9*H*-carbazole-2-carboxylate (17b). This compound was prepared as a white solid in 67% yield by condensation

between **7e** and methyl crotonate, following general procedure for the LDA promoted annulation (method A). Mp 122–24 °C; FTIR (KBr) cm^{-1} 3035, 2923 (s), 2852, 1660 (s), 1639, 1444, 1317 (m), 1263, 1157, 1022, 746; ^1H NMR (200 MHz, $CDCl_3$): δ 12.34 (s, 1H), 8.03 (d, 1H, J=8.0 Hz), 7.45–7.36 (m, 3H), 7.28–7.12 (m, 6H), 5.94 (s, 2H), 4.0 (s, 3H), 2.68 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 173.4, 151.9, 150.7, 142.2, 138.9, 130.7, 128.4, 127.5, 127.0, 126.9, 126.4, 122.2, 120.93, 119.3, 113.7, 109.8, 108.1, 52.0, 48.4, 24.5; HRMS ESI: for $C_{22}H_{19}NO_3$ $[M+H]^+$ calcd 346.1443, found 346.1442.

4.4.29. Methyl 1-hydroxy-3-methyl-9*H*-carbazole-2-carboxylate (17c). To a stirred solution of **17b** (0.05 g, 0.145 mmol) in dry CH_2Cl_2 (20 mL) solution at room temperature was added anhydrous $AlCl_3$ (0.095 g, 0.725 mmol) under nitrogen atmosphere. The mixture was stirred overnight and the resulting mass was poured into cold water (30 mL). The white material precipitated was filtered off and the filtrate was extracted with CH_2Cl_2 (3×30 mL). The combined organic extracts were washed with H_2O (20 mL), brine (20 mL), and dried (Na_2SO_4). Concentration of the organic layer gave a solid residue. This was purified by column chromatography (1:3 EtOAc/petroleum ether, R_f=0.65) to give **17c** (0.03 g, 81%) as a white solid. Mp 138–40 °C; FTIR (KBr) cm^{-1} 3373 (s), 2945, 1668 (s), 1627, 1448, 1326 (s), 1261 (m), 1141, 1002, 808, 748; ^1H NMR (200 MHz, $CDCl_3$): δ 12.0 (s, 1H), 8.41 (br s, 1H), 8.01 (d, 1H, J=8.0 Hz), 7.48–7.42 (m, 1H), 7.40 (s, 1H), 7.24–7.16 (m, 2H), 4.0 (s, 3H), 2.68 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 173.1, 150.2, 140.4, 130.8, 127.2, 127.1, 127.0, 122.7, 121.1, 119.6, 113.8, 111.3, 107.7, 51.9, 24.4; HRMS ESI: for $C_{15}H_{13}NO_3$ $[M+H]^+$ calcd 256.0974, found 256.0964.

4.4.30. Dimethyl 1-hydroxy-9-(phenylmethyl)-9*H*-carbazole-2,3-dicarboxylate (17d). This compound was prepared as a white solid in 85% yield by condensation between **7e** and dimethyl maleate, following the general procedure for the LDA promoted annulation (method A). Mp 158–160 °C; ^1H NMR (200 MHz, $CDCl_3$) δ 11.38 (s, 1H), 8.02 (d, 1H, J=8.0 Hz), 7.83 (s, 1H), 7.53–7.40 (m, 2H), 7.35–7.12 (m, 6H), 5.97 (s, 2H), 3.94 (s, 3H), 3.93 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 170.5, 169.7, 149.5, 141.8, 137.9, 128.9, 128.3, 127.3, 126.9, 126.3, 126.1, 125.0, 122.3, 120.7, 120.09, 112.7, 109.9, 106.2, 52.4, 52.2, 48.3; HRMS ESI: for $C_{23}H_{19}NO_5$ $[M+H]^+$ calcd 390.1341, found 390.1332. Anal. Calcd for $C_{23}H_{19}NO_5$: C, 70.94; H, 4.92; N, 3.60. Found: C, 70.82; H, 4.77; N, 3.78.

4.4.31. Methyl 1-hydroxy-6-methoxy-3-methyl-9-(phenylmethyl)-9*H*-carbazole-2-carboxylate (17e). This compound was prepared as a white solid in 58% yield by condensation between **7f** and methyl crotonate, following the general procedure for the LDA promoted annulation (method A). Mp 146–48 °C; FTIR (KBr) 3235, 2923 (s), 2852, 1666 (s), 1626 (s), 1623, 1560, 1498 (m), 1310, 1239 (m), 1155, 983, 756; ^1H NMR (200 MHz, $CDCl_3$) δ 12.34 (s, 1H), 7.45 (d, 1H, J=2.5 Hz), 7.38 (s, 1H), 7.30–7.0 (m, 7H), 5.91 (s, 2H), 4.0 (s, 3H), 3.90 (s, 3H), 2.67 (s, 3H); MS ESI $[M+H]^+$ 376.2. Anal. Calcd for $C_{23}H_{21}NO_4$: C, 73.58; H, 5.64; N, 3.73. Found: C, 73.86; H, 5.78; N, 3.86. ^{13}C NMR could not be recorded due to the poor solubility in common deuterated solvents.

4.4.32. Methyl 1-hydroxy-6-methoxy-3-methyl-9*H*-carbazole-2-carboxylate (17f). This compound was obtained as a light brown solid in 71% yield from *N*-benzyl compound **17d**, following the procedure adopted for compound **17c**. Mp 162–64 °C; FTIR (KBr) 3402 (s), 2948, 1672 (s), 1625, 1622, 1552, 1488 (m), 1320, 1235 (m), 1160, 860 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 12.0 (s, 1H), 8.30 (br s, 1H), 7.45 (d, 1H, J=2.3 Hz), 7.40 (s, 1H), 7.36 (s, 1H), 7.13 (d, 1H, J=2.3 Hz), 4.0 (s, 3H), 3.93 (s, 3H), 2.68 (s, 3H); MS ESI $[M+H]^+$ 286.2. Anal. Calcd for $C_{16}H_{15}NO_4$: C, 67.36; H, 5.30; N, 4.91. Found: C, 67.02; H, 5.12; N, 5.04.

4.4.33. 1-Hydroxy-3-methyl-9-phenylmethyl-9*H*-carbazole-2-carboxylic acid (18). A mixture of carbazole **17b** (0.01 g, 0.289 mmol), aqueous NaOH solution (40%, 8 mL), MeOH (10 mL), and H_2O (8 mL) was heated at reflux for 5 h. The reaction mixture was then diluted with water (30 mL) and extracted with ethyl acetate (3×25 mL). The combined organic extracts were washed with water (20 mL) and 5% HCl (10 mL), brine (20 mL), dried (Na_2SO_4), and concentrated. Purification of the crude residue by chromatography (1:2 ethyl acetate/petroleum ether, R_f=0.30) gave compound **18** (0.07 g, 74%) as a yellow solid. Mp 180–82 °C; FTIR (KBr) cm^{-1} 3435 (br s), 2925, 1641 (s), 1619 (m), 1496, 1451, 1375, 1269, 1166, 744; ^1H NMR (200 MHz, d_6-DMSO): δ 10.02 (br s, 1H), 8.01 (d, 1H, J=8.0 Hz), 7.50–7.32 (m, 3H), 7.30–7.10 (m, 6H), 5.93 (s, 2H), 2.64 (s, 3H); ^{13}C NMR (50 MHz, d_6-DMSO): δ 152.8, 143.6, 141.5, 140.6, 139.5, 131.4, 128.5, 127.2, 126.8, 126.6, 125.5, 122.8, 120.9, 119.3, 113.4, 110.2, 109.8, 47.6, 24.2. Anal. Calcd for $C_{20}H_{15}NO_3$: C, 75.70; H, 4.76; N, 4.41. Found: C, 76.04; H, 4.94; N, 4.27.

4.4.34. 3-Methyl-9-phenylmethyl-9*H*-carbazole-1-ol (19). A mixture of carbazole **17b** (0.01 g, 0.289 mmol), aqueous KOH solution (40%, 8 mL), MeOH (10 mL), and H_2O (8 mL) was heated at reflux for 5 h. The reaction mixture was diluted with water (30 mL) and extracted with ethyl acetate (3×25 mL). The combined organic extracts were washed with water (30 mL) and 5% HCl (15 mL), brine (20 mL), dried (Na_2SO_4), and concentrated. Purification of the crude residue by chromatography (3:7 ethyl acetate/petroleum ether, R_f=0.56) gave compound **19** (0.047 g, 56%) as a brownish liquid. FTIR (KBr) cm^{-1} 3042, 2922, 2852, 1616, 1587, 1500, 1454, 1296, 1227, 1120, 1090, 975, 748; ^1H NMR (200 MHz, $CDCl_3$) δ 8.03 (d, 1H, J=8.0 Hz), 7.52 (s, 1H), 7.42–7.10 (m, 8H), 6.60 (s, 1H), 5.85 (s, 2H), 4.90 (br s, 1H), 2.46 (s, 3H). No attempt was made for preparing an analytical sample due to its propensity to decomposition on silica gel chromatography or standing.

4.4.35. 1-Methoxy-3-methyl-9-phenylmethyl-9*H*-carbazole (20). This compound was prepared from **19** as a light brown solid in 77% yield, following general procedure for the O-methylation of phenolic compounds (as in Section 4.4). Mp 95–97 °C; ^1H NMR (200 MHz, $CDCl_3$) δ 8.04 (d, 1H, J=8.0 Hz), 7.53 (s, 1H), 7.40–7.30 (m, 2H), 7.23–7.10 (m, 6H), 6.76 (s, 1H), 5.85 (s, 2H), 3.86 (s, 3H), 2.53 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 146.6, 141.1, 139.3, 129.2, 128.4, 128.2, 126.8, 126.3, 125.5, 124.8, 123.0, 120.2, 118.8, 112.7, 109.3, 109.1, 55.6, 48.6, 21.6; HRMS: for $C_{21}H_{19}NO$ $[M+H]^+$ calcd 302.1545, found 302.1538.

Anal. Calcd for $C_{21}H_{19}NO$: C, 83.69; H, 6.35; N, 4.65. Found: C, 83.52; H, 6.42; N, 4.54.

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