A Novel CAN-SiO_2-Mediated One-Pot Oxidation of 1-Keto-1,2,3,4-tetrahydrocarbazoles to Carbazoloquinones: Efficient Syntheses of Murrayaquinone A and Koeniginequinone A

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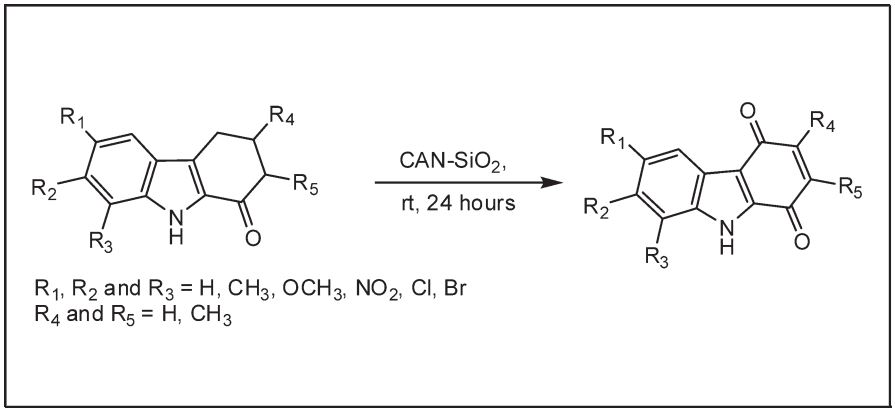

One-pot oxidations of substituted 1-keto-1,2,3,4-tetrahydrocarbazoles (**1**) to carbazole-1,4-quinones (**2**) are efficiently carried out by CAN-SiO_2-mediated reaction. This generalized protocol was successfully extended to the synthesis of two naturally occurring carbazoloquinones: murrayaquinone A (**2b**) and koeniginequinone A (**2g**). A plausible mechanism for this novel reaction involves formation of a 9-hydroxy-2,3,4,9-tetrahydro-1*H*-carbazole-1-one followed by rearrangement to 1-hydroxycarbazole derivatives, which are further oxidized by cerium (IV) to carbazoloquinones.

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INTRODUCTION

As part of a larger project in our laboratory, we faced the problem of synthesizing, in quantity, the carbazole-1,4-quinone (**2a**). To date, there is only one report [1] for direct oxidation of 1-keto-1,2,3,4-tetrahydrocarbzoles to carbazole-1,4-quinones and each cited example uses 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ). In our hands, however, this method proved unsuccessful in the transformation of **1a** into **2a** (Scheme 1).

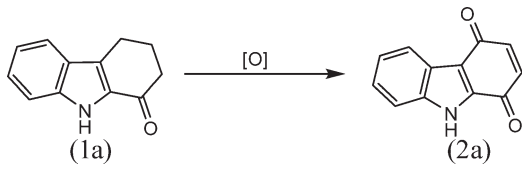
This failure motivated us to study the similar oxidation of 1-keto-1,2,3,4-tetrahydrocarbzoles by using the time-honored single-electron oxidant, CAN [2–4]. A survey of the literature [5] revealed that CAN, a single-electron oxidant is a reagent of choice for the synthesis quinones.

It is worth mentioning that substituted 1-keto-1,2,3,4-tetrahydrocarbazoles have been extensively used as an intermediate in the synthesis of naturally occurring carbazole alkaloids [6]. Cabazole-1,4-quinones are present in a large group of alkaloids that includes murrayaquinones A and B [7,8], pyrrayaquinones A and B [9], and koeniginequinones A and B [10]. Murrayaquinone A is known to have cardiotonic activity on guinea-pig papillary muscle [11]. Further carbazole-1,4-quinones [12] have been used as intermediates in the synthesis of a novel class of antibiotics, carbazomycines G and H [13].

In addition to the aforementioned oxidations [1] using DDQ, there are several reported syntheses of carbazole-1,4-quinones from 1- or 4-oxygenated carbazoles [10,14–16] *via* oxidation with Fremy's salt. A Japanese team [17] has developed a facile palladium (II) assisted intramolecular ring closure of arylamino-1,4-benzoquinones to carbazole-1,4-quinones. Knolker and coworkers [18,19] have taken advantage of this oxidative cyclization to obtain koeniginequinones A and B and carbazomycines G and H. Chowdhury *et al*. [20] have reported a photochemical oxidation of 3-methyl carbazole to obtain murrayaquinone A. Recently, Mal *et al*. [21] have developed a new strategy using [4 + 2] cycloaddition to obtain carbazole quinones from furoindolone and Michael acceptors.

Considering the importance of carbazole-1,4-quinones and the easy availability of 1-keto-1,2,3,4-tetrahydrocabazoles, we have studied the oxidation of 1-keto-1,2,3,4-tetrahydrocarbazole (**1a**) with CAN and CAN/DDQ

Scheme 1. Attempted oxidation of **1a** to **2a**.



under different conditions. However, because it could not be accomplished satisfactorily in solution phase, we had to carry out this reaction on a solid support.

RESULTS AND DISCUSSION

The strong oxidizing power of cerium (IV) salts often leads to undesired over oxidized products [22]. The concept of moderating the effect of reagents by immobilizing them on an inorganic solid support has achieved considerable popularity in organic syntheses [23,24]. Taking advantage of the moderated activity of CAN when it is immobilized on silica gel, we oxidized **1a** in solid phase under solvent-free conditions and obtained **2a** in moderate yield.

Using this finding as a starting point, a new and environmentally safe method for the oxidation of substituted 1-keto-1,2,3,4-tetrahydrocarbazoles (**1**) to carbazole-1,4-quinones (**2**) in single step using CAN-SiO_2 has been developed. The analysis of our observations and characterization of the products is the subject of this communication. Finally, we extend the scope of the reaction to the synthesis of the naturally occurring carbazoloquinones: murrayaquinone A (**2b**) and koeniginequinone A (**2g**) (Fig. 1).

The required substituted 1-keto-1,2,3,4-tetrahydrocarbazoles (**1**) were prepared through Fischer indole cyclization [25] of substituted cyclohexane-1,2-dione-1-phenylhydrazones obtained by Japp-Klingemann procedure from diazonium salts and 1,3-dicarbonyl compounds. CAN was dissolved in acetonitrile and then mixed with requisite amount of silica gel (see Experimental Section). Solvent was then evaporated and replaced by a solution of the substituted 1-keto-1,2,3,4-tetrahydrocarbazole (**1**). After re-evaporation, the mixture was kept at room temperature overnight [monitored by thin layer chromatography (TLC)], and the product was isolated and purified (Scheme 2). The results are summarized in Table 1.

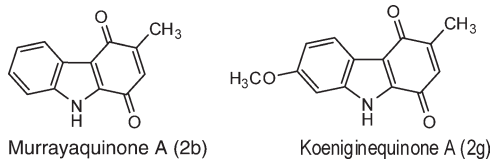
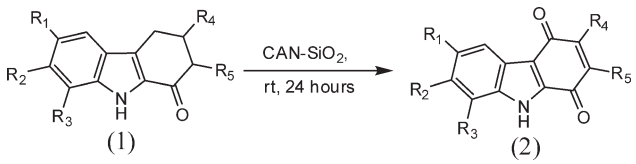


Figure 1. Representative carbazoloquinones.

Scheme 2. CAN-SiO_2-mediated oxidation to obtain carbazole-1,4-quinones.



The apparently favorable effect of 3-substitution on yields in the oxidation reaction of **1** provoked to also examine the effect of 2-substitution. However, no perceptible change was observed when compared with that of 3-methyl isomer. Again, presence of an electron-donating methoxy group in the benzene moiety of **1** lowers the yield of **2**, probably because of over oxidation [22]. However, this observation prompted us to investigate the oxidations of 1-keto-1,2,3,4-tetrahydrocarzoles (**1**) with electron-withdrawing group in the phenyl ring. On the basis of this insight, we successfully synthesized several carbazole-1,4-quinones with electron-withdrawing group (Table 1). It is worth mentioning that, with carbazole-1,4-quinones containing electron-withdrawing group on the phenyl ring, optimum yields are formed by heating the reaction for at least 4 h in an oil bath maintained at ca. 150°C or by microwave irradiation for 20 s at the power level 80% of 720 W.

It was noted by TLC that a compound with R_f 0.65 (solvent system, benzene–chloroform–diethyl amine 14:5:1) formed alongside quinone **2t** (R_f 0.26). The less polar by-product was isolated by column chromatography and identified as 9-hydroxy-6-methoxy-3,7-dimethyl-2,3,4,9-tetrahydro-1*H*-carbazol-1-one (**3**) for which there is a good literature precedent [26] and the reaction is assumed to proceed as in Scheme 3.

The key steps of the reaction sequence shown above (Scheme 3) are the oxidation of **1t** to **3** followed by 1,4-elimination of a water molecule and subsequent 1,5-shift of the hydrogen atom to afford a 1-hydroxycarbazole, which is oxidized further by CAN to the final product, a 1,4-carbazoloquinone **2t**. Further identification of **3** was established through *O*-acetylation and *O*-methylation to obtain 6-methoxy-3,7-dimethyl-1-oxo-3,4-dihydro-1*H*-carbazol—9(2*H*)-yl acetate (**13**) and 6,9-dimethoxy-3,7-dimethyl-1-oxo-3,4-dihydro-1*H*-carbazol-1-one (**14**), respectively.

We then turned our attention to the conversion of **3** to a 1-hydroxycarbazole under several solid acid catalyzed conditions using SiO_2, acidic Al_2O_3, SiO_2-NH_4Cl, montmorillonite-K10, and montmorillonite-KSF. However, all these attempts were unsuccessful and in each case, the unreacted starting material **3** was almost completely recovered. Finally, we tried the CAN-SiO_2-mediated oxidation on **3** and obtained the desired 1,4-carbazoloquinone **2t**. This observation led to the idea that Ce (IV) may

Table 1

CAN-SiO_2 mediated oxidation of 1-keto-1,2,3,4-tetrahydrocarbazoles (1) to carbazole-1,4-quinones (2).

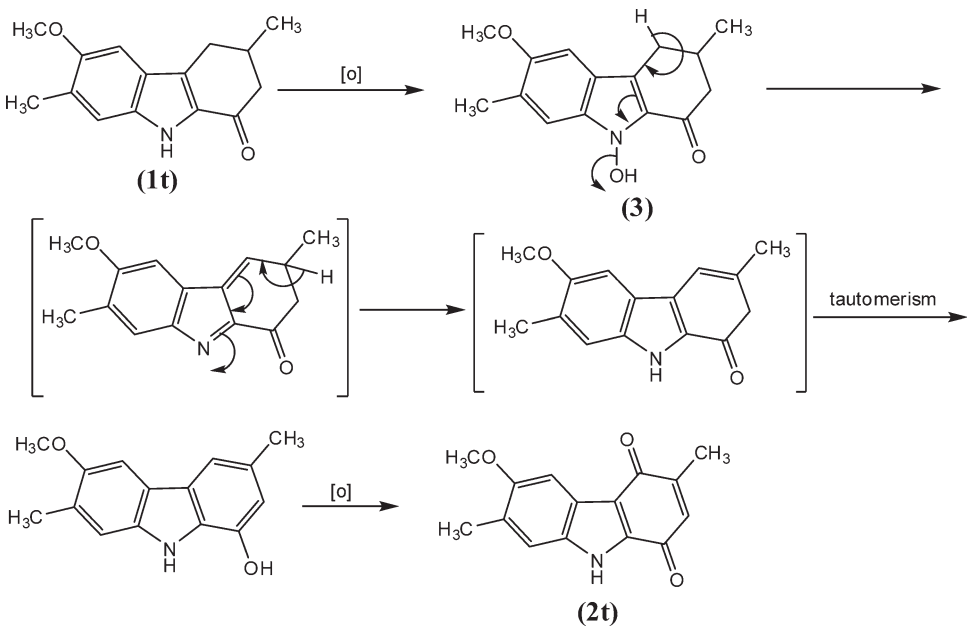
Entry	Substrate	Product	Yield (%)[a]	References
1	1a. $R_1 = R_2 = R_3 = R_4 = R_5 = H$	2a	55	26
2	1b. $R_1 = R_2 = R_3 = R_5 = H$, $R_4 = CH_3$	2b	62	1,8,14,15,17,18
3	1c. $R_1 = CH_3$, $R_2 = R_3 = R_4 = R_5 = H$	2c[b]	50	–
4	1d. $R_1 = R_4 = CH_3$, $R_2 = R_3 = R_5 = H$	2d	60	17
5	1e. $R_1 = R_3 = R_4 = CH_3$, $R_2 = R_5 = H$	2e[b]	54	–
6	1f. $R_1 = OCH_3$, $R_2 = R_3 = R_5 = H$, $R_4 = CH_3$	2f	50	17
7	1g. $R_1 = R_3 = R_5 = H$, $R_2 = OCH_3$, $R_4 = CH_3$	2g	56	10,17,18
8	1h. $R_1 = R_2 = R_3 = R_4 = H$, $R_5 = CH_3$	2h	58	17
9	1i. $R_1 = R_5 = CH_3$, $R_2 = R_3 = R_4 = H$	2i	54	17
10	1j. $R_1 = R_3 = R_5 = CH_3$, $R_3 = R_4 = H$	2j[b]	52	–
11	1k. $R_1 = OCH_3$, $R_2 = R_3 = R_4 = H$, $R_5 = CH_3$	2k	50	17
12	1l. $R_1 = NO_2$, $R_2 = R_3 = R_4 = R_5 = H$	2l[b]	88	–
13	1m. $R_1 = NO_2$, $R_2 = R_3 = R_5 = H$, $R_4 = CH_3$	2m[b]	92	–
14	1n. $R_1 = Cl$, $R_2 = R_3 = R_4 = R_5 = H$	2n[b]	81	–
15	1o. $R_1 = Cl$, $R_2 = R_3 = R_5 = H$, $R_4 = CH_3$	2o	85	17
16	1p. $R_1 = Cl$, $R_2 = R_3 = R_4 = H$, $R_5 = CH_3$	2p	85	17
17	1q. $R_1 = Br$, $R_2 = R_3 = R_4 = R_5 = H$	2q[b]	83	–
18	1r. $R_1 = Br$, $R_2 = R_3 = R_5 = H$, $R_4 = CH_3$	2r[b]	89	–
19	1s. $R_1 = Br$, $R_2 = R_3 = R_4 = H$, $R_5 = CH_3$	2s[b]	88	–

[a] yields are reported after isolation in pure form.
[b] spectral data of these unknown compounds are incorporated in the Experimental Section.

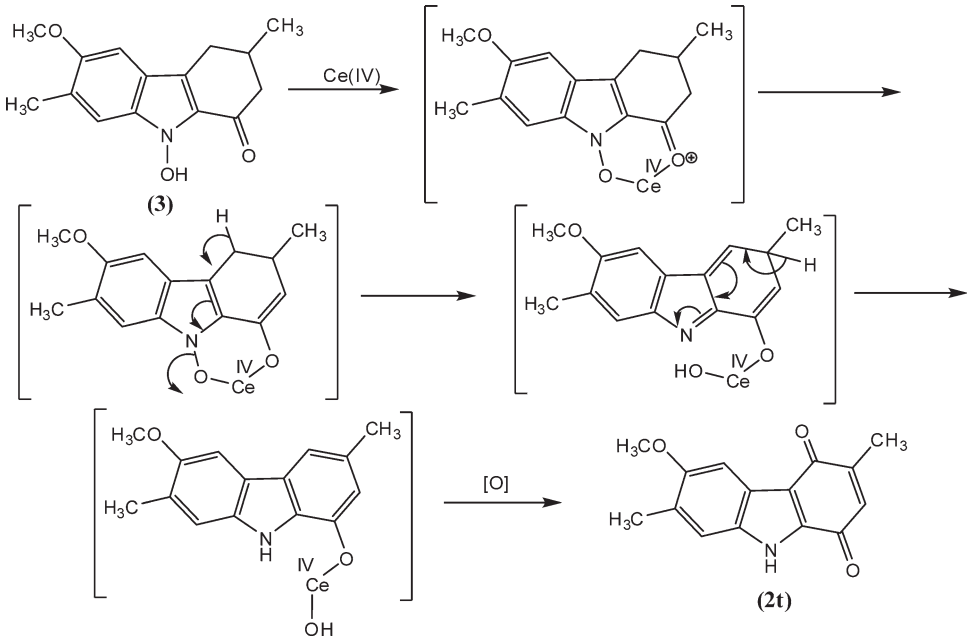
participate in the process by forming a complex as shown in Scheme 4. The ability of Ce (IV) to complex with aromatic OH groups is previously documented in literature [27].

To synthesize the starting compound 6-methoxy-3,7-dimethyl-2,3,4,9-tetrahydro-1*H*-carbazol-1-one (**1t**), the amine hydrochloride **9** was prepared from *o*-cresol (Scheme 5) using a method different from that reported in literature [28]. *o*-Cresol (**4**) was converted to the nitroso derivative [29] **5** which on reduction with H_2S, NH_3 furnished the corresponding amine **6**. The amine **6** on acetylation furnished the acetyl derivative **7** which on methylation with CH_3I and $NaOC_2H_5$ gave **8**. Compound **8** on hydrolysis with concentrated hydrochloric acid (HCl) in ethanol afforded the required amine hydrochloride **9**. Diazotization of **9** followed by coupling with 2-(hydroxymethylene)-5-methylcyclohexanone (**10**) under Japp-Klingemann conditions furnished 2-(4-methoxy-3-

Scheme 3. Plausible mechanistic details for the oxidation of 1-keto-1,2,3,4-tetrahydrocarbazoles.



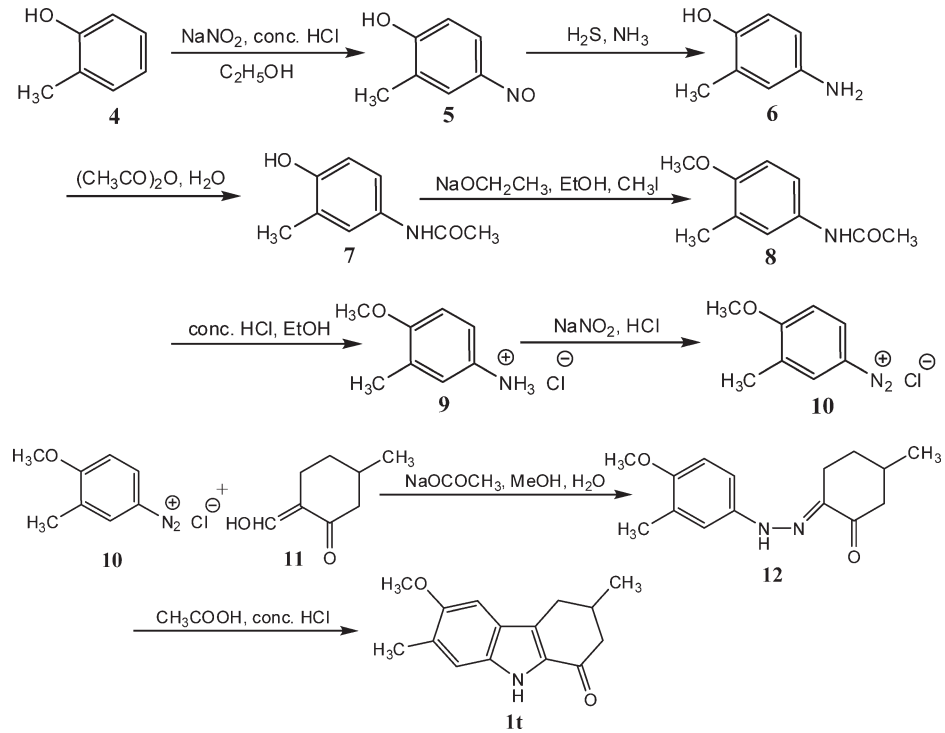
Scheme 4. Plausible mechanism for Ce (IV)-mediated pathway for the conversion of **3** to **2t**.



methylphenyl)hydrazono-5-methylcyclohexanone (**11**), which was cyclized to **1t**.

The presence of a carbazole-1,4-quinone moiety **2a–t** was confirmed by their UV and IR spectra [8] and the presence of two carbonyl signals at around δ 180 in the ^{13}C-NMR spectrum. In the ^{1}H-NMR spectrum, the C-5 proton was deshielded at around δ 7.20–8.20 due to the carbonyl moiety at 4-C. In addition, the C-5 proton of **2e**, **2j**, and **2t** showed unexpected lower intensity in ^{1}H-NMR spectra. Moreover, Nuclear Overhauser Effect (NOE) analysis [8,30] suggested orientation of the 6-*O*-methyl group toward C-5 hydrogen.

Scheme 5. Synthesis of 6-methoxy-3,7-dimethyl-2,3,4,9-tetrahydro-1*H*-carbazol-1-one.



In summary, we have developed a very simple, inexpensive, nontoxic, and eco-friendly one-pot oxidation of substituted 1-keto-1,2,3,4-tetrahydrocarbazoles to carbazole-1,4-quinones and applied it to the synthesis of the naturally occurring carbazoloquinones murrayaquinone A (**2b**) and koeniginequinone A (**2g**). The method is fairly general, although product yields are higher when the phenyl ring of the 1-keto-1,2,3,4-tetrahydrocarbazole starting material contains an electron-withdrawing substituent. Isolation of 9-hydroxy-6-methoxy-3,7-dimethyl-2,3,4,9-tetrahydro-1*H*-carbazol-1-one (**3**) during the CAN-SiO_2 oxidation of 6-methoxy-3,7-dimethyl-2,3,4,9-tetrahydro-1*H*-carbazol-1-one (**1t**) as an intermediate product, followed by its subsequent oxidation to 6-methoxy-3,7-dimethyl-1*H*-carbazole-1,4(9*H*)-dione (**2t**) suggested a plausible mechanism for the reaction. The present study expands the application of CAN-SiO_2-mediated oxidation in synthetically useful transformations.

EXPERIMENTAL

General methods and materials. Melting points were determined in open capillaries and are uncorrected. Reagent-grade chemicals were purchased from a commercial source and used without further purification. All reaction mixtures and column eluents were monitored by TLC using commercial aluminum TLC plates (Merck Kieselgel 60 F_{254}). The plates were observed under UV light at 254 and 365 nm. IR spectra were recorded in KBr discs on Schimadzu FTIR-8300 and NMR spectra were recorded on Bruker AV 500. Results of attached proton test—^{13}C-NMR experiments are shown in parentheses where (+) denotes CH_3 or CH and (−) denotes CH_2 or C. High-resolution mass spectra (HRMS) were performed on Qtof Micro YA263.

Typical experimental procedure for CAN-SiO_2-mediated oxidation of 1b to murrayaquinone A (2b). Ceric ammonium nitrate (15 mmol) was dissolved in dry acetonitrile (30 mL) and then mixed with silica gel (35 gm). Solvent was then evaporated at room temperature and the reagent was impregnated with the solution of **1b** (2.5 mmol) in dichloromethane (20 mL) followed by evaporation of solvent in air. The mixture was then kept over night at room temperature. After the reaction, the mixture was extracted with dichloromethane (3 × 50 mL). The solvent was evaporated to dryness and the residue was chromatographed over silica gel by eluting successively with hexane and hexane–dichloromethane (2:3). The eluent furnished a red-colored solid which was purified by crystallization from dichloromethane–hexane to yield murrayaquinone A (**2b**), m.p. 242–243°C (lit. m.p. [1] 240–241°C).

6-Methyl-1H-carbazole-1,4(9H)-dione (2c). m.p. 238°C (dec.); UV (MeOH): 224 (sh), 255.5, 388; IR (KBr): ν = 3178, 2928, 1662,1636 cm^{-1}; ^{1}H-NMR (DMSO-d_6, 500 MHz) 2.41 (s, 3H, Ar—CH_3), 6.69 (s, 1H × 2, C_2—H & C_3—H), 7.20 (s, 1H, C_7—H), 7.41 (s, 1H, C_8—H), 7.80 (s, 1H, C_5—H), 12.76 (s, 1H, N—H, exch.); ^{13}C-NMR (DMSO-d_6, 125 MHz): 21.20 (+), 113.46 (+), 114.92 (+), 120.93 (+), 123.61 (−), 128.32 (−), 133.28 (−), 135.28 (+), 135.28 (+), 135.84 (−),138.72 (−),179.77 (−), 183.11 (−); HRMS *m/z* calcd for $C_{13}H_9NO_2Na$ $[M + Na]^+$ 234.0531; found 234.0581.

3,6,8-Trimethyl-1H-carbazole-1,4(9H)-dione (2e). m.p. 236°C (dec.); UV (MeOH): 219 (sh), 258.7, 378.5; IR (KBr): ν = 3324, 2920, 1669,1647 cm^{-1}; ^{1}H-NMR (DMSO-d_6, 500 MHz): 1.99 (s, 3H, Ar—CH_3), 2.12 (s, 3H, Ar—CH_3), 2.25 (s, 3H, C_3—CH_3), 6.52 (s, 1H, C_2—H), 7.10 (s, 1H, C_7—H), 7.60 (s, 1H, C_5—H), 13.16 (s, 1H, N—H, exch.); ^{13}C-NMR (DMSO-d_6, 125 MHz): 15. 42 (+), 15.74 (+), 16.42 (+), 113.28 (+), 114.42 (−), 124.12 (+), 126.99 (−), 128.84 (−), 131.42 (−), 136.29 (−), 137.28 (+), 141.74 (−), 148.21 (−), 179.47 (−), 181.14 (−); HRMS *m/z* calcd for $C_{15}H_{13}NO_2Na$ $[M + Na]^+$ 262.0844; found 262.0846.

2,6,8-Trimethyl-1H-carbazole-1,4(9H)-dione (2j). m.p. 239°C (dec.); UV (MeOH): 223 (sh), 257.7, 370.5; IR (KBr): ν = 3313, 2929, 1662, 1651 cm^{-1}; ^{1}H-NMR (DMSO-d_6, 500 MHz): 1.98 (s, 3H, Ar—CH_3), 2.28 (s, 3H, Ar—CH_3), 2.55 (s, 3H, C_2—CH_3), 6.56 (s, 1H, C_3—H), 7.18 (s, 1H, C_7—H), 7.25 (s, 1H, C_5—H), 13.25 (s, 1H, N—H, exch.); ^{13}C-NMR (DMSO-d_6, 125 MHz): 14.79 (+), 16.42 (+), 16.87 (+), 113.53 (+), 114.30 (−), 124.16 (+), 127.01 (−), 128.99 (−), 135.05 (−), 136.51 (+), 137.24 (−), 141.82 (−143.86 (−), 179.77 (−), 181.42 (−); HRMS *m/z* calcd for $C_{15}H_{14}NO_2$ $[M + H]^+$ 240.1024; found 240.1028.

6-Nitro-1H-carbazole-1,4(9H)-dione (2l). m.p. 233°C (dec.); UV (MeOH): 246.5, 375; IR (KBr): ν = 3244, 2956, 2928, 1728, 1649 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): 6.80 (d, J = 6.0, 1H, C_2—H), 6.82 (d, J = 6.0, 1H, C_3—H), 7.52 (dd, J_{13} = 15.5, J_{24} = 26, 1H, C_7—H), 8.40 (d, J = 8, 1H, C_8—H), 8.65 (d, J = 7.5, 1H, C_5—H), 10.64 (s, 1H, N—H, exch.); ^{13}C-NMR ($CDCl_3$, 125 MHz): 117.06 (−), 123.47 (+), 123.84 (+), 126.88 (−), 129.97 (−), 131.14 (+), 134.26 (−), 135.32 (+), 136.33 (−), 139.02 (+), 179.11 (−), 182.85 (−); HRMS *m/z* calcd for $C_{12}H_6N_2O_4Na$ $[M + Na]^+$ 265.0225; found 265.0235.

3-Methyl-6-nitro-1H-carbazole-1,4(9H)-dione (2m). m.p. 230°C (dec.); UV (MeOH): 246.5, 283, 371; IR (KBr): ν = 3298, 2958, 2920, 1726, 1649 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): 2.20 (s, 3H, C_3—CH_3), 6.63 (s, 1H, C_2—H), 7.50 (dd, J_{13} = 7.5, J_{24} = 7.5, 1H, C_7—H), 8.38 (d, J = 7.5, 1H, C_8—H), 8.66 (d, J = 7.5, 1H, C_5—H), 10.56 (s, 1H, N—H, exch.); ^{13}C-NMR ($CDCl_3$, 125 MHz): 15.23 (+), 117.06 (−), 122.95 (+), 123.34 (+), 128.04 (−), 129.5 (−), 131.42 (+), 132.20 (+), 135.32 (−), 136.30 (−), 148.70 (−), 179.11 (−), 182.85 (−); HRMS *m/z* calcd for $C_{13}H_8N_2O_4Na$ $[M + Na]^+$ 279.0382; found 279.0382.

6-Chloro-1H-carbazole-1,4(9H)-dione (2n). m.p. 248°C (dec.); UV (MeOH): 225.5, 258.7, 383; IR (KBr): ν = 3201, 2991, 1666, 1635 cm^{-1}; ^{1}H-NMR (DMSO-d_6, 500 MHz): 6.76 (s, 1H × 2, C_2—H & C_3—H), 7.52 (d, J = 8.5, 1H, C_7—H), 7.54 (d, J = 8.5, 1H, C_8—H), 7.95 (s, 1H, C_5—H), 13.08 (s, 1H, N—H, exch.); ^{13}C-NMR (DMSO-d_6, 125 MHz): 114.69 (−), 115.53 (+), 120.42 (+), 124.06 (−), 126.56 (+), 128.43 (−), 135.48 (+), 135.77 (−), 136.40 (−), 138.67 (+), 179.66 (−), 182.80 (−); HRMS *m/z* calcd for $C_{12}H_7NO_2Cl$ $[M + H]^+$ 232.0165; found 232.0168.

6-Bromo-1H-carbazole-1,4(9H)-dione (2q). m.p. 254°C (dec.); UV (MeOH): 224, 259, 388; IR (KBr): ν = 3200, 2987, 1664, 1637 cm^{-1}; ^{1}H-NMR (DMSO-d_6, 500 MHz): 6.78 (s, 1H × 2, C_2—H & C_3—H), 7.53 (s, 1H × 2, C_7—H & C_8—H), 8.14 (s, 1H, C_5—H), 13.11 (s, 1H, N—H, exch.); ^{13}C-NMR (DMSO-d_6, 125 MHz): 114.55 (−), 115.91 (+), 116.48 (−), 123.54 (+), 124.66 (−), 129.09 (+), 135.55 (+), 136.02 (−), 136.25 (−),

138.70 (+), 179.70 (−), 182.88 (−); HRMS *m/z* calcd for $C_{12}H_6NO_2BrNa$ $[M + Na]^+$ 297.9479; found 297.9482.

3-Methyl-6-bromo-1H-carbazole-1,4(9H)-dione (2r). m.p. 257°C (dec.); UV (MeOH): 225.5, 258.7, 322, 392; IR (KBr): ν = 3205, 2985, 1667, 1640 cm^{-1}; ^{1}H-NMR (DMSO-d_6, 500 MHz): 2.03 (s, 3H, C_3—CH_3), 6.57 (s, 1H, C_2—H), 8.06 (s, 1H, C_7—H), 8.20 (s, 1H × 2, C_5—H & C_8—H), 12.94 (s, 1H, N—H, exch.); ^{13}C-NMR (DMSO-d_6, 125 MHz): 15.49 (+), 114.49 (−), 116.31 (+), 124.13 (+), 124.84 (−), 129.31 (+), 131.65 (+), 135.98 (−), 136.32 (−), 139.37 (−), 147.89 (−), 179.66 (−), 182.53 (−); HRMS *m/z* calcd for $C_{13}H_8NO_2BrNa$ $[M + Na]^+$ 311.9636; found 311.9638.

2-Methyl-6-bromo-1H-carbazole-1,4(9H)-dione (2s). m.p. 258°C (dec.); UV (MeOH): 224, 258.7, 325, 397; IR (KBr): ν = 3203, 2983, 1668, 1645 cm^{-1}; ^{1}H-NMR (DMSO-d_6, 500 MHz): 2.02 (s, 3H, C_2—CH_3), 6.56 (s, 1H, C_3—H), 7.43—7.53 (m, 1H × 2, C_7—H & C_8-H), 8.18 (s, 1H, C_5—H), 12.97 (s, 1H, N—H, exch.); ^{13}C-NMR (DMSO-d_6, 125 MHz): 15.19 (+), 114.65 (−), 115.74 (+), 124.03 (+), 124.35 (−), 124.50 (−), 128.81 (+), 134.66 (+), 136.35 (−), 139.44 (−), 144.20 (−), 179.85 (−), 182.83 (−); HRMS *m/z* calcd for $C_{13}H_9NO_2Br$ $[M + H]^+$ 289.9816; found 289.9816.

Preparation and oxidation of 6-methoxy-3,7-dimethyl-2,3,4,9-tetrahydro-1*H*-carbazol-1-one (1t). ***2-Methyl-4-nitrosophenol (5).*** To a solution of *o*-cresol (**4**, 10.8 gm, 0.1 mol) in 95% ethanol (80 mL), concentrated HCl (75 mL) was added. The mixture was cooled to 0°C and to the stirred solution sodium nitrite (10.5 gm, 0.15 mol) was added in portions of about 1 gm each while maintaining the reaction temperature at 0–5°C. Initially, a brown precipitate appeared which turned greenish within half an hour. The reaction mixture was then poured in ice water (400 mL). The light yellow solid (yield 7.5 gm) was collected by filtration and washed with cold water (100 mL). This crude product was used in the next step without further purification.

4-Amino-2-methylphenol (6). The crude nitroso derivative (**5**, 30 gm) was dissolved in a mixture of 28% aqueous ammonia (300 mL) and water (400 mL). The brown solution was then filtered and H_2S was passed until light yellow amino compound (**6**) was precipitated out. The reaction mixture was kept over night in refrigerator for complete crystallization of **6** (22 g, 81%), m.p. 173°C (lit. m.p. [31] 175.4°C). IR: 3390 (—OH), 3300 (—NH_2), and 1600, 1555, 1500 cm^{-1} (aromatic).

4-Acetamido-2-methylphenol (7). 4-Amino-2-methylphenol (**6**, 24.6 gm, 0.20 mol) was suspended in water (60 mL) and acetic anhydride (24 mL, 0.25 mol) was added with vigorous stirring. The mixture was warmed at about 60–65°C for 30 min. On cooling, a solid was separated out which was collected by filtration and washed with cold water. The acetyl derivative **7** was crystallized from water with charcoal treatment to yield colorless needle-shaped crystals (27.75 gm, 84%), m.p. 178°C (lit. m.p. [28] 179°C). IR: 3315 (—OH), 3285 (—NH), 1652 (C=O), and 1605, 1542, 1500 cm^{-1} (aromatic).

4-Methoxy-3-methylacetanilide (8). Clean sodium (1.5 gm, 0.065 mol) was placed in absolute alcohol (40 mL). After the dissolution of sodium, the mixture was cooled and 4-acetamido-2-methylphenol (10 gm, 0.06 mol) was added. Iodomethane (15.6 gm, 0.11 mol) was added slowly to the mixture under reflux using pressure equalizer. After 1-h reaction, mixture was poured in ice water (100 mL), cooled in ice bath, and crude methylated product was thus separated out. The crude product was leached with 1% NaOH solution (150 mL), filtered, and washed with ice cooled water (100 mL). Compound **8** was crystallized from MeOH-H_2O to furnish colorless needles (8 gm, 75%), m.p. 105°C (lit. m.p. [32] 103–3.5°C). IR: 3310 (—NH), 1654 (C=O), and 1560, 1510 cm^{-1} (aromatic).

4-Methoxy-3-methylaniline hydrochloride (9). 4-Methoxy-3-methylacetanilide (**7**, 35.8 gm, 0.20 mol) was dissolved in ethanol (100 mL) by boiling and concentrated HCl (100 mL) was added dropwise under reflux during 1 h. After 3 h, the solution was cooled when the crystals of amine hydrochloride (**9**) separated out, which was collected by filtration to furnish colorless crystals (27.8 gm, 80%), IR: 3440–3400 (—NH_3^+) and 1600, 1540, 1510 cm^{-1} (aromatic).

2-(4-Methoxy-3-methylphenyl)hydrazono-5-methylcyclohexanone (12). 2-Hydroxymethylene-5-methylcyclohexanone [10] (**11**, 16.20 gm, 0.12 mol) in methanol (150 mL) was added to an aqueous solution of sodium acetate (26 gm, 100 mL of water). To this a solution of 4-methoxy-3-methylphenyldiazonium chloride [10] (**10**, prepared from 20.8 gm, 0.12 mol of 4-methoxy-3-methylaniline hydrochloride) was added during 1 h under mechanical agitation when red crystals of **12** were obtained. Filtration and crystallization from methanol–dichloromethane yielded reddish brown crystals (**12**, 26.50 gm, 85%), m.p. 111–112°C. MS: *m/z* 260 (M^+); IR: 3450 (—NH), 1630 (C=O), and 1600, 1510 cm^{-1} (aromatic).

6-Methoxy-3,7-dimethyl-2,3,4,9-tetrahydro-1H-carbazol-1-one (1t). 2-(4-Methoxy-methyl phenyl)hydrazono-5-methylcyclohexanone (**12**, 5.2 gm, 0.02 mol) was refluxed with glacial acetic acid (30 mL) containing concentrated HCl (7 mL) for 5 min and the hot reaction mixture was poured in ice water (200 mL). The solid thus obtained was collected by filtration, washed with water, dried, and then chromatographed over silica gel (50 gm) and the column was eluted with hexane–dichloromethane (2:1). The eluent gave a colorless solid which on crystallization from dichloromethane–hexane furnished colorless crystals (**1t**, 3.2 gm, 66%), m.p. 248°. IR (KBr): ν = 3255, 2997, 2829, 1648 cm^{-1}; ^{1}H-NMR ($CDCl_3$ + DMSO-d_6, 500 MHz): 1.15 (d, J = 3.50 Hz, 3H, C_3—CH_3), 2.25 (s, 3H, Ar—CH_3), 2.29–2.54 (m, 3H, C_2—2H & C_3—1H), 3.06 (d, J = 15.30 Hz, 2H, C_4—2H), 3.82 (s, 3H, Ar—OCH_3), 6.97 (s, 1H, C_8—H), 7.15 (s, 1H, C_5—H), 11.22 (br, 1H, N—H, exch); ^{13}C-NMR ($CDCl_3$ + DMSO-d_6, 125 MHz): 17.22 (+), 21.06 (+), 29.29 (−), 32.47 (+), 46.16 (−), 55.11 (+), 99.29 (+), 113.59 (+), 122.39 (−), 126.82 (−), 127.37 (−), 130.47 (−), 133.36 (−), 152.39 (−), 189.15 (−); HRMS *m/z* calcd for $C_{15}H_{17}NO_2Na$ $[M + Na]^+$ 266.1156; found 266.1176.

9-Hydroxy-6-methoxy-3,7-dimethyl-2,3,4,9-tetrahydro-1H-carbazol-1-one (3) and 6-Methoxy-3,7-dimethyl-1H-carbazole-1,4(9H)-dione (2t). The immobilized CAN-SiO_2 reagent was impregnated with the solution of **1u** (603 mg, 2.5 mmol) in dichloromethane–acetonitrile mixture (1:1, 80 mL) followed by evaporation of solvent in air. The mixture was then kept over night at room temperature. After the reaction, the mixture was extracted with dichloromethane (4 × 50 mL). The solvent was evaporated to dryness and the residue so obtained was chromatographed over silica gel (15 gm) by eluting successively with hexane and mixtures of hexane and dichloromethane in the ratio 1:1 followed by 2:3. The eluent from hexane–dichloromethane (1:1) furnished a reddish brown-colored solid which was purified by crystallization from dichloromethane–hexane to yield **3** (100 mg, 16%), m.p. 206°C; UV

(MeOH): 233 (sh), 316.5; IR (KBr): ν = 3244, 2959, 2928, 2871, 1649 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz): 1.18 (d, J = 4.11 Hz, 3H, C_3—CH_3), 1.81 (s, 1H, N—OH), 2.37–2.54 (m, 1H, & C_3—1H), 2.46 (s, 3H, Ar—CH_3), 2.66 (d, J = 10.23, 2H, C_2—2H), 2.91 (d, J = 14.43 Hz, 2H, C_4—2H), 3.90 (s, 3H, Ar—OCH_3), 7.26 (s, 1H, C_8—H), 7.45 (s, 1H, C_5—H); ^{13}C-NMR ($CDCl_3$, 75 MHz): 17.03 (+), 21.28 (+), 29.66 (−), 32.61 (+), 46.12 (−), 62.75 (+), 116.37 (+), 117.33 (+), 125.95 (−), 132.79 (−), 132.88 (−), 135.50 (−), 136.47 (−), 145.59 (−), 191.97 (−); HRMS m/z calcd for $C_{15}H_{18}NO_3$ $[M + H]^+$ 260.1286; found. 260.1258. Further the eluent from hexane–dichloromethane (2:3) provide a red-colored solid which on crystallization from dichloromethane–hexane yielded **2t** (350 mg, 55%), m.p. 222°C (dec.); UV (MeOH): 222, 258.5, 378.5; IR (KBr): ν = 3323, 2924, 1724, 1651, 1616 cm^{-1}; ^{1}H-NMR (DMSO-d_6, 500 MHz) 2.03 (s, 3H, Ar—CH_3), 2.43 (s, 3H, C_3—CH_3), 3.81 (s, 3H, Ar—OCH_3), 6.67(s, 1H, C_2—H), 7.47 (s, 1H, C_8—H), 7.58 (s, 1H, C_5—H); ^{13}C-NMR (DMSO-d_6, 125 MHz): 15.72 (+), 16.31 (+), 62.58 (+), 113.22 (−), 113.39 (−), 117.54 (+), 131.55 (+), 131.65 (−), 134.68 (−), 137.55 (−), 138.16 (+), 146.08 (−), 148.24 (−), 179.48 (−), 181.28 (−); HMQC spectrum: δ_H (ppm):7.58 (C_5—H) δ_C (ppm): 118.41 (C_5); HRMS m/z calcd for $C_{15}H_{13}NO_3Na$ $[M + Na]^+$ 278.0793; found 278.0794.

6-Methoxy-3,7-dimethyl-1-oxo-3,4-dihydro-1H-carbazol—9(2H)-yl acetate (13). A mixture **3** (130 mg, 0.5 mmol), dry acetic anhydride (4.0 mL, 4.4 gm, 43 mmol), 4-(dimethylamino)pyridine (50.0 mg), and dry pyridine (two drops) was heated on water bath for 8 h. The reaction mixture was cooled and poured in ice water (50 mL), the whole mixture was extracted with ether (4 × 25 mL), the combined ether extract was washed with 5% $NaHCO_3$ solution until the evolution of carbon dioxide ceased, and then the organic phase was washed with brine solution (50 mL). Ether layer was dried over anhydrous Na_2SO_4 and evaporated. The residue was chromatographed over silica gel (10 gm) and elution with hexane–dichloromethane (3:2) furnished a light yellow-colored solid which on crystallization yielded **13** (120 mg, 80%), m.p. 123°C; UV (MeOH): 237 (sh), 320; IR (KBr): ν = 2956, 2929, 1716, 1678 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) 1.12 (d, J = 5.1 Hz, 3H, C_3—CH_3), 2.18–2.47 (m, 1H, C_3—1H), 2.44 (s, 3H, Ar—CH_3), 2.53 (s, 3H, $OCOCH_3$), 2.65 (d, J = 14.15, 2H, C_2—2H), 2.77 (d, J = 13.74 Hz, 2H, C_4—2H), 3.82 (s, 3H, Ar—OCH_3), 7.32 (s, 1H, C_8—H), 8.11 (s, 1H, C_5—H); ^{13}C-NMR ($CDCl_3$, 75 MHz): 17.25 (+), 20.86 (+), 27.55 (+), 29.82 (−), 31.17 (+), 46.83 (−) 62.75 (+), 116.79 (−), 119.78 (+), 128.65 (+), 133.47 (−), 133.57 (−), 135.55 (−), 135.65 (−), 146.73 (−), 171.95 (−), 189.38 (−).

6,9-Dimethoxy-3,7-dimethyl-1-oxo-3,4-dihydro-1H-carbazol-1-one (14). The compound **3** (100 mg, 0.38 mmol) was dissolved in dry benzene–*N*,*N*-dimethylformamide (DMF) mixture (2:1, 15 mL). After cooling the solution to 0°C, 60% sodium hydride in paraffin (60 mg, 1.5 mmol) was added to it. The reaction mixture was cooled in ice bath and iodomethane (600 mg, 4.2 mmol) was added with stirring. The stirring was continued for 7 h. The reaction mixture was poured in ice water (50 mL) and the whole mixture was extracted with dichloromethane (4 × 25 mL). The combined dichloromethane extract was washed with brine solution (25 mL), dried over anhydrous Na_2SO_4, and evaporated, and the residue was chromatographed over silica gel (8.5 gm) and elution with hexane–dichloromethane (3:2) furnished a light yellow-colored solid which was crystallized to obtain **14** (90 mg, 85%), m.p. 143°C; UV (MeOH): 240 (sh), 325; IR (KBr): ν = 2968, 2933, 1681 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 600 MHz) 1.18 (d, J = 5.4 Hz, 3H, C_3—CH_3), 2.41 (s, 3H, Ar—CH_3), 2.50 (q, 1H, C_3—1H), 2.71 (d, J = 14.15, 2H, C_2—2H), 2.75 (d, J = 13.74 Hz, 2H, C_4—2H), 3.82 (s, 3H, Ar—OCH_3), 3.97 (s, 3H, N—OCH_3), 7.19 (s,1H, C_8—H), 7.23 (s, 1H, C_5—H); ^{13}C-NMR ($CDCl_3$, 125 MHz): 17.26 (+), 20.22 (+), 29.33 (+) , 31.79 (−), 46.89 (−) 62.80 (+), 65.73 (+), 94.85 (+), 114.47 (+), 114.90 (−), 122.73 (−), 130.49 (−), 131.64 (−), 137.10 (−), 145.02 (−), 198.19 (−).

Oxidation of 3. The CAN-SiO_2 reagent was soaked with the solution of **3** (130 mg, 0.5 mmol) in dichloromethane (7 mL) and solvent was removed. The mixture was then kept over night at room temperature. The reaction mixture was then extracted with dichloromethane (2 × 50 mL). The solvent was removed and the residue so obtained was chromatographed over silica gel (10 gm) by eluting successively with hexane and hexane–dichloromethane (2:3). The eluent provided a red-colored solid which was crystallized from dichloromethane–hexane to yield **2t** (100 mg, 78%).

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