A Versatile Construction of the 8*H*-Quino[4,3-*b*]carbazole Ring System as a Potential DNA Binder

Arasambattu K. Mohanakrishnan and Panayencheri C. Srinivasan*

Department of Organic Chemistry, University of Madras, Guindy Campus, Madras - 600 025, Tamil Nadu, India

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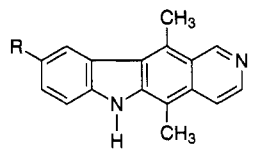
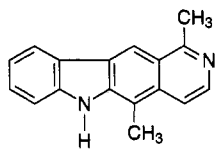
A short synthesis of the quino[4,3-*b*]- and quino[3,4-*b*]carbazoles is reported. The key step of the synthesis involves the preparation of suitable 2,3-divinylindoles by consecutive Wittig reactions. The thermal electrocyclic reaction of the divinylindole with concomitant dehydrogenation in the presence of Pd–C gave the (nitroaryl)carbazole which on reductive cyclization led to the quinocarbazole. The cleavage of the phenylsulfonyl group followed by phosphorus oxychloride treatment and subsequent displacement of the chlorine with 3-(dimethylamino)-1-propylamine gave the title compound in 25% overall yield.

Introduction

The plant alkaloid ellipticine (**1a**), 9-methoxyellipticine (**1b**), 9-hydroxyellipticine (**1c**), and olivacine (**2**) are potent antitumor agents, and elliptinium (**3**) is used clinically as a drug to treat advanced breast cancer, myeloblastic leukemia, and some solid tumors.[1]



1a–c
a; R = H
b; R = OCH_3
c; R = OH



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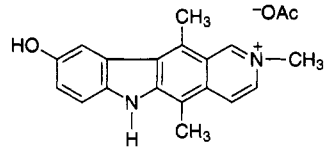
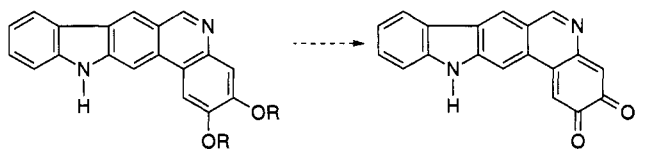


3

In recent years many second generation ellipticine-derived antitumor agents like datelliptium and retelliptine have been developed. The molecular basis for their antitumor activity stems from their ability to intercalate between the base pairs in DNA. 9-Hydroxyellipticine exhibits enhanced antitumor activity relative to ellipticine, since the presence of the 9-hydroxyl group could stabilize the intercalating complex by hydrogen bonding with the phosphate groups or base pairs present in the DNA.[2] Further, 9-hydroxyellipticine undergoes oxidation in vivo resulting in the formation of electrophilic quinone imines. This type of quinone imines could covalently bind to biomolecules such as proteins and nucleic acids.[3] It was conceived that quinolino carbazole **4** having adjacent methoxy groups at the E ring may undergo similar in vivo oxidation to give quinone derivatives **5** which in turn may covalently bind to DNA or proteins.



4 **5**

The promising anticancer activity of ellipticine and its analogues prompted chemists to develop many synthetic routes to the ellipticine nucleus and to synthesize a number of analogues for pharmacological evaluation.[4] The Diels–Alder approach for quinocarbazole was reported[5] from our lab. To the best of our knowledge no other report dealing with the synthesis of quinocarbazole analogues is available. So in continuation of our work in carbazole-containing natural products,[6–8] we report here a new synthetic route with complete details on the construction of quino[4,3-*b*]- and quino[3,4-*b*]carbazole analogues oxygenated in A, D, and E rings as potential DNA binders.

Results and Discussion

The utilization of thermal electrocyclic reaction for the synthesis of carbazole alkaloids hyellazole and its derivatives has received considerable attention in recent years.[9,10] Synthesis of genotoxic heterocyclic amines **Tryp-1** and **Tryp-2** has also been reported[11] using thermal electrocyclic reaction of the 1-azahexa-1,3,5-triene system involving the indole (b) bond. Our original methodology

[⊗] Abstract published in *Advance ACS Abstracts,* March 1, 1995.

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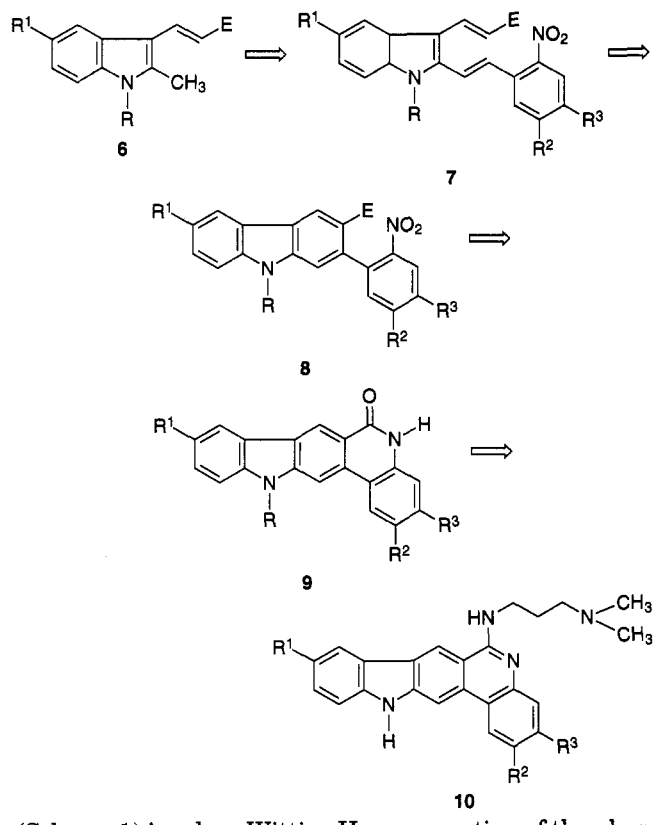
Scheme 1



(Scheme 1) involves Wittig–Horner reaction of the phosphonate ester **7** with 2-nitrobenzaldehydes followed by thermal electrocyclization and subsequent reductive cyclization to furnish amides **9** which could be converted to the quinocarbazole analogues **10** (Scheme 1).

8*H*-Quino[4,3-*b*]carbazole 25a–c. Our synthesis of the desired divinylindole and the subsequent conversion into quino[4,3-*b*]carbazole is illustrated in Scheme 2. 2-Methylindole-3-carboxaldehyde (**11**) was converted to 1-(phenylsulfonyl)-2-methylindole-3-carboxaldehyde (**13**) in 82% yield by treatment[12] with NaH and phenylsulfonyl chloride in DME. The Wittig reaction of **13** with (carbethoxymethylene)triphenylphosphorane in THF gave the 1-(phenylsulfonyl)-2-methyl-3-(β-carbethoxyvinyl)indole (**15**) in 75% yield. The bromination of **15** followed by subsequent Arbuzov reaction with triethyl phosphite gave the phosphonate ester **19** which underwent Wittig–Horner reaction with 2-nitrobenzaldehydes in NaH/THF condition to give **21** (Scheme 3). Boiling a xylene solution of **21** in the presence of 10% Pd–C gave the expected carbazole **23** as a single product. The reductive cyclization of the carbazole **23** with W_2 Ra–Ni in boiling THF followed by cleavage of the phenylsulfonyl group gave the expected amide **25**. The structure of the amide **25** is supported by IR, which shows carbonyl absorption at 1640 cm^{-1} consistent with the amide chromophore, and also by D_2O exchange studies (^1H NMR, 400 MHz).

The known[13] indole **12** was reduced by LAH at rt without cleaving the phenylsulfonyl group. Oxidation of the resulting alcohol by MnO_2 in refluxing dichloromethane gave the expected indole-3-carboxaldehyde **14** in 80% yield. The remaining synthetic steps for the synthesis of 11-methoxy-8*H*-quino[4,3-*b*]carbazole **26** are similar to that of 8*H*-quino[4,3-*b*]carbazole **25**.

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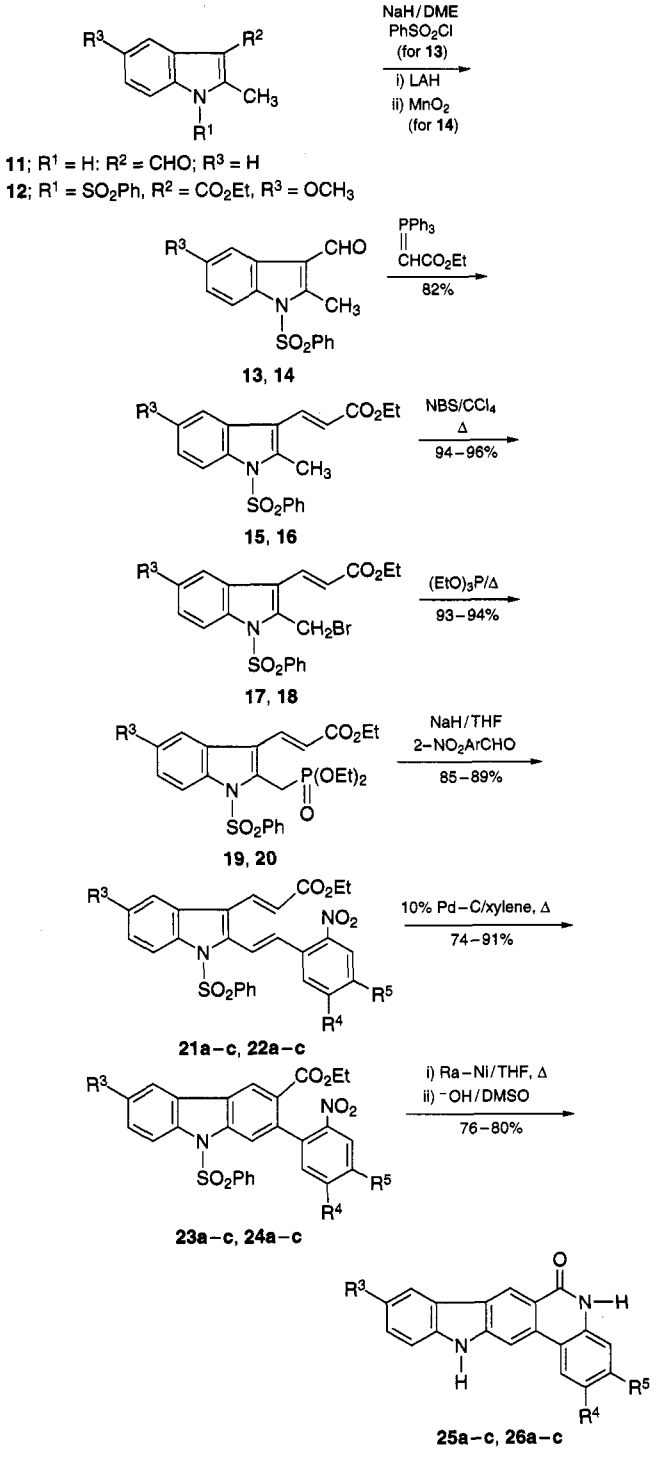
Scheme 2



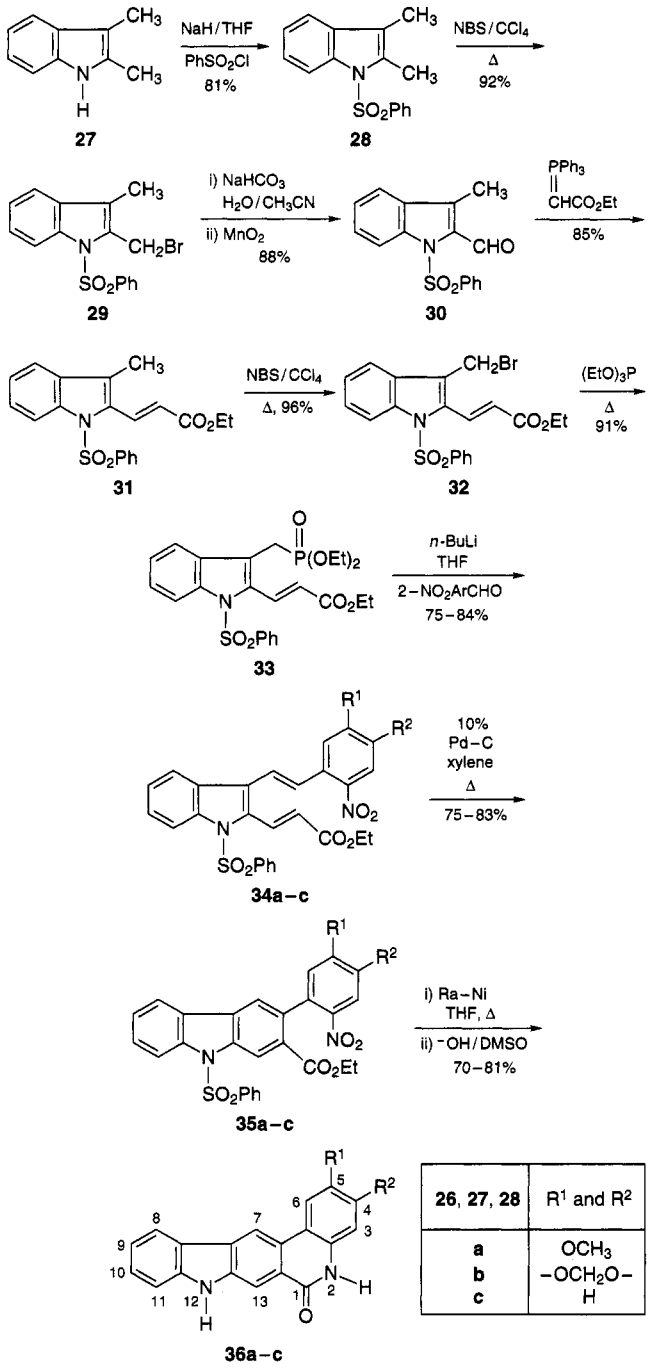
13, 15, 17, 19, 21, 23, 25	R^3 = H
14, 16, 18, 20, 22, 24, 26	R^3 = OCH_3

21, 22, 23, 24, 25, 26	R^4 and R^5
a	OCH_3
b	$-OCH_2O-$
c	H

The quino[3,4-*b*]carbazole **36** was synthesized using the same methodology (Scheme 3).

The conventional phenylsulfonylation of the 2,3-di-

Scheme 3



27 28 29 30 31 32 33 34a–c 35a–c

26, 27, 28	R¹ and R²
a	OCH_3
b	$-OCH_2O-$
c	H

36a–c

methylindole **27** using PTC[14] was unsuccessful. Hence it was phenylsulfonylated by treatment with NaH and phenylsulfonyl chloride in THF. Bromination of **28** with 1 equiv of NBS in boiling CCl_4 gave the monobromo compound **29** in almost quantitative yield.[15a] The subsequent hydrolysis of **29** using $NaHCO_3$ in CH_3CN followed by oxidation with[15b] MnO_2 in boiling 1,2-dichloroethane gave the known[16] 1-(phenylsulfonyl)-3-methylindole-2-carboxaldehyde **30** in 80% yield. The remaining synthetic steps for the synthesis of quino[3,4-*b*]carbazole **36** are similar to that of Scheme 2.

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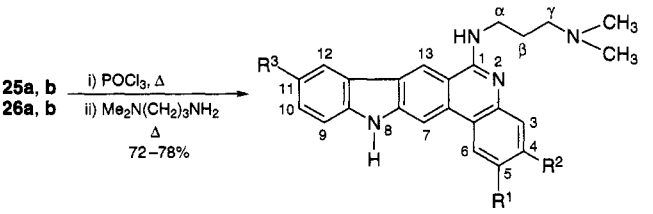
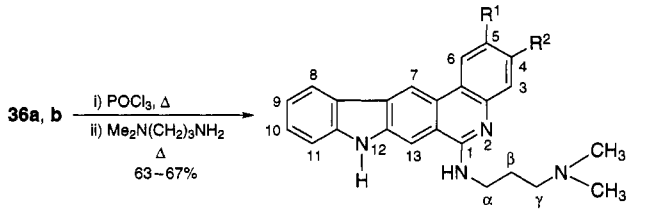
It is well known that aminoalkyl substituents are crucial structural features in pharmacologically active synthetic compounds. Particularly 9-methoxy-5,11-dimethyl-6*H*-pyrido[4,3-*b*]carbazole bearing a [3-(dialkylamino)propyl]amino moiety at the C-1 position shows a higher anticancer activity against myeloblastic leukemias and solid tumors compared with the parent ellipticine.[17] Hence the quinocarbazole analogues **25**, **26**, and **36** were converted[18] to the corresponding [(dimethylamino)propyl]-amino derivatives **37** and **38** as follows:



37a–d

37	R¹ and R²	R³
a	OCH_3	H
b	$-OCH_2O-$	H
c	OCH_3	OCH_3
d	$-OCH_2O-$	OCH_3



38a, b

38a; $R^1 = R^2 = OCH_3$
38b; $R^1 = R^2 = -OCH_2O-$

Synthesis of 1-Methyl-(4,5-dimethoxy)-8*H*-quino-[4,3-*b*]carbazoles 45 (Scheme 4). Wittig reaction of **13** with 1-(triphenylphosphoranylidene)-2-propanone in THF gave the 1′-[1-(phenylsulfonyl)-2-methylindol-3-yl]buten-3′-one **39**, bromination of which gave the monobromo compound **40**. In this case, the Arbuzov reaction of bromo compound gave a complex mixture. So use of Ph_3P gave the corresponding phosphonium salt **42** and the subsequent Wittig reaction was carried out with 2-nitrobenzaldehydes to give the 2,3-divinylindole **43**. Electrocyclization followed by reductive cyclization and hydrolysis gave the quinocarbazole analogues **45**.

Wittig reaction of the isomeric phosphonium salt **48** gave the 2,3-divinylindole **49** as the sole product with concurrent cleavage of phenylsulfonyl group. Attempted electrocyclization of **49** was found to be vain. So it seems that *N*-phenylsulfonyl group is indispensable for electrocyclization of 2,3-divinylindoles (Scheme 5).

Conclusion

For the first time the electrocyclization of 1-(phenylsulfonyl)-2,3-divinylindoles has been utilized for the synthesis of quinocarbazole analogues. The subsequent reductive cyclization followed by hydrolysis and the

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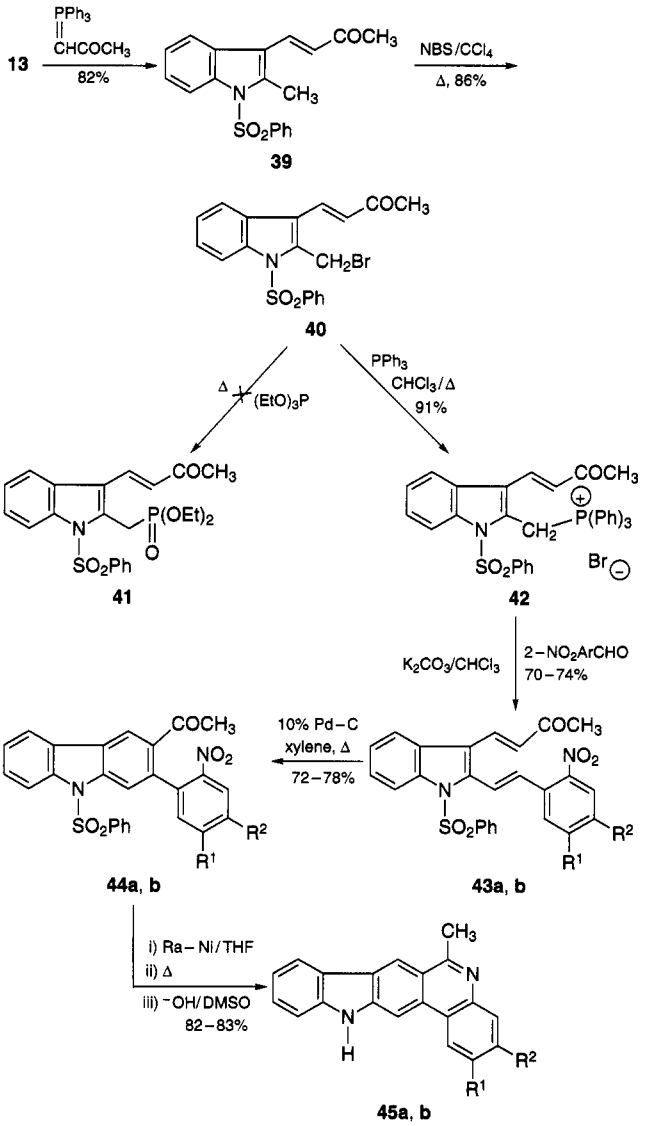
(18) (a) Ducroc, C.; Bisagni, E.; Rivalle, C.; Lhoste, J.-M. *J. Chem. Soc. Perkin Trans. 1* **1979**, 142. (b) Bisagni, E.; Ducrocq, C.; Lhoste, J.-M.; Rivalle, C.; Civier, A. *J. Chem. Soc. Perkin Trans. 1* **1979**, 1706.

Scheme 4



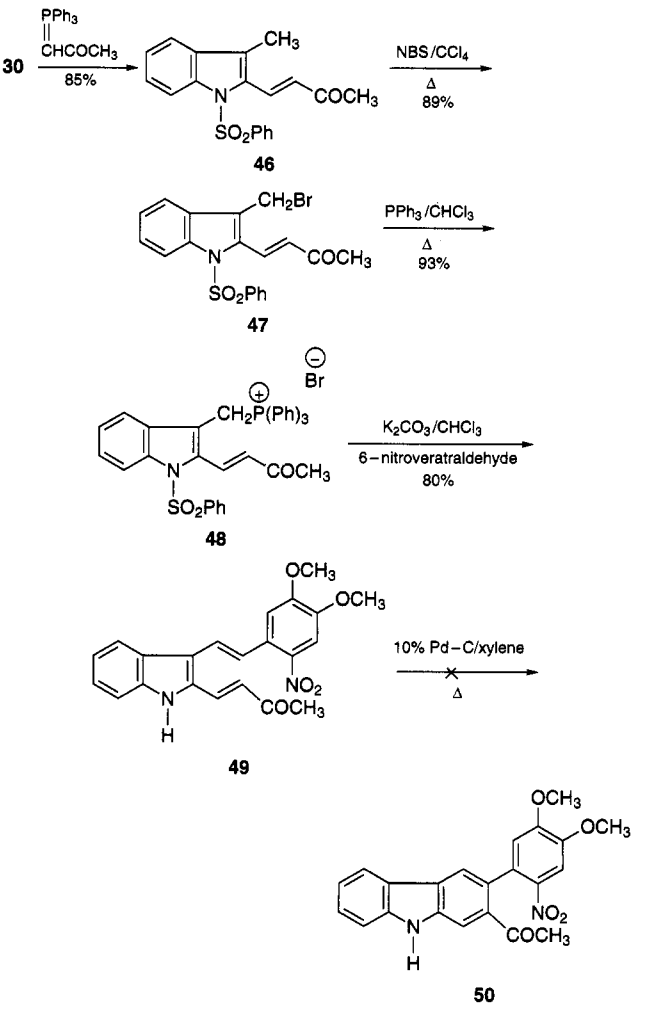
43, 44, 45	R^1 and R^2
a	OCH_3
b	$-OCH_2O-$

conversion into the corresponding [(dimethylamino)-propyl]amino derivative takes place with an overall yield of 25–30% starting from respective indole.

Experimental Section

All melting points are uncorrected. ^1H NMR spectra were recorded at 400, 300, 200, 90, and 60 MHz. ^{13}C NMR spectra were recorded at 75 MHz. Chemical shifts were reported in ppm (δ) using Me_4Si as standard, and coupling constants were expressed in hertz. Tetrahydrofuran was distilled from Na/benzophenone ketyl before use. n-Butyllithium (15% solution in n-hexane) purchased from Merck-Schuchardt was used. Elemental analyses were performed using a Perkin-Elmer 240 B elemental analyzer. HRMS data were obtained using a Finnigan MAT 8230 mass spectrometer. TLC chromatograms were developed on glass plates coated with silica gel-G (ACME) of 0.25 mm thickness and visualized with iodine. Column chromatography was carried out either with SiO_2 (silica gel, ACME, 100–200 mesh) or neutral Al_2O_3 (alumina, ACME, washed with ethyl acetate and activated). Glassware used was thoroughly dried in an oven, cooled, and assembled under a

Scheme 5



stream of nitrogen. The organic extracts of crude products were dried over anhydrous magnesium sulfate or sodium sulfate.

5-Methoxy-1-(phenylsulfonyl)-2-methylindole-3-carboxaldehyde (14). To a solution of LAH (0.57 g, 15 mmol) in dry THF (50 mL) was slowly added the ester[13] **12** (7.5 g, 20 mmol) in dry THF (200 mL) and stirred for 1 h. The excess LAH was destroyed (CH_3OH), and 10% NaOH (2 mL) was added and stirred. Then the THF solution was decanted, and the residue was washed with THF (3 × 20 mL). The solvent was then removed from the dried (K_2CO_3) extract. The residue was then dissolved in CH_2Cl_2 (300 mL). To this freshly prepared MnO_2 (10 g) was added and refluxed for 8 h. Then the MnO_2 was filtered and washed with CH_2Cl_2 (3 × 30 mL). The removal of the solvent gave 6 g (91%) of aldehyde **14** as colorless solid: mp 132–134 °C (benzene–hexane); IR (KBr) 1660, 1600, 1370, 1170 cm^{-1}; ^1H NMR ($CDCl_3$, 90 MHz) δ 10.4 (s, 1 H), 7.8–6.8 (m, 8 H), 3.9 (s, 3 H), 2.9 (s, 3 H). The compound was used as such for the next step without purification.

Ethyl 3′-[1-(Phenylsulfonyl)-2-methylindole-3-yl]acrylate (15). A solution of aldehyde **13** (2.9 g, 10 mmol) and (carbethoxymethylene)triphenylphosphorane (4.2 g, 12 mmol) in dry THF (70 mL) was refluxed for 12 h. The solution was then poured over ice (200 g), and the solid formed was filtered immediately and washed with MeOH. The crude product was recrystallized from MeOH to give 3 g (82%) of **15** as colorless crystals; mp 118 °C; IR (KBr) 1695, 1610, 1360, 1170 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 8.3–8.2 (d, J = 8 Hz, 1 H), 7.8–7.2 (m, 9 H), 6.6–6.4 (d, J = 17 Hz, 1 H), 4.3–4.2 (q, J = 8 Hz, 2 H), 2.7 (s, 3 H), 1.3 (t, J = 8 Hz, 3 H). Anal. Calcd for $C_{20}H_{19}NO_4S$: C, 65; H, 5.2; N, 3.8. Found: C, 64.7; H, 5.2; N, 3.9.

Ethyl 3′-[1-(Phenylsulfonyl)-2-(bromomethyl)indole-3-

yl]acrylate (17). A solution of **15** (3.7 g, 10 mmol) and benzoyl peroxide (0.05 g) containing finely powdered NBS (1.83 g, 10.3 mmol) in dry CCl_4 (200 mL) was refluxed for 2 h. The reaction mixture was cooled to rt and filtered, and the filtrate was concentrated in vacuo to give **17** as a colorless solid. The residue from the filtration was stirred for 1 h with CCl_4 (100 mL), filtered and concentrated in vacuo to give additional bromo compound. The combined solids were recrystallized from MeOH to give 4.2 g (94%) of bromo compound **17** as colorless crystals: mp 146 °C; IR (KBr) 1700, 1530, 1370, 1270, 1160 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 8.1–8 (d, J = 10 Hz, 1 H), 7.95–7 (m, 9 H), 6.8 (d, J = 18 Hz, 1 H), 5.15 (s, 2 H), 4.3 (q, J = 8 Hz, 2 H), 1.4 (t, J = 8 Hz, 3 H).

Diethyl [[1-(Phenylsulfonyl)-3-(β-carbethoxyvinyl)indol-2-yl]methyl]phosphonate (19). A mixture of (bromomethyl)indole **17** (4 g, 8.9 mmol) and triethyl phosphite (3 g, 18 mmol) was refluxed under N_2 at 170 °C for 3 h. The sticky oil was then poured over ice (200 g) and then acidified with concd HCl (1 mL). The solid was filtered and dried. The crude product was recrystallized from MeOH to give 4.2 g of phosphonate ester **19** as colorless crystals: mp 110 °C; IR (KBr) 1690, 1350, 1240, 1160, 1010 cm^{-1}; ^1H NMR ($CDCl_3$ FT 90 MHz) δ 8.3–7.2, (m, 10 H), 6.7 (d, J = 19 Hz, 1 H), 4.4–4.2 (m, 8 H), 1.4 (m, 9 H). Anal. Calcd for $C_{24}H_{28}NO_7PS$: C, 57; H, 5.6; N, 2.8. Found: C, 57; H, 5.7; N, 2.7.

General Procedure for the Wittig–Horner Reaction of the Phosphonate Ester 19 with Nitrobenzaldehydes. To a suspension of NaH (0.15 g, 6 mmol) in dry THF (20 mL) at −10 °C was slowly added the phosphonate ester **19** (2 g, 4 mmol) in dry THF (40 mL) under N_2 and stirred for 1 h. Then a solution of nitrobenzaldehyde (15 mmol) in dry THF (20 mL) was added. Stirring was continued for another 2 h. The yellow solution was poured over ice (200 g) and then acidified with concd HCl (1 mL). The solid was filtered and washed with MeOH. The crude product was recrystallized from MeOH.

3-(β-Carbethoxyvinyl)-1-(phenylsulfonyl)-2-[β′-(6′-nitroveratryl)vinyl]indole (21a). The Wittig–Horner reaction of phosphonate ester **19** with 6-nitroveratraldehyde as above afforded 2 g (89%) of **16a**: mp 162 °C; IR (KBr) 1690, 1610, 1500, 1380, 1330, 1170 cm^{-1}; ^1H NMR ($CDCl_3$, FT 90 MHz) δ 8.3 (d, J = 9 Hz, 1 H), 8–7.1 (m, 13 H), 6.55 (d, J = 19 Hz, 1 H), 4.2 (q, J = 8.4 Hz, 2 H), 4.1 (s, 3 H), 4 (s, 3 H), 1.31 (t, J = 8.4 Hz, 3 H). Anal. Calcd for $C_{29}H_{26}N_2O_8S$: C, 61.9; H, 4.7; N, 5.0. Found: C, 61.7; H, 4.7; N, 4.9.

3-(β-Carbethoxyvinyl)-1-(phenylsulfonyl)-2-[β′-[3′,4′-(methylenedioxy)-6′-nitrophenyl]vinyl]indole (21b). The Wittit–Horner reaction of **19** with 6-nitropiperonal as above gave 1.9 g (87%) of **21b**: mp 178 °C; IR (KBr) 1690, 1600, 1460, 1370, 1160 cm^{-1}; ^1H NMR ($CDCl_3$, FT 90 MHz) δ 8.3 (d, J = 9 Hz, 1 H), 8–7.1 (m, 13 H), 6.5 (d, J = 19 Hz, 1 H), 6.18 (s, 2 H), 4.28 (q, J = 8.4 Hz, 2 H), 1.2 (t, J = 8.4 Hz, 3 H). Anal. Calcd for $C_{28}H_{22}N_2O_8S$: C, 61.5; H, 4.1; N, 5.1. Found: C, 61.2; H, 4.2; N, 5.1.

3-(β-Carbethoxyvinyl)-[1-(phenylsulfonyl)-2-[β′-(2′-nitrophenyl)vinyl]indole (21c). Following the general procedure as above gave 1.9 g (87%) of **21c**: mp 166 °C; IR (KBr) 1700, 1620, 1500, 1370, 1340, 1170 cm^{-1}; ^1H NMR ($CDCl_3$, FT 90 MHz) δ 8.4–6.5 (m, 17 H), 4.2 (q, J = 8.4 Hz, 2 H), 1.24 (t, J = 8.4 Hz, 3 H). Anal. Calcd for $C_{27}H_{22}N_2O_6S$: C, 64.5; H, 4.4; N, 5.6. Found: C, 64.2; H, 4.5; N, 5.6.

General Procedure for Wittig–Horner Reaction of Phosphonate Ester 20 with Nitrobenzaldehydes. The procedure was similar to that of phosphonate ester **19** except that the reaction was performed at rt. The crude product was recrystallized from EtOH–$CHCl_3$.

5-Methoxy-3-(β-carbethoxyvinyl)-1-(phenylsulfonyl)-2-[β′-(6′-nitroveratryl)vinyl]indole (22a): 2.1 g (88%) mp 190 °C; IR (KBr) 1710, 1630, 1510, 1470, 1380, 1330, 1170 cm^{-1}; ^1H NMR ($CDCl_3$, FT 90 MHz) δ 8.15 (d, J = 13 Hz, 1 H), 8–6.9 (m, 12 H), 6.4 (d, J = 19 Hz, 1 H), 4.2 (q, J = 8.4 Hz, 2 H), 4.09 (s, 3 H), 4.01 (s, 6 H), 1.32 (t, J = 8.4 Hz, 3 H). Anal. Calcd for $C_{30}H_{28}N_2O_9S$: C, 60.8; H, 4.8; N, 4.7. Found: C, 60.4; H, 4.7; N, 4.6.

5-Methoxy-3-(β-carbethoxyvinyl)-1-(phenylsulfonyl)-2-[β′-(6′-nitropiperonyl)vinyl]indole (22b): 2 g (87%); mp 192 °C; IR (KBr) 1710, 1630, 1610, 1510, 1500, 1370, 1330, 1170 cm^{-1}; ^1H NMR ($CDCl_3$, FT 90 MHz) δ 8.15 (d, J = 13 Hz, 1 H), 7.9–7 (m, 12 H), 6.4 (d, J = 19 Hz, 1 H), 6.17 (s, 2 H), 4.28 (q, J = 8.4 Hz, 2 H), 3.86 (s, 3 H), 1.38 (t, J = 8.4 Hz, 3 H). Anal. Calcd for $C_{29}H_{24}N_2O_9S$: C, 60.4; H, 4.2; N, 4.9. Found: C, 60.1; H, 4.4; N, 4.7.

5-Methoxy-3-(β-carbethoxyvinyl)-1-(phenylsulfonyl)-2-[β′-(2′-nitrophenyl)vinyl]indole (22c): 1.8 g (85%); mp 168 °C; IR (KBr) 1710, 1620, 1510, 1370, 1330, 1160 cm^{-1}; ^1H NMR ($CDCl_3$, FT 90 MHz) δ 8.4–7 (m, 15 H), 6.4 (d, J = 19 Hz, 1 H), 4.2 (q, J = 8.4 Hz, 2 H), 3.8 (s, 3 H), 1.24 (t, J = 8.4 Hz, 3 H). Anal. Calcd for $C_{28}H_{24}N_2O_7S$: C, 63.1; H, 4.5; N, 5.3. Found: C, 62.7; H, 4.7; N, 5.1.

3-Carbethoxy-9-(phenylsulfonyl)-2-(6′-nitroveratryl)-carbazole (23a). A solution of **21a** (1.1 g, 2 mmol) in dry xylene (60 mL) containing 10% Pd–C (0.1 g) was refluxed for 24 h. The solution was filtered and the residue washed with hot xylene (3 × 10 mL). The removal of xylene from the combined filtrate gave the carbazole as pale yellow solid. It was boiled with EtOH (20 mL). On cooling 1 g (91%) of **23a** was obtained as colorless crystals: mp 200 °C; IR (KBr) 1700, 1500, 1370, 1340, 1330, 1240, 1160 cm^{-1}; ^1H NMR ($CDCl_3$, FT 90 MHz) δ 8.6 (s, 1 H, 4-H), 8.3 (d, J = 5.6 Hz, 1 H, 5-H), 8.2 (s, 1 H, 1-H), 8–7.3 (m, 9 H), 6.7 (s, 1 H), 4.1 (q, J = 8.4 Hz, 2 H), 4.05 (2s, 6 H), 1.16 (t, J = 8.4 Hz, 3 H). Anal. Calcd for $C_{29}H_{24}N_2O_8S$: C, 62.1; H, 4.3; N, 5.0. Found: C, 61.8; H, 4.4; N, 4.7.

3-Carbethoxy-9-(phenylsulfonyl)-2-[3′,4′-(methylenedioxy)-6′-nitrophenyl]carbazole (23b). Following the same procedure as above gave 0.95 g (88%) of **23b** as colorless crystals: mp 234 °C; IR (KBr) 1720, 1470, 1370, 1330, 1240, 1160 cm^{-1}; ^1H NMR ($CDCl_3$, FT 90 MHz) δ 8.6 (s, 1 H, 4-H), 8.2 (d, 1 H, 5-H), 8.1 (s, 1 H, 1-H), 7.9–7.2, (m, 9 H), 6.7 (s, 1 H), 6.17 (s, 2 H), 4.2 (q, J = 8.4 Hz, 2 H), 1.17 (t, J = 8.4 Hz, 3 H). Anal. Calcd for $C_{28}H_{20}N_2O_8S$: C, 61.8; H, 3.7; N, 5.1. Found: C, 61.5; H, 3.8; N, 4.8.

3-Carbethoxy-9-(phenylsulfonyl)-2-(2′-nitrophenyl)-carbazole (23c): 0.8 g (80%); mp 218 °C; IR (KBr) 1720, 1360, 1340, 1260, 1170 cm^{-1}; ^1H NMR ($CDCl_3$, FT 90 MHz) δ 8.6 (s, 1 H, 4-H), 8.4–7.3 (m, 14 H), 4.15 (q, J = 8.4 Hz, 2 H), 1.07 (t, J = 8.4 Hz, 3 H). Anal. Calcd for $C_{27}H_{20}N_2O_6S$: C, 64.8; H, 4.0; N, 5.6. Found: C, 64.6; H, 4.2; N, 5.4.

6-Methoxy-3-carbethoxy-9-(phenylsulfonyl)-2-(6′-nitroveratryl)carbazole (24a). The procedure was similar to that of **23**: 0.88 g (75%); mp 184 °C; IR (KBr) 1730, 1590, 1510, 1370, 1330, 1250, 1170 cm^{-1}; ^1H NMR ($CDCl_3$, FT 90 MHz) δ 8.5 (s, 1 H, 4-H), 8.2–7 (m, 11 H), 4.2 (q, J = 8.4 Hz, 2 H), 4.15 (s, 3 H), 4 (s, 3 H), 3.95 (s, 3 H), 1.06 (t, J = 8.4 Hz, 3 H). Anal. Calcd for $C_{30}H_{26}N_2O_9S$: C, 61; H, 4.4; N, 4.7. Found: C, 60.8; H, 4.5; N, 4.8.

6-Methoxy-3-carbethoxy-9-(phenylsulfonyl)-2-[3′,4′-(methylenedioxy)-6′-nitrophenyl)carbazole (24b): 0.85 g (74%); mp 208 °C; IR (KBr) 1720, 1480, 1370, 1330, 1240, 1170 cm^{-1}; ^1H NMR ($CDCl_3$, FT 90 MHz) δ 8.4–7 (m, 12 H), 6.1 (s, 2 H), 4.1 (q, J = 8.4 Hz, 2 H), 3.8 (s, 3 H), 1.17 (t, J = 8.4 Hz, 3 H). Anal. Calcd for $C_{29}H_{22}N_2O_9S$: C, 60.6; H, 3.9; N, 4.9. Found: C, 60.5; H, 4; N, 4.9.

6-Methoxy-3-carbethoxy-9-(phenylsulfonyl)-2-(2′-nitrophenyl)carbazole (24c): 0.8 g (75%); mp 202 °C; IR (KBr) 1710, 1600, 1520, 1370, 1340, 1170 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ 8.7 (s, 1 H, 4-H), 8.3–7.1 (m, 13 H), 4.1 (q, J = 8 Hz, 2 H), 3.9 (s, 3 H), 1.1 (t, J = 8 Hz, 3 H). Anal. Calcd for $C_{28}H_{22}N_2O_7S$: C, 63.4; H, 4.2; N, 5.3. Found: C, 63.1; H, 4.3; N, 5.3.

General Procedure for Reductive Cyclization and Subsequent Hydrolysis of the Carbazoles 23. To a solution of carbazole (2 mmol) in dry THF (100 mL) was added freshly prepared W_2 grade Ra-Ni (6–7 g) and refluxed for 4 h. Then the nickel was filtered and washed with hot THF (3 × 30 mL). The combined filtrate was evaporated. To this were added DMSO (40 mL) and 50% NaOH (5 mL). The reaction mixture was stirred at rt for 10 h and poured over ice (300 g). The solution is slightly warmed to avoid the emulsification, and the solid formed was filtered and dried ($CaCl_2$). The crude product was recrystallized from DMSO.

4,5-Dimethoxy-8*H*-quino[4,3-*b*]carbazol-1(2*H*)-one (25a). Following the general procedure as above gave 0.55 g (80%) of **25a**: mp > 350 °C; IR (KBr) 3490, 1650, 1600 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz) δ 11.58 (s, 1 H, amide NH, exchangeable with D_2O), 11.28 (s, 1 H, indole NH, exchangeable with D_2O), 9.1 (s, 1 H, 13-H), 8.35 (s, 1 H, 7-H), 8.3 (d, J = 10 Hz, 1 H, 12-H), 7.85 (s, 1 H, 6-H), 7.6 (d, J = 10 Hz, 1 H, 9-H), 7.5 (m, 1 H, 11-H), 7.28 (m, 1 H, 10-H), 6.98 (s, 1 H, 3-H), 3.95 (s, 3 H), 3.85 (s, 3 H); MS *m/e* 344 (M^+). Anal. Calcd for $C_{21}H_{16}N_2O_3$: C, 73.2; H, 4.7; N, 8.1. Found: C, 72.9; H, 4.9; N, 7.9.

4,5-(Methylenedioxy)-8*H*-quino[4,3-*b*]carbazol-1(2*H*)-one (25b): 0.5 g (76%); mp > 350 °C; IR (KBr) 3480, 1660, 1600 cm^{-1}; ^1H NMR (DMSO-d_6, FT 90 MHz) δ 11.35 (s, 1 H, amide NH, exchangeable with D_2O), 11.3 (s, 1 H, indole NH, exchangeable with D_2O), 9 (s, 1 H, 13-H), 8.07–7.3 (m, 6 H), 7 (s, 1 H, 3-H), 5.9 (s, 2 H); MS *m/e* 328 (M^+). Anal. Calcd for $C_{20}H_{12}N_2O_3$: C, 73.2; H, 3.7; N, 8.5. Found: C, 72.8; H, 3.9; N, 8.4.

8*H*-Quino[4,3-*b*]carbazol-1(2*H*)-one (25c): 0.44 g (78%); mp > 350 °C; IR (KBr) 3500, 1660, 1610 cm^{-1}; ^1H NMR (DMSO-d_6, FT 90 MHz) δ 11.5 (s, 1H, amide NH, exchangeable with D_2O), 11.45 (s, 1 H, indole NH, exchangeable with D_2O), 9.1 (s, 1 H, 13-H), 8.4–7.3 (m, 9 H); MS *m/e* 284 (M^+). Anal. Calcd for $C_{19}H_{12}N_2O$: C, 80.3; H, 4.2; N, 9.8. Found: C, 80; H, 4.4; N, 9.7.

General Procedure for Reductive Cyclization and Subsequent Hydrolysis of the Carbazoles 24. To a solution of carbazole (2 mmol) in dry THF (100 mL) was added freshly prepared W_2 grade Ra-Ni (10 g) and then refluxed for 4 h. Then the nickel was filtered and washed with hot DMSO (5 × 50 mL). The combined filtrate was poured over ice (500 g), and the solid was filtered. Then it was dissolved in DMSO (50 mL). To this was added 50% NaOH (5 mL), and the reaction mixture was stirred at rt for 16 h and poured over ice (300 g). The solution is then slightly warmed to avoid emulsification, and the solid formed was filtered and dried ($CaCl_2$). The crude product was recrystallized from DMSO.

4,5,11-Trimethoxy-8*H*-quino[4,3-*b*]carbazol-1(2*H*)-one (26a). Following the general procedure as above gave 0.58 g (77%) of the amide **26a** as colorless solid; mp > 350 °C; IR (KBr) 3400, 1650, 1600 cm^{-1}; ^1H NMR (DMSO-d_6, 300 MHz) δ 9.9 (bs, 1 H, amide NH, exchangeable with D_2O), 9.8 (bs, 1 H, indole NH, exchangeable with D_2O), 9.1 (s, 1 H, 13-H), 8.3 (s, 1 H, 7-H), 7.89 (s, 1 H, 12-H), 7.81 (s, 1 H, 3-H), 7.47–7.45 (d, J = 8 Hz, 1 H, 9-H), 7.1–7.08 (d, J = 8 Hz, 1 H, 10-H), 6.95 (s, 1 H, 6-H), 3.93 (s, 3 H), 3.87 (s, 3 H), 3.83 (s, 3 H). ^{13}C NMR (DMSO-d_6, 75 MHz) δ 161, 154, 150, 144.7, 143, 136, 132, 131, 122.9, 122.7, 120, 116.8, 115.7, 111.7, 110.7, 106, 104, 102, 99, 56, 55.5, 55.4. Anal. Calcd for $C_{22}H_{18}N_2O_4$: C, 70.6; H, 4.8; N, 7.5. Found: C, 70.1; H, 5; N, 7.4. HRMS calcd for $C_{22}H_{18}N_2O_4$ 374.1266, found M^+ 374.1259.

11-Methoxy-4,5-(methylenedioxy)-8*H*-quino[4,3-*b*]carbazol-1(2*H*)-one (26b): 0.55 g (77%); mp > 350 °C; IR (KBr) 3460, 1650, 1630, 1600 cm^{-1}; ^1H NMR (DMSO-d_6, 300 MHz) δ 10 (s, 1 H, amide NH, exchangeable with D_2O), 9.8 (s, 1 H, indole NH, exchangeable with D_2O), 9.1 (s, 1 H, 13-H), 8.2 (s, 1 H, 7-H), 7.88 (s, 1 H, 12-H), 7.87 (s, 1 H, 3-H), 7.46–7.43 (d, J = 9.7 Hz, 1 H, 9-H), 7.1–7.07 (m, 1 H, 10-H), 6.89 (s, 1 H, 6-H), 6.06 (s, 2 H), 3.9 (s, 3 H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 161.5, 153.6, 148.2, 143.5, 136.1, 132.2, 132, 123, 122.8, 120.4, 116.6, 115.9, 112, 111.8, 103.8, 102.1, 102, 101.4, 96.3, 55.6; HRMS calcd for $C_{21}H_{14}N_2O_4$ 358.0954, found M^+ 358.0940.

11-Methoxy-8*H*-quino[4,3-*b*]carbazol-1(2*H*)-one (26c): 0.5 g (80%); mp > 350 °C; IR (KBr) 3350, 1650, 1600 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz) δ 11.5 (s, 1 H, amide NH, exchangeable with D_2O), 11.4 (s, 1 H, indole NH, exchangeable with D_2O), 9.18 (s, 1 H, 13-H), 8.45 (d, 1 H, 9-H), 8.4 (s, 1 H, 7-H), 7.95 (s, 1 H, 12-H), 7.45–7.15 (m, 5 H, ArH), 3.9 (s, 3 H). Anal. Calcd for $C_{20}H_{14}N_2O_2$: C, 76.4; H, 4.5; N, 8.9. Found: C, 75.9; H, 4.7; N, 8.9. HRMS calcd for $C_{20}H_{14}N_2O_2$ 314.1055, found M^+ 314.1025.

1-(Phenylsulfonyl)-3-methyl-2-(bromomethyl)indole (29). The procedure was similar to that of **17**: 13.4 g (92%); mp 136 °C; ^1H NMR ($CDCl_3$, FT 90 MHz) δ 8.1–7.4 (m, 9 H), 5.1 (s, 2 H), 2.2 (s, 3 H).

1-(Phenylsulfonyl)-3-methylindole-2-carboxaldehyde (30). To a solution of **29** (10.9 g, 30 mmol) in CH_3CN (200 mL) and H_2O (30 mL), $NaHCO_3$ (5 g, 60 mmol) was added and refluxed for 2 h. Then the solvent was completely removed and the sticky residue was extracted with CH_2Cl_2 (3×50 mL) and dried (Na_2SO_4) and the solvent was completely removed. The residue was dissolved in dry 1,2-dichloroethane (300 mL). To this was added freshly prepared MnO_2 (15 g) and refluxed for 12 h. The progress of the reaction was monitored by TLC. Then the MnO_2 was filtered and washed with hot 1,2-dichloroethane (4×50 mL), and the combined filtrate was concentrated to give 7.9 g (88%) of **30** as white solid: mp 210 °C; IR (KBr) 1670, 1370, 1180 cm^{-1}; ^1H NMR ($CDCl_3$, 90 MHz) 10.5 (s, 1 H), 8.1–6.8 (m, 9 H), 2.34 (s, 3 H).

Ethyl 3′-[1-(Phenylsulfonyl)-3-methylindol-2-yl]acrylate (31). The procedure was similar to that of **15**: 3.2 g (85%); mp 156 °C; IR (KBr) 1700, 1360, 1170 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ 8.4–7.2 (m, 10 H), 6.15 (d, J = 18 Hz, 1 H), 4.4 (q, J = 8 Hz, 2 H), 2.2 (s, 3 H), 1.3 (t, J = 8 Hz, 3 H). Anal. Calcd for $C_{20}H_{19}NO_4S$: C, 65; H, 5.2; N, 3.8. Found: C, 65.1; H, 5.3; N, 3.7.

Ethyl 3′-[1-(Phenylsulfonyl)-3-(bromomethyl)indol-2-yl]acrylate (32). The procedure was similar to that of **17**; 4.4 g (96%); mp 150 °C; IR (KBr) 1710, 1360, 1170 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ 8.3–7.2 (m, 10 H), 6.2 (d, J = 18 Hz, 1 H), 4.7 (s, 2 H), 4.3 (q, J = 8 Hz, 2 H), 1.4 (t, J = 8 Hz, 3 H).

Diethyl [[1-(Phenylsulfonyl)-2-(β-carbethoxyvinyl)indol-3-yl]methyl]phosphonate (33). The procedure was similar to that of **19**: 4.1 g (91%); mp 130 °C; IR (KBr) 1700, 1620, 1360, 1170 cm^{-1}; ^1H NMR ($CDCl_3$, FT 90 MHz) δ 8.3–7.3 (m, 10 H), 6.8–6.6 (d, J = 19 Hz, 1 H), 4.37 (q, J = 8.4 Hz, 2 H), 3.8 (m, 4 H), 3.3 (d, J = 24 Hz, 2 H), 1.45 (t, J = 8.4 Hz, 3 H), 1.14 (t, J = 8.4 Hz, 6 H). Anal. Calcd for $C_{24}H_{28}NO_7PS$: C, 57; H, 5.6; N, 2.8. Found: C, 57; H, 5.8; N, 2.5.

General Procedure for Wittig–Horner Reaction of the Phosphonate Ester 33 with Nitrobenzaldehydes. To a solution of phosphonate ester **33** (2 g, 4 mmol) in dry THF (50 mL) at −10 °C under N_2 was slowly added *n*-BuLi (2.6 mL, 5 mmol) followed by the addition of nitrobenzaldehyde (5 mmol) in dry THF (20 mL). Stirring was continued for 2 h. The yellow solution was poured over ice (200 g), and the solid was filtered and washed with MeOH. The crude product was recrystallized from EtOAc or EtOH–$CHCl_3$.

2-(β-Carbethoxyvinyl)-1-(phenylsulfonyl)-3-[β′-(6′-nitroveratryl)vinyl]indole (34a): 1.9 g (84%); mp 176 °C; IR (KBr) 1710, 1610, 1500, 1370, 1330, 1270, 1170 cm^{-1}; ^1H NMR ($CDCl_3$, FT 90 MHz) δ 8.2–8 (m, 2 H), 7.9–6.8 (m, 12 H), 6.1 (d, J = 19 Hz, 1 H), 4.3 (q, J = 8.4 Hz, 2 H), 3.9 (s, 3 H), 3.8 (s, 3 H), 1.3 (t, J = 8.4 Hz, 3 H). Anal. Calcd for $C_{29}H_{26}N_2O_8S$: C, 61.9; H, 4.7; N, 5.0. Found: C, 61.5; H, 4.9; N, 5.1.

2-(β-Carbethoxyvinyl)-1-(phenylsulfonyl)-3-[β′-[3′,4′-(methylenedioxy)-6′-nitrophenyl]vinyl]indole (34b): 1.7 g (77%); mp 162 °C; IR (KBr) 1710, 1500, 1370, 1330, 1170 cm^{-1}; ^1H NMR ($CDCl_3$, FT 90 MHz) δ 8.2–8 (m, 2H), 7.9–6.8 (m, 12 H), 6.1 (m, 3H, ArH + -OCH_2O-), 4.4 (q, J = 8.4 Hz, 2 H), 1.4 (t, J = 8.4 Hz, 3 H). Anal. Calcd for $C_{28}H_{22}N_2O_8S$: C, 61.5; H, 4.1; N, 5.1. Found: C, 61.4; H, 4.2; N, 5.0.

2-(β-Carbethoxyvinyl)-1-(phenylsulfonyl)-3-[β′-(2′-nitrophenyl)vinyl]indole (34c): 1.5 g (75%); mp 142 °C; IR (KBr) 1720, 1600, 1500, 1370, 1330, 1180 cm^{-1}; ^1H NMR ($CDCl_3$, FT 90 MHz) δ 8.4–7.3 (m, 15 H), 6.9 (d, J = 19 Hz, 1 H), 6.1 (d, J = 19 Hz, 1 H), 4.3 (q, J = 8.4 Hz, 2 H), 1.4 (t, 3 H).

2-Carbethoxy-9-(phenylsulfonyl)-3-[6′-nitroveratryl)]-carbazole (35a). The procedure was similar to that of **23**: 0.9 g (80%); mp 200 °C; IR (KBr) 1700, 1500, 1360, 1320, 1260, 1200, 1170 cm^{-1}; ^1H NMR ($CDCl_3$, FT 90 MHz) δ 8.9 (s, 1 H, 1-H), 8.3–6.8 (m, 11 H), 6.6 (s, 1 H), 4.2 (q, J = 8.4 Hz, 2 H), 3.9 (s, 3 H), 3.8 (s, 3 H), 1.1 (t, J = 8.4 Hz, 3 H). Anal. Calcd for $C_{29}H_{24}N_2O_8S$: C, 62.1; H, 4.3; N, 5.0. Found: C, 61.8; H, 4.4; N, 5.1.

2-Carbethoxy-9-(phenylsulfonyl)-3-[3′,4′-(methylenedioxy)-6′-nitrophenyl]carbazole (35b): 0.9 g (83%); mp 214 °C; IR (KBr) 1710, 1500, 1370, 1320, 1160 cm^{-1}; ^1H NMR ($CDCl_3$, FT 90 MHz) δ 8.96 (s, 1 H, 1-H), 8.4–6.5 (m, 11 H), 6.3 (s, 1 H), 6.05 (s, 2 H), 4.2 (q, J = 8.4 Hz, 2 H), 1.2 (t, J =

8.4 Hz, 3 H). Anal. Calcd for $C_{28}H_{20}N_2O_8S$: C, 61.8; H, 3.7; N, 5.2. Found: C, 61.4; H, 3.7; N, 5.2.

2-Carbethoxy-9-(phenylsulfonyl)-3-(2′-nitrophenyl)-carbazole (35c): 0.75 g (75%); mp 184 °C; IR (KBr) 1700, 1510, 1360, 1340, 1260, 1170 cm^{-1}; ^1H NMR ($CDCl_3$, FT 90 MHz) δ 8.9 (s, 1 H, 1-H), 8.3–7.2 (m, 14 H), 4.1 (q, J = 8.4 Hz, 2 H), 1.1 (t, J = 8.4 Hz, 3 H). Anal. Calcd for $C_{27}H_{20}N_2O_6S$: C, 64.8; H, 4.0; N, 5.6. Found: C, 64.4; H, 4.3; N, 5.3.

4,5-Dimethoxy-8*H*-quino[3,4-*b*]carbazol-1(2*H*)-one (36a). The procedure was similar to that of **25**: 0.56 g (81%); mp > 350 °C; IR (KBr) 3300, 1650 cm^{-1}; ^1H NMR (DMSO-d_6, FT 90 MHz) δ 11.45 (s, 1 H, amide NH, exchangeable with D_2O), 11.4 (s, 1 H, indole NH, exchangeable with D_2O), 9.2 (s, 1 H, 13-H), 8.44 (s, 1 H, 7-H), 8.3 (d, 1 H, 11-H), 8 (s, 1 H, 3-H), 7.7–7.2 (m, 3 H), 7 (s, 1 H, 6-H), 4.02 (s, 3 H), 3.9 (s, 3 H). HRMS calcd for $C_{21}H_{16}N_2O_3$ 344.1160, found M^+ 344.1119.

4,5-(Methylenedioxy)-8*H*-quino[3,4-*b*]carbazol-1(2*H*)-one (36b): 0.48 g (73%); mp > 350 °C; IR (KBr) 3400, 1650, 1620 cm^{-1}; ^1H NMR (DMSO-d_6, FT 90 MHz) δ 11.44 (s, 1 H, amide NH, exchangeable with D_2O), 11.4 (s, 1 H, indole NH, exchangeable with D_2O), 9.14 (s, 1 H, 13-H), 8.33 (s, 1 H, 7-H), 8.31 (m, 1 H, 11-H), 8.1 (s, 1 H, 3-H), 7.5–7.2 (m, 3 H), 6.9 (s, 1 H, 6-H), 6.60 (s, 2 H). HRMS calcd for $C_{20}H_{12}N_2O_3$ 328.0848, found M^+ 328.0895.

8*H*-Quino[3,4-*b*]carbazol-1(2*H*)-one (36c): 0.43 g (70%); mp > 350 °C; ^1H NMR (DMSO-d_6, FT 90 MHz) δ 11.3 (bs, 2 H, amide NH and indole NH, exchangeable with D_2O), 9.2 (s, 1 H, 13-H), 8.3 (s, 1 H, 7-H), 7.9 (s, 1 H, 12-H), 7.8 (s, 1 H, 3-H), 7.5–7.4 (d, 1 H, 9-H), 7.1 (d, 1 H, 10-H), 6.9 (s, 1 H, 6-H). HRMS calcd for $C_{19}H_{12}N_2O$ 284.0949, found M^+ 284.0923.

General Procedure for Quino[4,3-*b*]carbazole 37 and quino[3,4-*b*]carbazole 38. Amide (1 mmol) in distilled $POCl_3$ (80 mL) was refluxed with stirring under N_2 for 24 h. Then the excess $POCl_3$ was removed in vacuo. To the cooled residue was added saturated solution of $NaHCO_3$ (50 mL) with stirring, and then the reaction mixture was allowed to settle for 1 h. The chloroquinoline was filtered and dried ($CaCl_2$). It was then dissolved in 3-(*N*,*N*-dimethylamino)-1-propylamine (20 mL) and refluxed under N_2 for 20 h. The excess amine was then removed in vacuo. The sticky residue was extracted with $CHCl_3$ (3 × 50 mL) and the extract was washed with H_2O (2 × 50 mL) and dried (Na_2SO_4). Removal of the solvent followed by purification by column chromatography (neutral-Al_2O_3, 30 g) using 1% MeOH/$CHCl_3$ as eluent gave the corresponding alkylamine derivatives (**37** and **38**).

1-[3′-(*N*,*N*-Dimethylamino)propyl]-4,5-dimethoxy-8*H*-quino[4,3-*b*]carbazole (37a): 0.345 g (77%); mp 140 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.67–8.62 (bs, 2 H, NH, exchangeable with D_2O), 8.42 (s, 1 H, 13-H), 8.15 (s, 1 H, 7-H), 8 (d, J = 7.5 Hz, 1 H, 12-H), 7.55 (s, 1 H, 3-H), 7.4 (m, 2 H, 9-H and 10-H), 7.3–7.2 (m, 2 H, 6-H and 11-H), 3.95–3.9 (2s, 6 H, OCH_3), 3.82–3.77 (t, J = 6.1 Hz, 2 H, CH_2-α), 2.57 (t, J = 6.1 Hz, 2 H, CH_2-γ), 2.4 (s, 6 H, NMe_2), 1.9 (m, 2 H, CH_2-β); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 153, 150.6, 146, 142.3, 141.8, 131.6, 127.2, 123.6, 122.8, 119.9, 114.8, 113.6, 111.5, 105.4, 103.4, 101.6, 93.4, 59, 56.1, 56, 45.4, 43.3, 24.5. Anal. Calcd for $C_{26}H_{28}N_4O_2{\cdot}H_2O$: C, 69.9; H, 6.8; N, 12.5. Found: C, 70; H, 6.7; N, 12.5.

1-[3′-(*N*,*N*-Dimethylamino)propyl]-4,5-(methylenedioxy)-8*H*-quino[4,3-*b*]carbazole (37b): 0.32 g (74.4%); mp 220 °C; ^1H NMR ($CDCl_3$, 300 MHz) δ 8.68–8.64 (bs, 2 H, NH, exchangeable with D_2O), 8.38 (s, 1 H, 13-H), 8–7.98 (m, 2 H, 7-H and 12-H), 7.52 (s, 1 H, 3-H), 7.41–7.40 (m, 2 H, 9-H and 10-H), 7.22–7.2 (m, 1 H, 11-H), 7.15 (s, 1 H, 6-H), 5.93 (s, 2 H, -OCH_2O-), 3.78–3.75 (t, J = 6 Hz, 2 H, CH_2-α), 2.55–2.52 (t, J = 6 Hz, 2 H, CH_2-γ), 2.38 (s, 6 H, NMe_2), 1.88–1.85 (m, 2 H, CH_2-β). Anal. Calcd for $C_{25}H_{24}N_4O_2{\cdot}H_2O$: C, 69.7; H, 6.1; N, 13.0. Found: C, 70; H, 6; N, 13.3.

11-Methoxy-1-[3′-(*N*,*N*-dimethylamino)propyl]-4,5-dimethoxy-8*H*-quino[4,3-*b*]carbazole (37c): 0.37 g (77.7%); mp 230 °C; ^1H NMR ($CDCl_3$, 300 MHz) δ 8.62 (bs, 1 H, indole NH, exchangeable with D_2O), 8.33 (s, 1 H, 13-H), 7.98 (s, 1 H, 7-H), 7.81 (bs, 1 H, 1′-NH, exchangeable with D_2O), 7.52 (s, 1 H, 3-H), 7.48 (d, 1 H, 12-H), 7.29–7.26 (m, 1 H, 9-H), 7.19 (s, 1 H, 6-H), 7 (m, 1 H, 10-H), 3.9 (s, 6 H, OCH_3), 3.85 (s, 3 H, OCH_3), 3.77 (t, J = 5.1 Hz, 2 H, CH_2-α), 2.54–2.51 (t, J = 5.1 Hz, 2 H, CH_2-γ), 2.36 (s, 6 H, -NMe_2), 1.88–1.85 (m, 2 H, CH_2-β). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 154.1, 150.5, 145.4, 142.3, 139.6, 136.2, 132.2, 128.3, 123.8, 123.4, 115.3, 114.4, 113.9, 112.5, 111.4, 107.5, 103.6, 103.5, 101.2, 59.5, 56.2, 55.98, 55.9, 45.7, 43, 25.5. Anal. Calcd for $C_{27}H_{30}N_4O_3{\cdot}H_2O$: C, 68; H, 6.8; N, 11.7. Found: C, 67.9; N, 6.8; N, 11.8.

11-Methoxy-1-[3′-(*N*,*N*-dimethylamino)propyl]-4,5-(methylenedioxy)-8*H*-quino[4,3-*b*]carbazole (37d): 0.35 g (72.2%); mp 220 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.43 (s, 1 H, 13-H), 8.35 (bs, 1 H, indole NH, exchangeable with D_2O), 8.03 (s, 1 H, 7-H), 7.65 (bs, 1 H, 1′-NH, exchangeable with D_2O), 7.62 (s, 1 H, 3-H), 7.58 (d, J = 3.5 Hz, 1 H, 12-H), 7.38–7.35 (d, J = 9 Hz, 1 H, 9-H), 7.25 (s, 1 H, 6-H), 7.13–6.98 (m, 1 H, 10-H), 6 (s, 2 H, -OCH_2O-), 3.98 (s, 3 H, OCH_3), 3.9 (t, J = 5.9 Hz, 2 H, CH_2-α), 2.62 (t, J = 5.9 Hz, 2 H, CH_2-γ), 2.45 (s, 6 H, NMe_2), 1.95–1.92 (m, 2 H, CH_2-β). Anal. Calcd for $C_{26}H_{26}N_4O_3$; C, 70.6; H, 5.9; N, 12.7. Found: C, 70.4; H, 6.2; N, 12.4.

1-[3′-(*N*,*N*-dimethylamino)propyl]-4,5-dimethoxy-12*H*-quino[3,4-*b*]carbazole (38a): 0.28 g (62.8%); mp 134 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.75–9.65 (bs, 1 H, NH, exchangeable with D_2O), 8.6 (s, 1 H, 13-H), 8.18 (d, J = 10 Hz, 1 H, 11-H), 8 (s, 1 H, 7-H), 7.66 (s, 1 H, 3-H), 7.5–7.4 (m, 2 H, 10-H and 9-H), 7.3–7.2 (m, 1 H, 8-H), 7 (s, 1 H, 6-H), 4.1 (s, 3 H, OCH_3), 3.95 (s, 3 H, OCH_3), 3.68 (m, 2 H, CH_2-α), 2.48 (m, 2 H, CH_2-γ), 2.3 (s, 6 H, NMe_2), 1.92 (m, 2 H, CH_2-β); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 153, 149.4, 145.4, 142.3, 138.7, 138.4, 127.3, 126.2, 125.6, 122, 121.6, 118.7, 117.1, 114.3, 113.7, 111, 107.8, 104.1, 103.5, 56.8, 56.1, 55.4, 44.2, 25.8 (The γ-carbon has merged with DMSO signal in CMR spectrum). Anal. Calcd for $C_{26}H_{28}N_4O_3{\cdot}H_2O$: C, 69.9; H, 6.8; N, 12.5. Found: C, 69.3; H, 6.7; N, 12.04.

1-[3′-(*N*,*N*-dimethylamino)propyl]-4,5-(methylenedioxy)-12*H*-quino[3,4-*b*]carbazole (38b): 0.29 g (67.4%); mp 132 °C; ^1H NMR ($CDCl_3$, 300 MHz) δ 9.65 (bs, 1 H, NH, exchangeable with D_2O), 8.85 (s, 1 H, 13-H), 8.5 (bs, 1 H, NH, exchangeable with D_2O), 8.16 (d, J = 8 Hz, 11-H), 7.8 (s 1 H, 7-H), 7.7 (s, 1 H, 3-H), 7.42 (m, 2 H, 9-H and 10-H), 7.24 (m, 1 H, 8-H), 7.13 (s, 1 H, 6-H), 5.98 (s, 2 H, -OCH_2O-), 3.72 (t, J = 5.8 Hz, 2 H, CH_2-α), 2.48 (t, J = 5.8 Hz, 2 H, CH_2-γ), 2.3 (s, 6 H, NMe_2), 1.88 (m, 2 H, CH_2-β); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 152.8, 147.3, 143.6, 142.3, 139.7, 138.8, 127.3, 126.2, 121.5, 118.8, 116.9, 115.5, 113.8, 110.9, 104.8, 103.1, 100.8, 100.2, 57.7, 45.4, 26.4 (The γ-carbon has merged with DMSO signal in the CMR spectrum). Anal. Calcd for $C_{25}H_{24}N_4O_2{\cdot}H_2O$: C, 69.7; H, 6.1; N, 13. Found: C, 69.6; H, 6.1; N, 13.1.

1′-[2-Methyl-1-(phenylsulfonyl)indol-3-yl]buten-3′-one (39). A mixture of aldehyde **13** (2.9 g, 10 mmol) and 1-(triphenylphosphoranylidene)-2-propanone (3.8 g, 12 mmol) in dry THF (50 mL) was refluxed for 16 h. The solution was then poured over ice (200 g), and the solid was filtered and dried. It was purified by column chromatography (silica gel, 80 g) using benzene–hexane (1:4) as eluent. Recrystallization from MeOH–$CHCl_3$ gave 2.8 g (82%) of vinylindole **39** as colorless solid: mp 174 °C; IR (KBr) 1660, 1360, 1180 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ 8.3–7.1 (m, 10 H), 6.6 (d, J = 18 Hz, 1 H), 2.8 (s, 3 H), 2.4 (s, 3 H); Anal. Calcd for $C_{19}H_{17}NO_3S$: C, 67.2; H, 5.0; N, 4.1. Found: C, 66.9; H, 5.1; N, 4.2.

1′-[2-(Bromomethyl)-1-(phenylsulfonyl)indol-3-yl)buten-3′-one (40). The procedure was similar to that of **17**: mp 124 °C (Et_2O); ^1H NMR (acetone-d_6, 60 MHz) δ 8.2–7.2 (m, 10 H), 6.7 (d, J = 20 Hz, 1 H), 4.8 (s, 2 H), 2.5 (s, 3 H).

Attempted Preparation of the Phosphonate Ester 41. A mixture of (bromomethyl)indole **40** (1.86 g, 4.45 mmol) and triethyl phosphite (1 g, 6 mmol) was heated under N_2 at 160 °C for 3 h). The sticky oil was then poured over ice (100 g) and acidified with concd HCl (0.5 mL). No characterizable product was obtained after column chromatography.

Preparation of the Phosphonium Salt 42. A solution of bromo compound **40** (4.2 g, 10 mmol) and triphenylphosphine (3.4 g, 13 mmol) in dry $CHCl_3$ (40 mL) was refluxed under N_2 for 2 h. Then it was poured into dry Et_2O (200 mL), and the precipitated phosphonium salt **42** was filtered and dried. Yield 6.2 g (91%); mp 212 °C; IR (KBr) 1650, 1610, 1430,

1360, 1250, 1170 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 8.2 (d, J = 17 Hz, 1 H), 7.9–7.2 (m, 25 H), 6.3 (d, J = 17 Hz, 2 H), 2.5 (s, 3 H).

Wittig Reaction of Phosphonium Salt 42 with 6-Nitroveratraldehyde. To a solution of phosphonium salt **42** (3.4 g, 5 mmol) in dry $CHCl_3$ (30 mL) was added 6-nitroveratraldehyde (1.5 g, 7 mmol) and stirred at rt for 16 h. It was diluted with more $CHCl_3$ (50 mL), and then the $CHCl_3$ layer was washed with H_2O (2 × 50 mL) and dried (Na_2SO_4). Complete removal of the solvent followed by recrystallization from EtOAc gave 2 g (74%) of **43a** as yellow crystals: mp 174 °C; IR (KBr) 1660, 1590, 1490, 1370, 1320, 1250, 1150 cm^{-1}; ^1H NMR ($CDCl_3$, FT 90 MHz) δ 8.3 (d, J = 13 Hz, 1 H), 8–7.3 (m, 13 H), 7.2 (d, J = 19 Hz, 1 H), 4.15 (s, 3 H), 4 (s, 3 H), 2.4 (s, 3 H). Anal. Calcd for $C_{28}H_{24}N_2O_7S$: C, 63.1; H, 4.5; N, 5.3. Found: C, 63.3; H, 4.8; N, 5.4.

Wittig Reaction of Phosphonium Salt 42 with 6-Nitropiperonal: 1.8 g (69.7%) of **43b**; mp 182 °C; IR (KBr) 1665, 1590, 1500, 1370, 1160 cm^{-1}; ^1H NMR ($CDCl_3$, FT 90 MHz) δ 8.5 (d, J = 14 Hz, 1 H), 8–7.2 (m, 13 H), 6.8 (d, J = 18 Hz, 1 H), 5.86 (s, 2 H), 2 (s, 3 H). Anal. Calcd for $C_{27}H_{20}N_2O_7S$: C, 62.8; H, 3.9; N, 5.4. Found: C, 62.5; H, 3.7; N, 5.5.

3-Acetyl-9-(phenylsulfonyl)-2-(6′-nitroveratryl)]carbazole (44a). The procedure was similar to that of **23**, **24**, and **35**: 800 mg (73%); mp 232 °C; IR (KBr) 1680, 1510, 1370, 1340, 1200, 1180 cm^{-1}; ^1H NMR ($CDCl_3$, FT 90 MHz) δ 8.2–6.64 (m, 13H), 3.95 (s, 3 H), 3.86 (s, 3 H), 2.4 (s, 3 H). Anal. Calcd for $C_{28}H_{22}N_2O_7S$: C, 63.4; H, 4.2; N, 5.3. Found: C, 63.1; H, 4.2; N, 5.3.

3-Acetyl-9-(phenylsulfonyl)-2-[3′,4′-(methylenedioxy)-6′-nitrophenyl]carbazole (44b): 800 mg (77.8%); mp 258 °C; ^1H NMR ($CDCl_3$, FT 90 MHz) δ 8.3–6.7 (m, 13 H), 6.2 (s, 2 H), 2.4 (s, 3 H). Anal. Calcd for $C_{27}H_{18}N_2O_7S$: C, 63; H, 3.5; N, 5.4. Found: C, 62.8; H, 3.6; N, 5.3.

1-Methyl-4,5-dimethoxy-8*H*-quino[4,3-*b*]carbazole (45a). To a solution of carbazole **44a** (0.53 g, 1 mmol) in dry THF (70 mL) was added freshly prepared W_2 grade Ra-Ni (5 g) and then stirred at rt for 2 h. The nickel was then filtered and washed with hot THF (3 × 20 mL). The combined filtrate was refluxed for 2 h and then the solvent removed completely. To this were added DMSO (30 mL) and 50% NaOH (5 mL). The reaction mixture was stirred at rt for 12 h and poured over ice (200 g). The solution was then slightly warmed to avoid the emulsification, and the solid formed was filtered and dried over $CaCl_2$. It was recrystallized from $CHCl_3$ to give 0.28 g (82%) of **45a** as colorless solid: mp 290 °C; IR (KBr) 1610, 1490, 1470, 1250, 1150 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 8.77 (s, 1 H, 13-H), 8.41 (bs, 1 H, indole NH, exchangeable with D_2O), 8.22 (s, 1 H, 7-H), 8.18–8.16 (d, J = 8 Hz, 1 H, 12-H), 7.75 (s, 1 H, 3-H), 7.47–7.41 (m, 3 H, 6-H, 9-H and 11-H), 7.29–7.24 (m, 1 H, 10-H), 4.04 (s, 3 H), 3.97 (s, 3 H), 3.06 (s, 3 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 157.4, 150.5, 148.4, 141.6, 141.5, 139, 131.2, 127.4, 124.3, 123.2, 120.9, 120.2, 119.8, 118.4, 117.9, 110.7, 109.6, 102.4, 100.5, 56.14, 56.08, 23.5. Anal. Calcd for $C_{22}H_{18}N_2O_2$: C, 77.2; H, 5.3; N, 8.2. Found: C, 76.8; H, 5.3; N, 8.3. HRMS calcd for $C_{22}H_{18}N_2O_2$ 342.1368, found M^+ 342.1350.

1-Methyl-4,5-(methylenedioxy)-8*H*-quino[4,3-*b*]carbazole (45b): 0.27 g, 82.8%; mp > 320 °C; ^1H NMR (DMSO-d_6, 400 MHz) δ 11.6 (s, 1 H, indole NH, exchangeable with D_2O), 9.1 (s, 1 H, 13-H), 8.53 (s, 1 H, 7-H), 8.4 (d, J = 7.5 Hz, 1 H, 12-H), 8.24 (s, 1 H, 3-H), 7.6 (d, 1 H, 9-H), 7.5 (m, 1 H, 11-H), 7.4 (s, 1 H, 6-H), 7.25 (m, 1 H, 10-H), 6.2 (s, 2 H), 3.1 (s, 3 H). HRMS calcd for $C_{21}H_{14}N_2O_2$ 326.1055, found M^+ 326.1051.

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Supplementary Material Available: Experimental and characterization data of **13**, **16**, **18**, **20**, **28**, and **46–49** (3 pages). This material contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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