

REGIOSPECIFIC HETERO DIELS-ALDER SYNTHESIS
OF PYRIDO[2,3-*b*]- AND PYRIDO[3,2-*b*]CARBAZOLE-5,11-DIONES

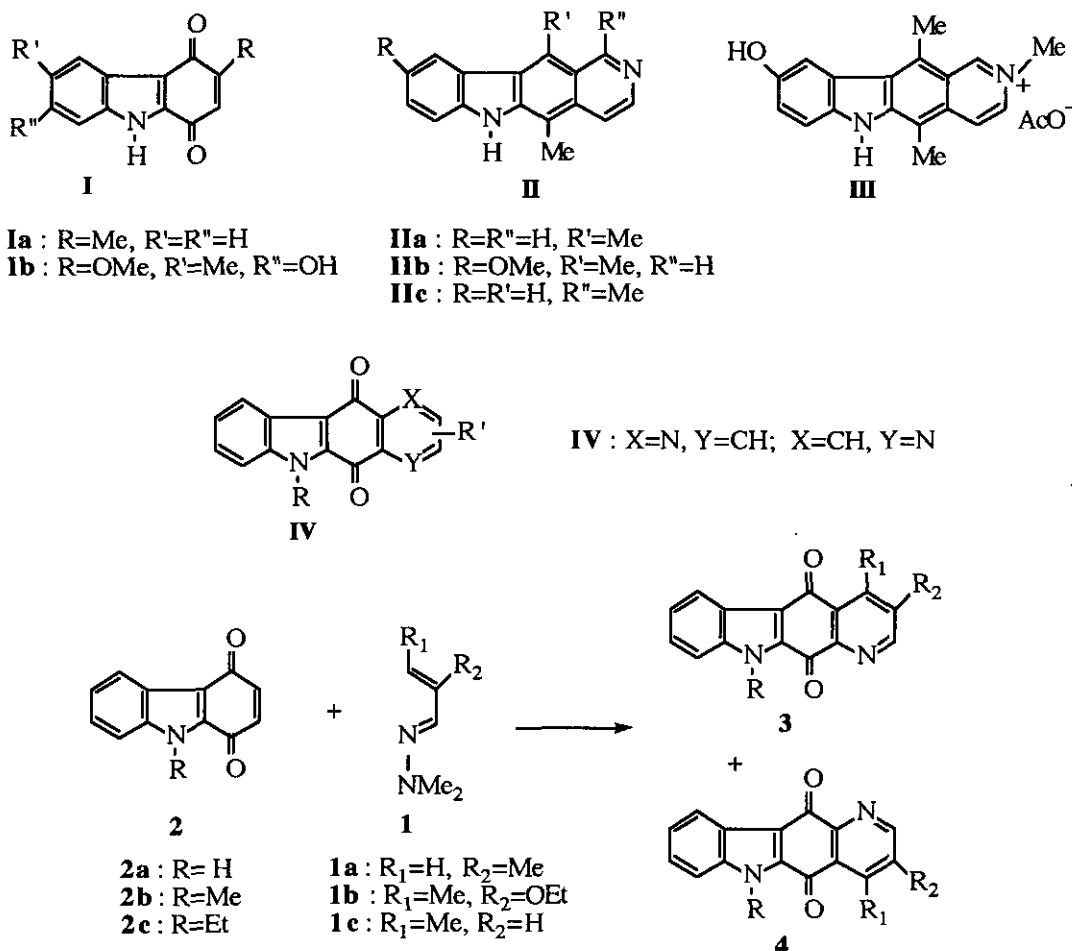
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Abstract - Diels-Alder reactions of 2- or 3-bromocarbazolequinones (**8**) or (**9**) with azadienes (**1**) afford regiospecifically pyrido[2,3-*b*]- or pyrido[3,2-*b*]carbazole-5,11-diones (**3**) or (**4**). Structural assignment of the regioisomers is made by ¹H-NMR NOE DIFF experiments. The orientation of the cycloadditions is under control of the bromine atom position on quinones (**8**) or (**9**). Calculations by the semiempirical method PM3 of the HOMO and LUMO orbital coefficients of azadienes (**1**) and quinones (**2c**), (**8**) and (**9**) indicate that the larger ones are situated at C-4 for azadienes (**1**) and C-3 for the dienophiles.

Carbazolequinone or pyridocarbazole skeletons exist in numerous naturally occurring compounds of biological interest. Among these, murrayaquinone-A¹ (**Ia**), isolated from *Murraya euchrestifolia hayata* shows a cardiotonic activity, clausenaquinone-A² (**Ib**) extracted from *Clausena excavata* inhibits the growth of tumor cells while indole alkaloids such ellipticine (**IIa**), 9-methoxyellipticine (**IIb**) and olivacine (**IIc**) are known for their antitumor properties.³ On the other hand, a synthetic derivative elliptinium (**III**) was used in chemotherapy in the treatment of breast cancer.³ These observations led us to synthesize some pyridocarbazolequinones (**IV**) in order to assess their pharmacological properties. Some structures analogous to **IV** were previously obtained by annulated methods.⁴ But, their direct access through [4+2] cycloaddition reactions had not yet been envisaged. In continuation of our program aimed to obtain new

compounds having a pyridine nucleus annulated to heterocyclic quinones, we planned to develop a hetero Diels-Alder strategy based on the use of α,β -unsaturated *N,N*-dimethylhydrazones⁵ towards carbazolequinones. Our first attempts start with azadienes (**1**) and quinones (**2**) (Scheme 1).



Scheme 1

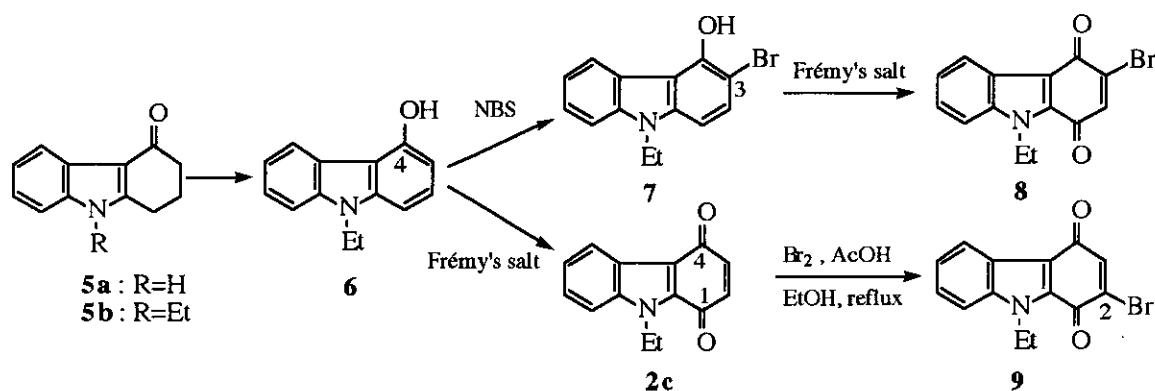
The Diels-Alder reactions between azadienes (**1a**) or (**1b**) and carbazolequinones (**2a**)⁶ or (**2b**)⁷ gave very insoluble products. Therefore, the [4+2] cycloadditions were performed with the *N*-ethyl derivative (**2c**). Starting from azadiene (**1b**) and quinone (**2c**) the reaction was found totally regioselective (Table 1, Entry 2). Thus, only pyridocarbazolequinone (**3b**) was obtained in good yield after spontaneous elimination of dimethylamine and oxidation. In contrast, the Diels-Alder reactions of azadienes (**1a**) or (**1c**) with quinone (**2c**) gave the respective mixtures of **3+4** (Entries 1 and 3).

Table 1. Cycloadditions of azadienes (**1**) with carbazolequinone (**2c**)

Entry	Azadiene (eq.)	Quinone	Conditions (solvent, time reflux, base)	Products (ratio 3 / 4)*	R	R ₁	R ₂	Yield (%)
1	1a (1.5)	2c	EtOH, 1.5 h	3a+4a (93/7)	Et	H	Me	81
2	1b (1.5)	2c	MeCN, 0.5 h basic alumina, 12 h	3b	Et	Me	OEt	85
3	1c (2.5)	2c	Toluene, 1 h basic alumina, 12 h	3c+4c (68/32)	Et	Me	H	77

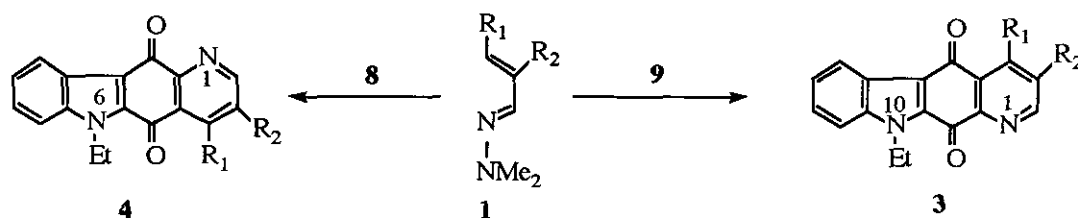
*Measured from the ¹H-NMR spectra.

To obtain pyridocarbazolequinones (**3**) or (**4**) regiospecifically, we turn our attention to the preparation and use of the unknown 3- or 2-bromocarbazole-1,4-diones (**8**) or (**9**). The presence of a bromine atom at C-2 or C-3 on these quinones was expected to afford regiospecificity.⁸ Bromoquinones (**8**) and (**9**) were prepared according to Scheme 2. Thus, tetrahydrocarbazolone (**5a**)^{9,10} was treated with potassium hydroxide and ethyl iodide to give **5b**. Dehydrogenation of the latter in the presence of 10% Pd-C in refluxing diphenyl ether yielded the corresponding 4-hydroxycarbazole (**6**). Treatment of **6** with NBS in acetonitrile yielded *o*-bromophenol (**7**) which was oxidized by Frémy's salt to give 3-bromocarbazolequinone (**8**). On the other hand, oxidation of **6** with Frémy's salt yielded carbazolequinone (**2c**). Addition of bromine in acetic acid to the latter, followed by hydrogen bromide elimination, afforded 2-bromocarbazolequinone (**9**).



Scheme 2

Compounds (**8**) and (**9**) are differentiated by their physical and spectroscopical data. Then, cycloadditions of azadienes (**1**) with bromocarbazolequinones (**8**) or (**9**), performed at reflux of an appropriate solvent in a basic medium, afforded regiospecifically the corresponding pyridocarbazolequinones (**3**) or (**4**) (Scheme 3 and Table 2).



Scheme 3

Table 2. Cycloadditions of azadienes (**1**) with carbazolequinones (**8**) and (**9**)

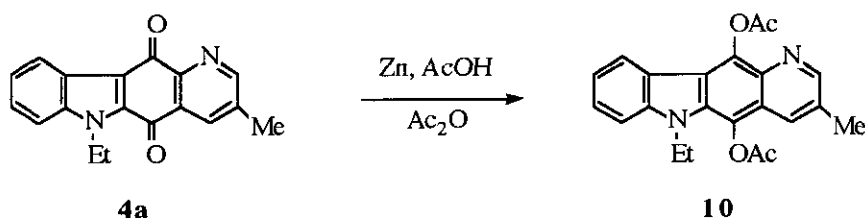
Azadiene (eq.)	Quinone	Conditions (solvent, time reflux, base)	Product	R_1	R_2	Yield (%)
1a (2.5)	9	Ethanol, $NaHCO_3$, 1.5 h	3a	H	Me	79
1b (2.5)	9	$ClCH_2CH_2Cl$, 1 h, basic alumina, 3 h	3b	Me	OEt	88
1c (2.5)	9	MeCN, 1 h, basic alumina, 12 h	3c	Me	H	55
1a (2.5)	8	Ethanol, $NaHCO_3$, 2.5 h	4a	H	Me	83
1b (2.5)	8	$ClCH_2CH_2Cl$, 1 h, basic alumina, 3 h	4b	Me	OEt	77
1c (2.5)	8	MeCN, 1 h, basic alumina, 5 h	4c	Me	H	71

Concerning the regiochemistry of the cycloadditions, opposite regioisomers were obtained from 3-bromocarbazolequinone (**8**) comparatively to those formed from 2-bromocarbazolequinone (**9**). To explain the regiospecificity, it was assumed that the unbrominated carbon atom of these quinones was exclusively attacked by the nucleophilic end of azadienes. The regioisomeric pyridocarbazolequinones (**3**) and (**4**) were identified from their 1H -NMR and IR spectra (Table 3).

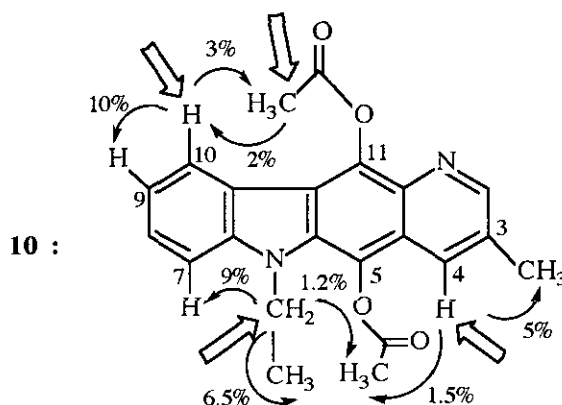
Table 3. ^1H -NMR and IR spectral data for pyridocarbazolequinones (**3**) and (**4**)

Compound	R_1	R_2	^1H -NMR (CDCl_3 , δ ppm)				IR (KBr) ν C=O
			H-2	H-6	H-10	N- CH_2CH_3	
3a	H	Me	8.78	8.46		4.82	1665, 1650
4a	H	Me	8.82		8.54	4.77	1665
3b	Me	OEt	8.46	8.46		4.79	1665, 1640
4b	Me	OEt	8.51		8.51	4.73	1660
3c	Me	H	8.77	8.46		4.80	1670, 1640
4c	Me	H	8.79		8.51	4.74	1660

Thus, for pyridocarbazolequinones (**3**), the ^1H -NMR chemical shifts of H-2 and H-6 are shifted to high fields comparatively to those of compounds (**4**) (H-2 and H-10). Otherwise, a deshielding was observed for the methylene protons of the *N*-ethyl substituent in compounds (**3**) comparatively to **4**. On the other hand, IR spectra of the 1,10-regioisomers (**3**) show two absorption bands for the carbonyl groups while in the 1,6-regioisomers (**4**), the latter are not differentiated. To assign the structure, pyridocarbazolequinone (**4a**) was converted to the diacetyl derivative (**10**) following a known procedure¹¹ (Scheme 4).



Scheme 4

Figure 1. ^1H -NMR NOE DIFF experiments performed on **10**.

Then, proof of the regiochemistry was made by $^1\text{H-NMR}$ NOE DIFF experiments performed on compound **10** (Figure 1). First, an irradiation at 7.82 ppm (H-4) gives two responses: one on 3- CH_3 ($\delta = 2.56$ ppm) and the other one on the acetate group at 2.60 ppm (OAc). Then, irradiation of the methylene at 4.45 ppm affords three responses: one on the same acetate, one on H-7 and the other one on the triplet at 1.48 ppm (CH_2CH_3). Finally irradiation of the proton at 8.20 ppm (H-10) gives two responses: one on H-9 and the other one on the acetyl group at 2.71 ppm (11-OAc) while irradiation of the latter provides only one response on H-10.

In order to better understand the behaviour of quinone (**2c**), (**8**) and (**9**) in their cycloaddition reactions towards azadienes (**1**), we calculated the respective LUMO and HOMO orbital coefficients by the semi-empirical method PM3.¹² Thus, the values given in Table 4 indicated that the larger coefficients were located at C-4 for azadienes (**1**) while they are at C-3 for quinones (**2c**), (**8**) and (**9**).

Table 4. Orbital coefficients of azadienes (**1**) and carbazolequinones (**2c**), (**8**) and (**9**)

Azadiene (HOMO)	N-1	C-4
1a	0.2397	0.3217
1b	0.3006	0.4085
1c	0.2738	0.3148
Carbazolequinone (LUMO)	C-2	C-3
2c	0.3113	0.3490
8	0.3393	0.3645
9	0.3277	0.3757

The regiochemistry observed in the cycloadditions between azadienes (**1**) and quinone (**2c**) agrees with the calculations. Indeed, C-4 of **1** attacks preferentially at C-3 of **2c**. In the case of 3-bromoquinone (**8**), the LUMO coefficient at C-3 is higher than that of C-2. The resulting regiochemistry can be explained by the blocking effect of the bromine atom. The nucleophilic end of **1** adds to the unbrominated carbon C-2 to give regiospecifically the 1,6-regioisomers (**4**). For 2-bromoquinone (**9**), both the value of LUMO coefficients and the blocking effect of the bromine atom orientate the attack of azadienes (**1**) on C-3. Thus, the 1,10-regioisomers (**3**) were exclusively obtained.

This work describes an efficient way to reach regiospecifically pyridocarbazolequinones (**3**) or (**4**) through Diels-Alder reactions between 1-azadienes (**1**) and 2- or 3-bromocarbazolequinones (**9**) or (**8**) respectively. Concerning the cycloadditions of **1** towards quinone (**2c**), the regiochemistry observed agrees with HOMO

and LUMO orbital coefficients. In the case of bromoquinones (**8**) and (**9**), the regiospecificity obtained may be explained by the orientational regiocontrol of the bromine atom.

EXPERIMENTAL SECTION

Melting points were taken in a capillary tube using a Büchi 510 apparatus and are corrected. IR spectra were performed on a Perkin-Elmer 1310 spectrophotometer. The ^1H -NMR spectra were recorded at 300 MHz on a Bruker AM 300 spectrometer. Elemental analysis were made at the Centre de Microanalyse du CNRS at Solaize. Column chromatography was carried out with Matrex (60 Å, 35-70 µm) acidic silica gel. Preparative circular thin layer chromatography was performed with a Chromatotron Harrison Research apparatus using silica gel 60 PF 254 containing gypsum as the adsorbant. Coefficients of the molecular frontier orbitals were calculated from MOPAC of SYBYL program on an IBM Risk 6000 workstation. Azadienes (**1a**),¹³ (**1b**),^{14,15} (**1c**),¹⁵ and tetrahydrocarbazolone (**5a**)⁹ were prepared according to procedures described in the respective literature.

9-Ethyl-1,2,3,9-tetrahydro-4H-carbazol-4-one (**5b**)

A suspension of **5a** (2 g, 10.8 mmol), freshly distilled iodoethane (2.53 g, 16.25 mmol), potassium hydroxide (1.2 g, 21.38 mmol) and benzyltriethylammonium chloride (0.246 g, 1.08 mmol) in acetone (150 mL) was heated to reflux for 30 min. After cooling at rt and filtration, the solution was evaporated under vacuum. The residue was dissolved in CH_2Cl_2 (150 mL), the organic solution washed with water and dried over MgSO_4 . Removal of the solvent afforded the crude product which was washed with cold ether and recrystallized from ether/hexane. Compound (**5b**) was obtained as a white solid in 78% yield, mp 108-112 °C (lit.,¹⁶ 107-109 °C).

9-Ethyl-4-hydroxy-9H-carbazole (**6**)

To a solution of **5b** (0.685 g, 3.2 mmol) in diphenyl ether (10 mL) was added 0.685 g of 10% Pd-C. Then, the mixture was heated to reflux for 1 h. After cooling, 100 mL of ethanol were added and the solution filtered on celite. Evaporation of the solvent left a residue which was purified by preparative circular thin layer chromatography using, first petroleum ether and then, a mixture of petroleum ether/ether (4:1) as the eluent. Compound (**6**) was obtained as a white powder (0.480 g, 71 %), mp 145 °C. IR (KBr): 3500 cm^{-1} . ^1H -NMR (CDCl_3 , 300 MHz) δ ppm 8.32 (d, 1H, $J=7.8$ Hz, H-5), 7.49 ~ 7.24 (m, 4H, H

aromat.), 7.00 (d, 1H, $J=8.2$ Hz, H aromat.), 6.57 (d, 1H, $J=7.7$ Hz, H aromat.), 5.38 (s, 1H, OH), 4.35 (q, 2H, $J=7.2$ Hz, CH_2CH_3), 1.43 (t, 3H, $J=7.2$ Hz, CH_2CH_3). Anal. Calcd for $\text{C}_{14}\text{H}_{13}\text{NO}$: C, 79.59; H, 6.20; N, 6.62. Found: C, 79.36; H, 6.30; N, 6.59.

9-Ethyl-1,4-dihydrocarbazole-1,4(9H)-dione (2c)

An aqueous solution (25 mL) of Frémy's salt (0.430 g, 1.6 mmol) and potassium dihydrogen orthophosphate (0.025 g, 0.183 mmol) was added to a solution of 4-hydroxycarbazole (**6**) (0.160 g, 0.76 mmol) in acetone (25 mL). The reaction mixture was stirred at room temperature for 1 h, extracted with CH_2Cl_2 , dried over MgSO_4 and concentrated under vacuum. The crude product was purified by column chromatography on silica gel using CH_2Cl_2 /hexane (1:1) as the eluent. Compound (**2c**) was obtained as a red solid (0.143 g, 83%), mp 136 °C. IR (KBr): 1660, 1640 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3 , 300 MHz) δ ppm 8.22 (d, 1H, $J=7.8$ Hz, H-4), 7.40 ~ 7.26 (m, 3H, H aromat.), 6.56 (AB system, 2H, $J=10.2$ Hz, H-2 and H-3), 4.58 (q, 2H, $J=7.2$ Hz, CH_2CH_3), 1.38 (t, 3H, $J=7.2$ Hz, CH_2CH_3). Anal. Calcd for $\text{C}_{14}\text{H}_{11}\text{NO}_2$, 0.4 H_2O : C, 72.34; H, 5.11; N, 6.02. Found: C, 72.47; H, 4.98; N, 5.86.

3-Bromo-9-ethyl-4-hydroxy-9H-carbazole (7)

N-Bromosuccinimide (0.126 g, 0.71 mmol) in acetonitrile (5 mL) was added dropwise at rt and under stirring to a solution of compound (**6**) (0.3 g, 1.42 mmol) in 10 mL of the same solvent. Stirring was maintained for 30 min. After removal of the solvent, bromophenol (**7**) was purified by column chromatography using EtOAc/hexane (1:9) as the eluent. It was obtained as an oil in quantitative yield calculated from NBS. The starting material (**6**) was then recovered from the further fractions in 45% yield. **7**: IR (CCl_4): 3520 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3 , 300 MHz) δ ppm 8.35 (d, 1H, $J=7.8$ Hz, H-5), 7.51 ~ 7.46 (m, 2H, H-2 and H-6), 7.39 (d, 1H, $J=8.1$ Hz, H-8), 7.31 ~ 7.28 (m, 1H, H-7), 6.90 (d, 1H, $J=8.6$ Hz, H-1), 6.1 (s, 1H, OH), 4.32 (q, 2H, $J=7.2$ Hz, CH_2CH_3), 1.41 (t, 3H, $J=7.2$ Hz, CH_2CH_3). Anal. Calcd for $\text{C}_{14}\text{H}_{12}\text{NOBr}$: C, 57.95; H, 4.17; N, 4.82. Found: C, 57.69; H, 4.10; N, 4.42.

3-Bromo-9-ethyl-1,4-dihydrocarbazole-1,4(9H)-dione (8)

Oxidation of 3-bromo-4-hydroxycarbazole (**7**) was performed with Frémy's salt following the procedure used for **2c**. Compound (**8**) was obtained as a red solid in 77 % yield, mp 155-158 °C. IR (KBr): 1655, 1645 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3 , 300 MHz) δ ppm 8.28 (m, 1H, H-5), 7.47 ~ 7.39 (m, 3H, H aromat.), 7.13 (s, 1H, H-2), 4.63 (q, 2H, $J=7.2$ Hz, CH_2CH_3), 1.44 (t, 3H, $J=7.2$ Hz, CH_2CH_3). Anal. Calcd for

$C_{14}H_{10}NO_2Br$, 0.15 H_2O : C, 54.80; H, 3.38; N, 4.56, Br, 26.04. Found: C, 54.60; H, 3.35; N, 4.55, Br, 26.09.

2-Bromo-9-ethyl-1,4-dihydrocarbazole-1,4(9H)-dione (9)

Bromine (0.240 g, 1.5 mmol) was added at rt under stirring to a solution of **2c** (0.338 g, 1.5 mmol) in glacial acetic acid (36 mL). Stirring was maintained for 20 min. Then, the reaction mixture was poured into ice-water and the yellow dibromo product was collected by filtration and immediately dissolved in ethanol (15 mL) and heated to reflux for 45 min. After cooling, a red precipitate of compound (**9**) was collected by filtration. The filtrate was poured into ice-water to give an additional fraction of **9**. Compound (**9**) was obtained as a red solid (0.370 g, 81 %), mp 187-189 °C. IR (KBr): 1665, 1640 cm^{-1} . 1H -NMR ($CDCl_3$, 300 MHz) δ ppm 8.25 (d, 1H, $J=8$ Hz, H-5), 7.46 ~ 7.30 (m, 3H, H arom.), 7.19 (s, 1H, H-3), 4.69 (q, 2H, $J=7.1$ Hz, CH_2CH_3), 1.45 (t, 3H, $J=7.1$ Hz, CH_2CH_3). Anal. Calcd for $C_{14}H_{10}NO_2Br$: C, 55.29; H, 3.31; N, 4.60, Br, 26.27. Found: C, 55.53; H, 3.32; N, 4.59, Br, 26.27.

Cycloadditions of azadiene (1a) to bromoquinones (8) and (9).

A solution of azadiene (**1**) (0.123 g, 1.1 mmol) in absolute ethanol (1 mL) was added to a solution of the corresponding bromoquinone (0.120 g, 0.394 mmol) in the same solvent (8 mL). Then, $NaHCO_3$ (0.067 g, 0.797 mmol) was added. The reaction mixture was stirred and heated to reflux until completion of the reaction, the reaction being followed by TLC. Then, the solvent was evaporated and the yellow residue purified by column chromatography using $CH_2Cl_2/MeOH$ (98 : 2) as the eluent.

10-Ethyl-3-methyl-10H-pyrido[2,3-b]carbazole-5,11-dione (3a)

Compound (**3a**) was obtained as a yellow solid in 79% yield, mp 242 °C. IR (KBr): 1665, 1650 cm^{-1} . 1H -NMR ($CDCl_3$, 300 MHz) δ ppm 8.78 (d, 1H, $J=2.1$ Hz, H-2), 8.46 (d, 1H, $J=7.9$ Hz, H-6), 8.32 (d, 1H, $J=2.1$ Hz, H-4), 7.54 to 7.39 (m, 3H, H arom.), 4.82 (q, 2H, $J=7.2$ Hz, CH_2CH_3), 2.53 (s, 3H, CH_3 -3), 1.51 (t, 3H, $J=7.2$ Hz, CH_2CH_3). Anal. Calcd for $C_{18}H_{14}N_2O_2$, 0.7 H_2O : C, 71.36; H, 5.12; N, 9.24. Found: C, 71.30; H, 4.80; N, 9.07.

6-Ethyl-3-methyl-6H-pyrido[3,2-b]carbazole-5,11-dione (4a)

Compound (**4a**) was obtained as a yellow solid in 83 % yield, mp 261-262 °C. IR (KBr): 1665 cm^{-1} . 1H -NMR ($CDCl_3$, 300 MHz) δ ppm 8.82 (d, 1H, $J=2$ Hz, H-2), 8.54 (d, 1H, $J=7.9$ Hz, H-10), 8.26 (d,

1H, $J=2$ Hz, H-4), 7.49 ~ 7.38 (m, 3H, H arom.), 4.77 (q, 2H, $J=7.2$ Hz, CH_2CH_3), 2.52 (s, 3H, CH_3 -3), 1.51 (t, 3H, $J=7.2$ Hz, CH_2CH_3). Anal. Calcd for $\text{C}_{18}\text{H}_{14}\text{N}_2\text{O}_2 \cdot 0.15 \text{ H}_2\text{O}$: C, 73.78; H, 4.92; N, 9.56. Found: C, 73.74; H, 4.91; N, 9.49.

Cycloadditions of azadiene (1b) to bromoquinones (8) and (9).

To a solution of the corresponding bromoquinone (0.120 g, 0.394 mmol) heated at reflux temperature in $\text{ClCH}_2\text{CH}_2\text{Cl}$ (60 mL), was added a solution of azadiene (1b) (0.156 g, 1 mmol) in the same solvent (2 mL). The reaction mixture was heated for 1 h. Then, basic alumina (1 g) was added. Stirring and heating were maintained for 3 h. After cooling, filtration and removing the solvent, the yellow residue was purified by column chromatography using the same eluent as above.

3-Ethoxy-10-ethyl-4-methyl-10H-pyrido[2,3-b]carbazole-5,11-dione (3b)

Compound (3b) was obtained as a yellow solid in 88 % yield, mp 245 °C. IR (KBr): 1665, 1640 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3 , 300 MHz) δ ppm 8.46 (m, 2H, H-2 and H-6), 7.49 ~ 7.36 (m, 3H, H arom.), 4.79 (q, 2H, $J=7.1$ Hz, CH_2CH_3), 4.28 (q, 2H, $J=6.9$ Hz, $\text{O-CH}_2\text{CH}_3$) 2.81 (s, 3H, CH_3 -4), 1.56-1.48 (m, 6H, CH_2CH_3 and $\text{O-CH}_2\text{CH}_3$). Anal. Calcd for $\text{C}_{20}\text{H}_{18}\text{N}_2\text{O}_3 \cdot 0.6 \text{ H}_2\text{O}$: C, 69.59; H, 5.60; N, 8.11. Found: C, 69.44; H, 5.58; N, 8.00.

3-Ethoxy-6-ethyl-4-methyl-6H-pyrido[3,2-b]carbazole-5,11-dione (4b)

Compound (4b) was obtained as a yellow solid in 77 % yield, mp 260 °C. IR (KBr): 1660 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3 , 300 MHz) δ ppm 8.51 (m, 2H, H-2 and H-10), 7.46 ~ 7.34 (m, 3H, H arom.), 4.73 (q, 2H, $J=7.1$ Hz, CH_2CH_3), 4.27 (q, 2H, $J=6.9$ Hz, $\text{O-CH}_2\text{CH}_3$) 2.74 (s, 3H, CH_3 -4), 1.55 to 1.48 (m, 6H, CH_2CH_3 and $\text{O-CH}_2\text{CH}_3$). Anal. Calcd for $\text{C}_{20}\text{H}_{18}\text{N}_2\text{O}_3 \cdot 0.5 \text{ H}_2\text{O}$: C, 69.96; H, 5.58; N, 8.16. Found: C, 69.72; H, 5.30; N, 8.31.

Cycloadditions of azadiene (1c) to bromoquinones (8) and (9).

To a solution of the corresponding bromoquinone (0.160 g, 0.526 mmol) in acetonitrile (12 mL), was added a solution of azadiene (1c) (0.148 g, 1.32 mmol) in the same solvent (2 mL). The reaction mixture was stirred and heated to reflux for 1 h. Then, basic alumina (1.6 g) was added. Stirring and heating were maintained until completion of the reaction, the reaction being followed by TLC. for 3 h. After cooling

and filtration, alumina was washed with CHCl_3 (2x20 mL). The filtrates were concentrated under vacuum and the yellow residue was purified by column chromatography using the same eluent as above.

10-Ethyl-4-methyl-10H-pyrido[2,3-b]carbazole-5,11-dione (3c)

Compound (3c) was obtained as a yellow solid in 55 % yield, mp 215-216 °C. IR (KBr): 1670, 1640 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3 , 300 MHz) δ ppm 8.77 (d, 1H, $J=4.8$ Hz, H-2), 8.46 (d, 1H, $J=8.1$ Hz, H-6), 7.50 ~ 7.38 (m, 4H, H aromat.), 4.80 (q, 2H, $J=7.1$ Hz, CH_2CH_3), 2.93 (s, 3H, CH_3 -4), 1.53 (t, 3H, $J=7.1$ Hz, CH_2CH_3). Anal. Calcd for $\text{C}_{18}\text{H}_{14}\text{N}_2\text{O}_2$, 0.4 H_2O : C, 72.66; H, 5.01; N, 9.41. Found: C, 72.69; H, 4.88; N, 9.36.

6-Ethyl-4-methyl-6H-pyrido[3,2-b]carbazole-5,11-dione (4c)

Compound (4c) was obtained as a yellow solid in 71 % yield, mp 258-260 °C. IR (KBr): 1660 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3 , 300 MHz) δ ppm 8.79 (d, 1H, $J=4.9$ Hz, H-2), 8.51 (d, 1H, $J=7.8$ Hz, H-10), 7.48 ~ 7.36 (m, 4H, H aromat.), 4.74 (q, 2H, $J=7.1$ Hz, CH_2CH_3), 2.88 (s, 3H, CH_3 -4), 1.51 (t, 3H, $J=7.1$ Hz, CH_2CH_3). Anal. Calcd for $\text{C}_{18}\text{H}_{14}\text{N}_2\text{O}_2$, 0.5 H_2O : C, 72.22; H, 5.05; N, 9.35. Found, C, 72.40; H, 4.78; N, 8.93.

5,11-Diacetyloxy-6-ethyl-3-methyl-6H-pyrido[3,2-b]carbazole (10)

Compound (10) was obtained as a pale yellow solid in 65 % yield, mp 235-240 °C. IR (KBr): 1750 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3 , 300 MHz) δ ppm 8.73 (d, 1H, $J=2$ Hz, H-2), 8.20 (dd, 1H, $J=8$ and 1 Hz, H-10), 7.82 (m, 1H, H-4), 7.54 (m, 1H, H-8), 7.40 (d, 1H, $J=8.2$ Hz, H-7), 7.30 (m, 1H, H-9), 4.45 (q, 2H, $J=7.2$ Hz, CH_2CH_3), 2.71 (s, 3H, OCOCH_3), 2.60 (s, 3H, OCOCH_3), 2.56 (s, 3H, CH_3 -3), 1.48 (t, 3H, $J=7.2$ Hz, CH_2CH_3). Anal. Calcd for $\text{C}_{22}\text{H}_{20}\text{N}_2\text{O}_4$: C, 70.20; H, 5.35; N, 7.44. Found: C, 70.00; H, 5.43; N, 7.26.

REFERENCES AND NOTES

1. K. Takeya, M. Itoigawa, and H. Furukawa, *Eur. J. Pharmacol.*, 1989, **169**, 137.
2. T.-S. Wu, S.-C. Huang, P.-L. Wu, and K.-H. Lee, *Bioorg. Med. Chem. Lett.*, 1994, **4**, 2395.
3. G. W. Gribble, *The alkaloids*, ed. by A. Brossi, Academic Press: New York, 1990, Vol. 39, 239.
4. W. R. Ashcroft, M. G. Beal, and J. A. Joule, *J. Chem. Soc., Chem. Commun.*, 1981, 994.

5. The synthetic usefulness of α,β -unsaturated *N,N*-dimethylhydrazones was established by :
 - (a) B. Serckx-Poncin, A.-M. Hesbain-Frisque, and L. Ghosez, *Tetrahedron Lett.*, 1982, **23**, 3261;
 - (b) L. Ghosez, B. Serckx-Poncin, M. Rivera, P. Bayard, F. Sainte, A. Demoulin, A.-M. Hesbain-Frisque, A. Mockel, L. Munoz, and C. Bernard-Henriet, *Lect. Heterocycl. Chem.*, 1985, **8**, 69.
6. T. Martin and C. J. Moody, *J. Chem. Soc., Perkin Trans. I*, 1988, 235.
7. A. Wada, S. Hirai, and M. Hanaoka, *Chem. Pharm. Bull.*, 1994, **42**, 416.
8. L. Chaker, F. Pautet, and H. Fillion, *Heterocycles*, 1995, **41**, 1169.
9. Tetrahydrocarbazolone (**5a**) was prepared following a Fischer indole synthesis from 1,3-cyclohexanedione monophenylhydrazone as described by G. R. Clemo and D. G. I. Felton, *J. Chem. Soc.*, 1951, 700. For other syntheses of **5a**, see references.¹⁰
10. (a) Y. Oikawa and O. Yonemitsu, *J. Org. Chem.*, 1977, **42**, 1213; (b) H. Iida, Y. Yuasa, and C. Kibayashi, *J. Org. Chem.*, 1979, **44**, 1236; (c) A. Osuka, Y. Mori, and H. Suzuki, *Chem. Lett.*, 1982, 2031; (d) D. Joseph, L. Martarello, and G. Kirsch, *J. Chem. Res.(M)*, 1995, 2257.
11. J. Lee and J. K. Snyder, *J. Org. Chem.*, 1990, **55**, 4995.
12. J. J. P. Stewart, *J. Comput. Chem.* 1989, **10**, 209.
13. A. Waldner, *Helv. Chim. Acta*, 1989, **72**, 1435.
14. P. Nebois, O. Cherkaoui, L. Benameur, H. Fillion, and B. Fenet, *Tetrahedron*, 1994, **50**, 8457.
15. T. Severin, G. Wanninger, and H. Lerche, *Chem. Ber.*, 1984, **117**, 2875.
16. H. Iida, Y. Yuasa, and C. Kibayashi, *J. Org. Chem.*, 1980, **45**, 2938.

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