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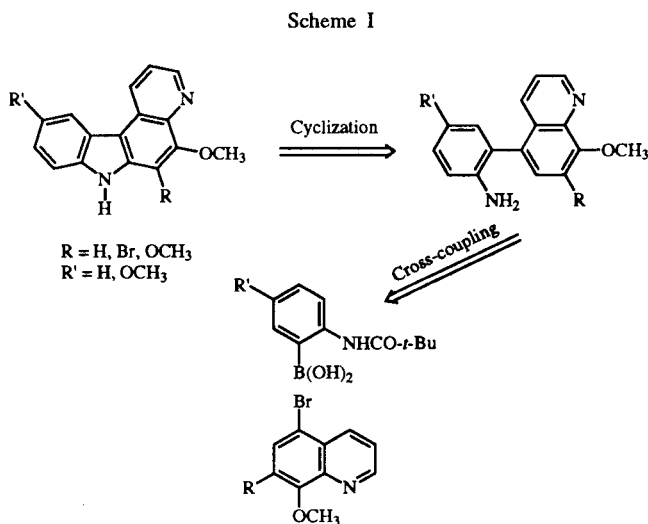
A new strategy for the synthesis of substituted 7H-pyrido[2,3-c]carbazoles has been developed from substituted 5-bromoquinolines by using cross-coupling reaction with (2-aminophenyl)boric acids, followed by a regioselective azide cyclization.

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Introduction.

It is well established that the pyridocarbazole ring is an appropriate skeleton to design DNA intercalating drugs [1]. Some compounds such as ellipticines and olivacines elicit high antitumor properties [1-2]. Since the discovery of the potent activity of 7H-pyridocarbazoles [2a-b,3], numerous syntheses have been reported [2a-c,4]; indoles [2a-b,4a], but also carbazoles [2c,4b-d] or benzenes [4e] were often used as starting materials.

Because of the usually low yields obtained in the methods described, mainly due to the large number of steps, we chose to construct 7H-pyrido[2,3-c]carbazoles from suitably substituted quinoline and benzene moieties (Scheme I).

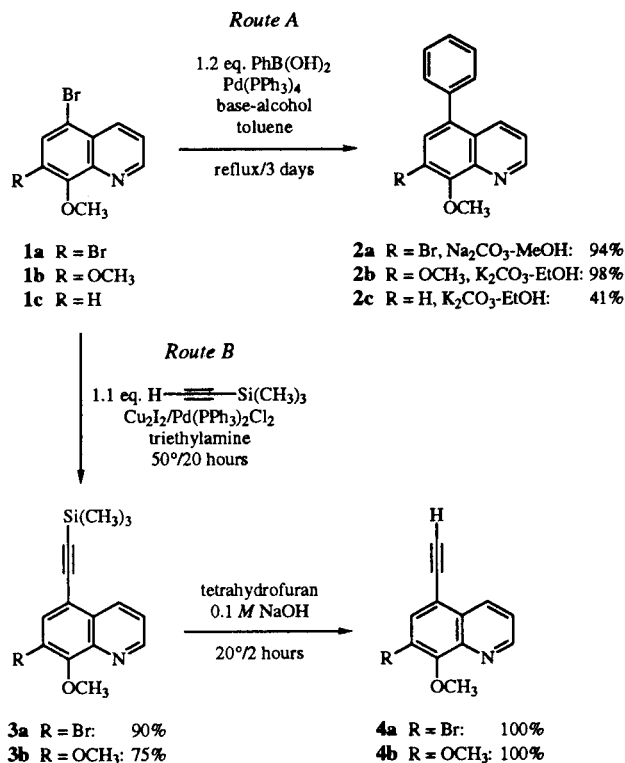


Results.

The cross-coupling reaction [5], largely described in the literature to create a C-C bond, was investigated with the easily available 5-bromoquinolines **1a-c** [6] under Suzuki's [5a] (Scheme II, *Route A*) and Sakamoto's [7] conditions (Scheme II, *Route B*). *Route A* conditions, tested with 5-bromoquinolines **1a-c** and commercial phenylboric acid, led to the corresponding 5-phenylquino-

lines **2a-c**. Even if quinolines bear two bromo groups, such as in **1a**, a total regioselectivity was observed at C-5 by using sodium carbonate-methanol pair [8]. *Route B* conditions, used with the 7-substituted 5-bromo-8-methoxyquinolines **1a-b** and commercial (trimethylsilyl)acetylene, gave the corresponding 5-(trimethylsilyl)ethynylquinolines **3a-b** in good yields. The trimethylsilyl cleavage under basic conditions led quantitatively to the 5-ethynylquinolines **4a-b**.

Scheme II



Under Suzuki's conditions [5a], the coupling reaction was also achieved with the (2-pivaloylamino)phenylboric acids **5a-b** [9] to give the amides **6a-f** (Scheme III, Table I). As far as monobromoquinolines **1b-c** are concerned,

yields were improved by using potassium carbonate-ethanol pair (Table I, Entries 3-6).

Scheme III

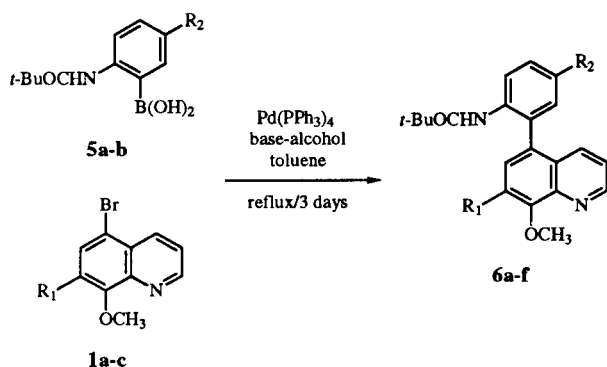


Table I

Entry	R ₁	R ₂	Base	Alcohol	Product	Yield %
1	Br	H	Na_2CO_3	MeOH	6a	90
2	Br	OCH_3	Na_2CO_3	MeOH	6b	52
3	OCH_3	H	K_2CO_3	EtOH	6c	94
4	OCH_3	OCH_3	K_2CO_3	EtOH	6d	76
5	H	H	K_2CO_3	EtOH	6e	36
6	H	OCH_3	K_2CO_3	EtOH	6f	40

Amides 6a-e thus obtained were hydrolyzed under acidic conditions to the corresponding amino derivatives 7a-e (Scheme IV, Table II).

Scheme IV

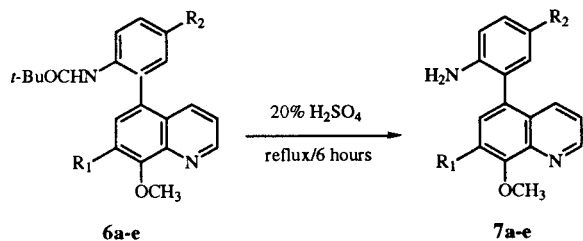
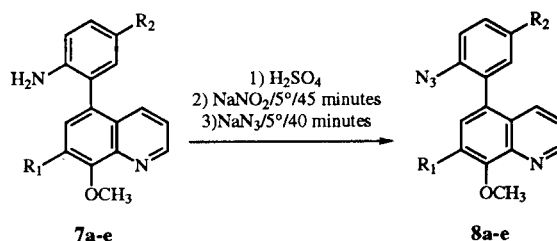


Table II

Entry	R ₁	R ₂	Amide	Amine	Yield %
1	Br	H	6a	7a	80
2	Br	OCH_3	6b	7b	57
3	OCH_3	H	6c	7c	81
4	OCH_3	OCH_3	6d	7d	84
5	H	H	6e	7e	72

Thus, the formation of diazonium salts from amino compounds 7a-e at 5° [10a], followed by the treatment with sodium azide [10a] afforded compounds 8a-e with good to quantitative yields (Scheme V, Table III). Thermocyclization attempts [10a] failed from the azide 8d; the pyridocarbazole 9b was only obtained in poor yield (13%) from 8b. In these two cases, the starting material could not be recovered (Table IV, Entries 4 and 2). Nevertheless, a regioselective thermocyclization at C-6 occurred from azides 8a,c,e affording 6-substituted 5-methoxy-7H-pyrido[2,3-c]carbazoles 9a,c,e in good yields (Scheme VI, Table IV).

Scheme V



Scheme VI

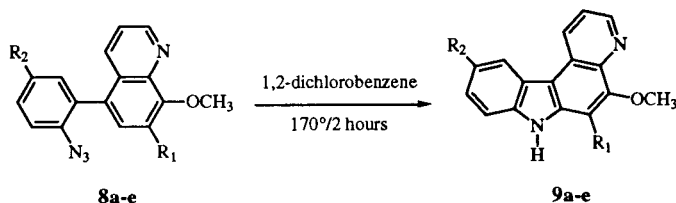


Table III

Entry	R ₁	R ₂	Amide	Azide	Yield %
1	Br	H	7a	8a	100
2	Br	OCH_3	7b	8b	90
3	OCH_3	H	7c	8c	100
4	OCH_3	OCH_3	7d	8d	75
5	H	H	7e	8e	100

Table IV

Entry	R ₁	R ₂	Azide	Product	Yield %
1	Br	H	8a	9a	81
2	Br	OCH_3	8b	9b	13
3	OCH_3	H	8c	9c	81
4	OCH_3	OCH_3	8d	9d	—
5	H	H	8e	9e	70

A literature survey showed that the cyclization of azido compounds *via* thermolysis has been successfully used to prepare various polycondensed heteroaromatics [10].

Conclusion.

Starting from easily available 5-bromo-8-methoxyquinolines 1a-c, coupling reaction allowed a facile syn-

thesis of 5-(2-aminophenyl)quinolines. Taking advantage, in our case, of a regioselective azide cyclization, new 7*H*-pyrido[2,3-*c*]carbazoles could be prepared. Thus, 6-substituted 5-methoxy-7*H*-pyrido[2,3-*c*]carbazoles were synthesized in four steps in 58, 62 and 18% overall yields, respectively, for compounds **9a**, **9c** and **9e**, which is particularly good, compared to earlier reported syntheses [2*a-c*,4] in the pyridocarbazole series.

EXPERIMENTAL

Melting points were measured on a Kofler hot stage and are uncorrected. The ^1H and ^{13}C nmr spectra were recorded in deuteriochloroform with tetramethylsilane as the internal standard on a Bruker 200 MHz spectrometer and δ are given in ppm. The ir spectra were obtained as potassium bromide pellets on a Perkin-Elmer FMR 1650 spectrometer. Mass spectra were obtained on a JEOL D700 instrument (electron impact or chemical ionization with ammonia), and elemental analyses were performed on a Carlo Erba CHNOS apparatus.

Starting Materials.

Tetrakis(triphenylphosphine)palladium(0) [11], (2-pivaloylaminophenyl) and (5-methoxy-2-pivaloylaminophenyl)boric acids [9] were synthesized by literature methods. 5-Bromo-8-methoxyquinolines **1a-c** were prepared from 5,7-dibromo-8-hydroxyquinoline [6].

General Procedure for the Reaction of 7-Substituted 5-Bromo-8-methoxyquinoline **1a-b** with (Trimethylsilyl)acetylene.

(Trimethylsilyl)acetylene (0.12 ml, 0.82 mmole) was added to a mixture of purified cuprous iodide [12] (0.15 g, 0.8 mmole) and triethylamine (20 ml) and the resulting mixture was stirred at room temperature for 10 minutes. Palladium bis(triphenylphosphine) dichloride (0.28 g, 0.8 mmole) was added and the mixture was stirred for 10 minutes. The required 5-bromoquinoline (8 mmole) and triethylamine were added. Stirring was continued for 10 minutes before addition of (trimethylsilyl)acetylene (1.17 ml, 8.2 mmole). The resulting mixture was heated at 50° for 20 hours. After cooling, the mixture was diluted with water (20 ml) and extracted 3 times with 100 ml of ether. Drying over magnesium sulphate and solvents removal afforded a crude product which was purified by preparative flash chromatography on a silica gel column.

7-Bromo-8-methoxy-5-(trimethylsilylethynyl)quinoline (**3a**).

The coupling reaction of **1a** (2.54 g, 8 mmole) according to the general procedure gave after purification by column chromatography with a mixture of tetrachloromethane and ether (4:1) as an eluent 2.41 g (90%) of **3a** as a yellow oil, bp 120° (0.2 millibar); ir: ν 2960, 2150, 1570, 1490, 1465, 1390, 1370, 1250, 1090, 1060 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 0.29 (s, 9H, Si(CH₃)₃), 4.15 (s, 3H, OCH₃), 7.47 (dd, J = 8.6-3.4 Hz, 1H, H₃), 7.85 (s, 1H, H₆), 8.52 (dd, J = 8.6-1.4 Hz, 1H, H₄), 8.91 (dd, J = 3.4-1.4 Hz, 1H, H₂); ^{13}C nmr (deuteriochloroform): δ -0.2, 62.2, 99.9, 100.8, 115.6, 117.5, 121.9, 129.2, 134.7, 134.9, 142.7, 150.3, 154.2.

Anal. Calcd. for C₁₅H₁₆BrNOSi (M = 334.30): C, 53.89; H, 4.82; N, 4.19. Found: C, 53.7; H, 4.8; N, 4.0.

7,8-Dimethoxy-5-(trimethylsilylethynyl)quinoline (**3b**).

The coupling reaction of **1b** (2.14 g, 8 mmole) according to the general procedure gave after purification by column chromatography with a mixture of trichloromethane and ether (85:15) as an eluent 1.71 g (75%) of **3b** as a yellow oil; ^1H nmr (deuteriochloroform): δ 0.33 (s, 9H, Si(CH₃)₃), 4.03 (s, 3H, OCH₃), 4.14 (s, 3H, OCH₃), 7.36 (dd, J = 8.5-4.1 Hz, 1H, H₃), 7.55 (s, 1H, H₆), 8.51 (dd, J = 8.5-1.7 Hz, 1H, H₄), 8.93 (dd, J = 4.1-1.7 Hz, 1H, H₂); ^{13}C nmr (deuteriochloroform): δ -0.5, 56.3, 61.4, 99.2, 101.0, 115.7, 119.0, 119.4, 124.5, 134.0, 142.4, 143.8, 150.1, 150.1.

Anal. Calcd. for C₁₆H₁₉NO₂Si (M = 285.42): C, 67.33; H, 6.71; N, 4.91. Found: C, 67.2; H, 6.6; N, 4.9.

General Procedure for the Trimethylsilyl Cleavage.

The required 5-(trimethylsilylethynyl)quinoline (2 mmole) was added to a mixture of tetrahydrofuran (10 ml) and 0.1 *M* aqueous sodium hydroxide (8 ml). Stirring at room temperature for 2 hours, extraction with ether, drying over magnesium sulphate, and solvents removal afforded a crude product which was purified by preparative flash chromatography on a silica gel column.

7-Bromo-5-ethynyl-8-methoxyquinoline (**4a**).

The reaction of **3a** (0.67 g, 2 mmole) according to the general procedure gave after purification by column chromatography with trichloromethane as an eluent 0.52 g (100%) of **4a** as a yellow solid, mp 128°; ir: ν 3260, 3160, 2940, 2090, 1570, 1490, 1460, 1365, 1085 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 3.48 (s, 1H, C $\equiv$ C-*H*), 4.19 (s, 3H, OCH₃), 7.50 (dd, J = 8.5-4.2 Hz, 1H, H₃), 7.90 (s, 1H, H₆), 8.57 (dd, J = 8.5-1.7 Hz, 1H, H₄), 8.97 (dd, J = 4.2-1.7 Hz, 1H, H₂); ^{13}C nmr (deuteriochloroform): δ 62.2, 78.9, 82.9, 115.8, 116.6, 122.0, 129.7, 134.7, 135.2, 143.3, 150.5, 154.9.

Anal. Calcd. for C₁₂H₈BrNO (M = 262.11): C, 54.99; H, 3.08; N, 5.34. Found: C, 54.9; H, 2.9; N, 5.4.

7,8-Dimethoxy-5-ethynylquinoline (**4b**).

The reaction of **3b** (0.57 g, 2 mmole) according to the general procedure gave after purification by column chromatography with trichloromethane as an eluent 0.43 g (100%) of **4b** as a yellow solid, mp 127°; ^1H nmr (deuteriochloroform): δ 3.47 (s, 1H, C $\equiv$ C-*H*), 4.02 (s, 3H, OCH₃), 4.15 (s, 3H, OCH₃), 7.36 (dd, J = 8.5-4.2 Hz, 1H, H₃), 7.58 (s, 1H, H₆), 8.54 (dd, J = 8.5-1.7 Hz, 1H, H₄), 8.94 (dd, J = 4.2-1.7 Hz, 1H, H₂); ^{13}C nmr (deuteriochloroform): δ 56.9, 62.0, 80.3, 82.1, 115.2, 120.1, 120.1, 125.3, 134.5, 143.1, 144.7, 150.9, 151.0.

Anal. Calcd. for C₁₃H₁₁NO₂ (M = 213.24): C, 73.23; H, 5.20; N, 6.57. Found: C, 73.0; H, 5.1; N, 6.4.

General Procedure for the Reaction of 5,7-Dibromo-8-methoxyquinoline (**1a**) with Phenylboric Acids.

5,7-Dibromo-8-methoxyquinoline (**1a**) (0.32 g, 1 mmole) and the required phenylboric acid (1.2 mmole) were added to a 2 *M* aqueous solution of sodium carbonate (1 ml) and methanol (0.5 ml) in deoxygenated toluene (10 ml). The resulting mixture was stirred for 30 minutes under an argon atmosphere. Tetrakis(triphenylphosphine)palladium(0) (0.035 g, 0.03 mmole) was added and this mixture was refluxed for 3 days. Cooling, filtration, extraction with toluene, drying over magnesium sulphate, and solvent removal afforded a crude product which was purified by preparative flash chromatography on a silica gel column.

7-Bromo-8-methoxy-5-phenylquinoline (**2a**) [7].

2,2-Dimethyl-*N*-(2-(7-bromo-8-methoxy-5-quinolyl)phenyl)propanamide (**6a**).

The coupling reaction of **1a** (0.32 g, 1 mmole) with (2-pivaloylaminophenyl)boric acid (**5a**) (0.27 g, 1.2 mmoles) according to the general procedure gave after purification by column chromatography with a mixture of dichloromethane and ether (95:5) as an eluent 0.45 g (90%) of **6a** as a yellow oil; ir: ν 3430, 3330, 2960, 2920, 1670, 1585, 1515, 1460, 1445, 1370, 1310, 1220, 1160, 1085 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 0.79 (s, 9H, $\text{C}(\text{CH}_3)_3$), 4.22 (s, 3H, OCH_3), 6.88 (bs, 1H, *NH*), 7.3 (m, 3H, $\text{H}_{3,4,5}$), 7.37 (dd, $J = 8.6\text{--}4.1$ Hz, 1H, H_3), 7.67 (s, 1H, H_6), 7.81 (dd, $J = 8.6\text{--}1.7$ Hz, 1H, H_4), 8.26 (m, 1H, H_6), 8.96 (dd, $J = 4.1\text{--}1.7$ Hz, 1H, H_2); ^{13}C nmr (deuteriochloroform): δ 26.9, 39.3, 62.2, 116.2, 121.8, 121.8, 124.3, 127.4, 127.7, 129.4, 130.4, 132.1, 132.1, 134.6, 134.6, 143.2, 150.5, 153.6, 176.0.

Anal. Calcd. for $\text{C}_{21}\text{H}_{21}\text{BrN}_2\text{O}_2$ ($M = 413.32$): C, 61.03; H, 5.12; N, 6.78. Found: C, 61.0; H, 5.0; N, 6.7.

2,2-Dimethyl-*N*-(2-(7-bromo-8-methoxy-5-quinolyl)-4-methoxyphenyl)propanamide (**6b**).

The coupling reaction of **1a** (0.32 g, 1 mmole) with (5-methoxy-2-pivaloylaminophenyl)boric acid (**5b**) (0.30 g, 1.2 mmoles) according to the general procedure gave after purification by column chromatography with a mixture of dichloromethane and ether (9:1) as an eluent 0.23 g (52%) of **6b** as a yellow oil; ir: ν 3348, 2963, 1652, 1578, 1502, 1462, 1368, 1246, 1221, 1083 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 1.24 (s, 9H, $\text{C}(\text{CH}_3)_3$), 3.62 (s, 3H, OCH_3), 4.16 (s, 3H, OCH_3), 6.89 (d, $J = 8.9$ Hz, 1H, H_6), 7.28 (dd, $J = 8.5\text{--}4.1$ Hz, 1H, H_3), 7.36 (d, $J = 2.7$ Hz, 1H, H_3), 7.55 (s, 1H, H_6), 7.57 (dd, $J = 8.9\text{--}2.7$ Hz, 1H, H_5), 7.81 (dd, $J = 8.5\text{--}1.7$ Hz, 1H, H_4), 8.88 (dd, $J = 4.1\text{--}1.7$ Hz, 1H, H_2); ^{13}C nmr (deuteriochloroform): δ 27.4, 39.3, 55.6, 61.9, 111.0, 116.0, 121.1, 121.9, 124.3, 126.5, 127.7, 131.2, 131.3, 133.3, 135.3, 142.7, 149.9, 152.7, 153.4, 176.7.

Anal. Calcd. for $\text{C}_{22}\text{H}_{23}\text{BrN}_2\text{O}_3$ ($M = 443.35$): C, 59.60; H, 5.23; N, 6.32. Found: C, 59.5; H, 5.1; N, 6.2.

General Procedure for the Reaction of other 5-Bromo-8-methoxyquinolines **1b**–**c** with Phenylboric Acids.

The required 5-bromo-8-methoxyquinoline (1 mmole) and phenylboric acid (1.2 mmoles) were added to a 2 *M* aqueous solution of potassium carbonate (1 ml) and ethanol (0.5 ml) in deoxygenated toluene (10 ml). The resulting mixture was stirred for 30 minutes under an argon atmosphere. Tetrakis(triphenylphosphine)palladium(0) (0.035 g, 0.03 mmole) was added and this mixture was refluxed for 3 days. Cooling, filtration, extraction with toluene, drying over magnesium sulphate, and solvent removal afforded a crude product which was purified by preparative flash chromatography on a silica gel column.

7,8-Dimethoxy-5-phenylquinoline (**2b**).

The coupling reaction of **1b** (0.27 g, 1 mmole) with phenylboric acid (0.15 g, 1.2 mmoles) according to the general procedure gave after purification by column chromatography with a mixture of dichloromethane and ether (95:5) as an eluent 0.26 g (98%) of **2b** as a yellow oil; ir: ν 3414, 2933, 1602, 1473, 1398, 1333, 1155, 1078 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 3.87 (s, 3H, OCH_3), 4.13 (s, 3H, OCH_3), 7.14 (dd, $J = 8.6\text{--}4.1$ Hz, 1H, H_3), 7.27 (s, 1H, H_6), 7.35 (m, 5H, phenyl), 8.07 (dd, $J = 8.6\text{--}1.7$ Hz, 1H, H_4), 8.87 (dd, $J = 4.1\text{--}1.7$ Hz, 1H, H_2); ^{13}C nmr (deu-

teriochloroform): δ 56.6, 61.6, 116.0, 118.9, 122.4, 127.5, 128.2, 129.7, 134.2, 136.1, 138.9, 142.2, 143.4, 150.1, 150.6.

Anal. Calcd. for $\text{C}_{17}\text{H}_{15}\text{NO}_2$ ($M = 265.31$): C, 76.96; H, 5.70; N, 5.28. Found: C, 76.8; H, 5.8; N, 5.2.

8-Methoxy-5-phenylquinoline (**2c**).

The coupling reaction of **1c** (0.24 g, 1 mmole) with phenylboric acid (0.15 g, 1.2 mmoles) according to the general procedure gave after purification by column chromatography with a mixture of dichloromethane and ether (9:1) as an eluent 0.096 g (41%) of **2c**, mp 120° ; ir: ν 1573, 1503, 1466, 1363, 1112 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 4.06 (s, 3H, OCH_3), 6.99 (d, $J = 8.2$ Hz, 1H, H_7), 7.24 (dd, $J = 8.6\text{--}4.0$ Hz, 1H, H_3), 7.95 (d, $J = 8.2$ Hz, 1H, H_6), 7.38 (s, 5H, phenyl), 8.14 (dd, $J = 8.6\text{--}1.7$ Hz, 1H, H_4), 8.88 (d, $J = 4.0\text{--}1.7$ Hz, 1H, H_2); ^{13}C nmr (deuteriochloroform): δ 55.8, 106.9, 121.4, 127.1, 127.1, 127.4, 128.2, 129.9, 132.0, 134.1, 139.2, 140.0, 148.8, 154.6.

Anal. Calcd. for $\text{C}_{16}\text{H}_{13}\text{NO}$ ($M = 235.29$): C, 81.68; H, 5.57; N, 5.95. Found: C, 81.5; H, 5.4; N, 5.9.

2,2-Dimethyl-*N*-(2-(7,8-dimethoxy-5-quinolyl)phenyl)propanamide (**6c**).

The coupling reaction of **1b** (0.27 g, 1 mmole) with (2-pivaloylaminophenyl)boric acid (**5a**) (0.27 g, 1.2 mmoles) according to the general procedure gave after purification by column chromatography with a mixture of ethyl acetate and hexane (1:1) as an eluent 0.34 g (94%) of **6c** as a yellow oil; ir: ν 3433, 3342, 2962, 2870, 1677, 1599, 1518, 1474, 1444, 1335, 1155, 1079 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 0.56 (s, 9H, $\text{C}(\text{CH}_3)_3$), 3.82 (s, 3H, OCH_3), 3.96 (s, 3H, OCH_3), 6.78 (bs, 1H, *NH*), 7.01 (dd, $J = 8.2\text{--}4.1$ Hz, 1H, H_3), 7.1 (m, 3H, $\text{H}_{3,4,5}$), 7.16 (s, 1H, H_6), 7.53 (dd, $J = 8.2\text{--}1.7$ Hz, 1H, H_4), 8.10 (m, 1H, H_6), 8.73 (dd, $J = 4.1\text{--}1.7$ Hz, 1H, H_2); ^{13}C nmr (deuteriochloroform): δ 26.4, 38.8, 56.5, 61.4, 116.8, 119.3, 121.1, 122.1, 123.7, 128.5, 128.7, 130.0, 130.7, 133.8, 135.6, 142.7, 142.8, 150.3, 150.6, 175.6.

Anal. Calcd. for $\text{C}_{22}\text{H}_{24}\text{N}_2\text{O}_3$ ($M = 364.45$): C, 72.51; H, 6.64; N, 7.69. Found: C, 72.3; H, 6.6; N, 7.6.

2,2-Dimethyl-*N*-(2-(8-methoxy-5-quinolyl)phenyl)propanamide (**6e**).

The coupling reaction of **1c** (0.24 g, 1 mmole) with (2-pivaloylaminophenyl)boric acid (**5a**) (0.27 g, 1.2 mmoles) according to the general procedure gave after purification by column chromatography with a mixture of ethyl acetate and dichloromethane (1:9) as an eluent 0.12 g (36%) of **6e** as a yellow oil; ^1H nmr (deuteriochloroform): δ 0.65 (s, 9H, $\text{C}(\text{CH}_3)_3$), 3.93 (s, 3H, OCH_3), 7.2 (m, 7H, $\text{H}_{3,4,5,6,7}$), 7.66 (dd, $J = 8.5\text{--}1.7$ Hz, 1H, H_4), 8.28 (m, 1H, H_6), 8.84 (dd, $J = 4.1\text{--}1.7$ Hz, 1H, H_2); ^{13}C nmr (deuteriochloroform): δ 26.8, 39.2, 55.9, 107.1, 120.8, 122.0, 123.8, 126.7, 127.4, 128.3, 128.6, 128.8, 130.6, 133.9, 136.1, 136.1, 149.4, 155.3, 175.9.

Anal. Calcd. for $\text{C}_{21}\text{H}_{22}\text{N}_2\text{O}_2$ ($M = 334.42$): C, 75.42; H, 6.63; N, 8.38. Found: C, 75.3; H, 6.6; N, 8.4.

2,2-Dimethyl-*N*-(2-(7,8-dimethoxy-5-quinolyl)-4-methoxyphenyl)propanamide (**6d**).

The coupling reaction of **1b** (0.27 g, 1 mmole) with (5-methoxy-2-pivaloylaminophenyl)boric acid (**5b**) (0.30 g, 1.2 mmoles) according to the general procedure gave after purification by column chromatography with a mixture of dichloromethane and ether (7:3) as an eluent 0.30 g (76%) of **6d** as a yellow

low oil; ir: ν 3330, 2959, 1654, 1598, 1499, 1474, 1334, 1158 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 1.19 (s, 9H, $\text{C}(\text{CH}_3)_3$), 3.56 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 4.04 (s, 3H, OCH_3), 6.84 (d, $J = 8.9$ Hz, 1H, H_6), 7.05 (dd, $J = 8.5$ –4.2 Hz, 1H, H_3), 7.17 (s, 1H, H_6), 7.35 (d, $J = 2.7$ Hz, 1H, H_3), 7.56 (dd, $J = 8.9$ –2.7 Hz, 1H, H_5), 7.70 (dd, $J = 8.5$ –1.7 Hz, 1H, H_4), 7.83 (bs, 1H, NH), 8.77 (dd, $J = 4.2$ –1.7 Hz, 1H, H_2); ^{13}C nmr (deuteriochloroform): δ 27.3, 39.2, 55.5, 56.5, 61.5, 111.0, 116.4, 118.8, 121.8, 122.8, 124.5, 127.6, 131.3, 131.6, 132.4, 134.9, 142.0, 142.9, 149.9, 150.6, 153.3.

Anal. Calcd. for $\text{C}_{23}\text{H}_{26}\text{N}_2\text{O}_4$ ($M = 394.47$): C, 70.03; H, 6.64; N, 7.10. Found: C, 69.8; H, 6.6; N, 7.0.

2,2-Dimethyl-*N*-(4-methoxy-2-(8-methoxy-5-quinolyl)phenyl)propanamide (**6f**).

The coupling reaction of **1c** (0.24 g, 1 mmole) with (5-methoxy-2-pivaloylamino)phenylboric acid (**5b**) (0.30 g, 1.2 mmole) according to the general procedure gave after purification by column chromatography with a mixture of dichloromethane and ether (9:1) as an eluent 0.15 g (40%) of **6f** as a yellow oil; ir: ν 3298, 2954, 2836, 1661, 1542, 1500, 1476, 1414, 1210, 1108 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 1.27 (s, 9H, $\text{C}(\text{CH}_3)_3$), 3.61 (s, 3H, OCH_3), 4.07 (s, 3H, OCH_3), 6.92 (d, $J = 8.9$ Hz, 1H, H_6), 7.02 (d, $J = 8.0$ Hz, 1H, H_7), 7.4 (m, 5H, $\text{H}_{3-5, 3'-6'}$, NH), 7.83 (dd, $J = 8.5$ –1.7 Hz, 1H, H_4), 8.87 (dd, $J = 4.1$ –1.7 Hz, 1H, H_2); ^{13}C nmr (deuteriochloroform): δ 27.4, 39.3, 55.6, 55.8, 106.9, 111.1, 121.2, 121.4, 124.6, 127.6, 127.8, 128.1, 131.2, 131.8, 134.8, 139.6, 148.7, 153.7, 154.7, 176.7.

Anal. Calcd. for $\text{C}_{22}\text{H}_{24}\text{N}_2\text{O}_3$ ($M = 364.45$): C, 72.51; H, 6.64; N, 7.69. Found: C, 72.3; H, 6.5; N, 7.5.

General Procedure for the Hydrolysis of Pivalamides **6a-f**.

The required pivaloylamino compound (1 mmole) was added to a 20% solution of sulphuric acid (10 ml) and refluxed for 6 hours. The resulting cold solution was poured into a mixture of ice and concentrated ammonia. Extraction with ethyl acetate, drying over magnesium sulphate and solvent removal afforded a crude product which was purified by preparative flash chromatography on a silica gel column.

5-(2-Aminophenyl)-7-bromo-8-methoxyquinoline (**7a**).

The reaction of **6a** (0.41 g, 1 mmole) according to the general procedure gave after purification by column chromatography with dichloromethane and ether (9:1) as an eluent 0.26 g (80%) of **7a** as a yellow solid, mp 216°; ir: ν 3380, 3290, 3020, 2920, 1620, 1575, 1500, 1460, 1400, 1255, 1185 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 3.5 (bs, 2H, NH_2), 4.26 (s, 3H, OCH_3), 7.0 (m, 4H, $\text{H}_{3-4, 5-6}$), 7.39 (dd, $J = 8.5$ –4.2 Hz, 1H, H_3), 7.69 (s, 1H, H_6), 7.96 (dd, $J = 8.5$ –1.6 Hz, 1H, H_4), 8.97 (dd, $J = 4.2$ –1.6 Hz, 1H, H_2); ^{13}C nmr (deuteriochloroform): δ 61.9, 115.1, 116.1, 118.2, 121.4, 122.5, 127.4, 129.3, 131.0, 131.7, 133.9, 135.2, 143.2, 144.2, 150.1, 152.8.

Anal. Calcd. for $\text{C}_{16}\text{H}_{13}\text{BrN}_2\text{O}$ ($M = 329.20$): C, 58.38; H, 3.98; N, 8.51. Found: C, 58.3; H, 3.9; N, 8.5.

5-(2-Amino-5-methoxyphenyl)-7-bromo-8-methoxyquinoline (**7b**).

The reaction of **6b** (0.44 g, 1 mmole) according to the general procedure gave after purification by column chromatography with dichloromethane and ethyl acetate (3:1) as an eluent 0.20 g (57%) of **7b** as a yellow viscous solid; ir: ν 3425, 3354, 2931, 1501, 1464, 1232, 1084 cm^{-1} ; ^1H nmr (deuteriochloroform): δ

3.5 (bs, 2H, NH_2), 3.56 (s, 3H, OCH_3), 4.17 (s, 3H, OCH_3), 6.56 (d, $J = 2.7$ Hz, 1H, H_6), 6.7 (m, 2H, H_{3-4}), 7.29 (dd, $J = 8.6$ –4.2 Hz, 1H, H_3), 7.57 (s, 1H, H_6), 7.90 (dd, $J = 8.6$ –1.7 Hz, 1H, H_4), 8.88 (dd, $J = 4.2$ –1.7 Hz, 1H, H_2); ^{13}C nmr (deuteriochloroform): δ 55.9, 61.9, 112.4, 116.0, 116.0, 118.9, 121.0, 127.2, 127.7, 131.2, 134.0, 135.6, 140.1, 142.9, 149.8, 149.8, 152.5.

Anal. Calcd. for $\text{C}_{17}\text{H}_{15}\text{BrN}_2\text{O}_2$ ($M = 359.23$): C, 56.84; H, 4.21; N, 7.80. Found: C, 56.7; H, 4.2; N, 7.7.

5-(2-Aminophenyl)-7,8-dimethoxyquinoline (**7c**).

The reaction of **6c** (0.36 g, 1 mmole) according to the general procedure gave after purification by column chromatography with dichloromethane and ether (1:1) as an eluent 0.23 g (81%) of **7c** as a yellow solid, mp 131°; ir: ν 3391, 3152, 1603, 1494, 1478, 1332, 1151, 1076 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 3.4 (bs, 2H, NH_2), 4.00 (s, 3H, OCH_3), 4.15 (s, 3H, OCH_3), 6.82 (dd, $J = 8.4$ –4.2 Hz, 1H, H_3), 7.0 (m, 4H, $\text{H}_{3-4, 5-6}$), 7.34 (s, 1H, H_6), 7.87 (dd, $J = 8.4$ –1.8 Hz, 1H, H_4), 8.90 (dd, $J = 4.2$ –1.8 Hz, 1H, H_2); ^{13}C nmr (deuteriochloroform): δ 56.8, 61.7, 115.3, 116.8, 118.2, 119.3, 122.6, 123.9, 129.2, 131.1, 132.9, 134.7, 142.5, 143.5, 144.3, 150.4, 151.1.

Anal. Calcd. for $\text{C}_{17}\text{H}_{16}\text{N}_2\text{O}_2$ ($M = 280.33$): C, 72.84; H, 5.75; N, 9.99. Found: C, 72.7; H, 5.6; N, 10.0.

5-(2-Amino-5-methoxyphenyl)-7,8-dimethoxyquinoline (**7d**).

The reaction of **6d** (0.39 g, 1 mmole) according to the general procedure gave after purification by column chromatography with dichloromethane and ethyl acetate (1:1) as an eluent 0.26 g (84%) of **7d** as a yellow solid, mp 181°; ir: ν 3344, 2926, 1600, 1498, 1473, 1338, 1234, 1155, 1077 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 3.5 (bs, 2H, NH_2), 3.55 (s, 3H, OCH_3), 3.95 (s, 3H, OCH_3), 4.11 (s, 3H, OCH_3), 6.58 (d, $J = 2.7$ Hz, 1H, H_6), 6.71 (dd, $J = 8.6$ –2.7 Hz, 1H, H_4), 6.82 (d, $J = 8.6$ Hz, 1H, H_3), 7.11 (dd, $J = 8.5$ –4.1 Hz, 1H, H_3), 7.24 (s, 1H, H_6), 7.82 (dd, $J = 8.5$ –1.6 Hz, 1H, H_4), 8.83 (dd, $J = 4.1$ –1.6 Hz, 1H, H_2).

Anal. Calcd. for $\text{C}_{18}\text{H}_{18}\text{N}_2\text{O}_3$ ($M = 310.36$): C, 69.66; H, 5.85; N, 9.03. Found: C, 69.4; H, 5.7; N, 8.9.

5-(2-Aminophenyl)-8-methoxyquinoline (**7e**).

The reaction of **6e** (0.33 g, 1 mmole) according to the general procedure gave after purification by column chromatography with dichloromethane and ethyl acetate (1:1) as an eluent 0.18 g (72%) of **7e** as a yellow solid, mp 188°; ir: ν 3410, 3336, 3241, 1630, 1505, 1472, 1448, 1365, 1309, 1111 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 3.4 (bs, 2H, NH_2), 4.10 (s, 3H, OCH_3), 6.8 (m, 5H, $\text{H}_{7-3, 4-5, 6}$), 7.33 (dd, $J = 8.5$ –4.1 Hz, 1H, H_3), 7.41 (d, $J = 7.9$ Hz, 1H, H_6), 7.91 (dd, $J = 8.5$ –1.7 Hz, 1H, H_4), 8.91 (dd, $J = 4.1$ –1.7 Hz, 1H, H_2); ^{13}C nmr (deuteriochloroform): δ 55.9, 107.3, 115.1, 118.2, 121.6, 124.1, 127.6, 127.9, 128.6, 128.8, 131.4, 134.5, 140.2, 144.5, 149.1, 154.9.

Anal. Calcd. for $\text{C}_{16}\text{H}_{14}\text{N}_2\text{O}$ ($M = 250.30$): C, 76.78; H, 5.64; N, 11.19. Found: C, 76.6; H, 5.5; N, 11.0.

General Procedure for the Synthesis of Azides **8a-e** from Amines **7a-e**.

The required amino compound (1 mmole) was added to a solution of water (1 ml) and concentrated sulfuric acid (0.3 ml). The resulting solution was stirred for 10 minutes and ice-cooled before addition of sodium nitrite (0.074 g, 1.05 mmole) in water (0.2 ml). After stirring for 45 minutes, sodium azide (0.084 g, 1.2 mmole) in water (0.3 ml) was added and stirring was continued for 40 minutes. Treatment with sodium

hydrogenocarbonate, extraction with dichloromethane, drying over magnesium sulphate and solvent removal afforded a crude product which was purified by preparative flash chromatography on a silica gel column.

5-(2-Azidophenyl)-7-bromo-8-methoxyquinoline (**8a**).

The reaction of **7a** (0.33 g, 1 mmole) according to the general procedure gave after purification by column chromatography with ethyl acetate as an eluent 0.36 g (100%) of **8a** as a yellow oil; ^1H nmr (deuteriochloroform): δ 4.27 (s, 3H, OCH_3), 7.4 (m, 5H, $\text{H}_{3-3',4'-5'-6'}$), 7.61 (s, 1H, H_6), 7.85 (dd, $J = 8.6\text{--}1.5$ Hz, 1H, H_4), 8.98 (dd, $J = 4.2\text{--}1.5$ Hz, 1H, H_2).

Anal. Calcd. for $\text{C}_{16}\text{H}_{11}\text{BrN}_4\text{O}$ ($M = 355.20$): C, 54.10; H, 3.12; N, 15.77. Found: C, 53.9; H, 3.0; N, 15.7.

5-(2-Azido-5-methoxyphenyl)-7-bromo-8-methoxyquinoline (**8b**).

The reaction of **7b** (0.36 g, 1 mmole) according to the general procedure gave after purification by column chromatography with dichloromethane and ethyl acetate (85:15) as an eluent 0.35 g (90%) of **8b** as a yellow oil; ir: ν 3005, 2964, 2936, 2835, 2109, 1575, 1500, 1463, 1284, 1242, 1084 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 3.67 (s, 3H, OCH_3), 4.20 (s, 3H, OCH_3), 7.0 (m, 3H, $\text{H}_{3-4'-6'}$), 7.34 (dd, $J = 8.5\text{--}4.1$ Hz, 1H, H_3), 7.58 (s, 1H, H_6), 7.82 (dd, $J = 8.5\text{--}1.7$ Hz, 1H, H_4), 8.93 (dd, $J = 4.1\text{--}1.7$ Hz, 1H, H_2); ^{13}C nmr (deuteriochloroform): δ 55.7, 61.9, 112.1, 116.0, 119.9, 121.1, 122.2, 127.6, 127.9, 131.4, 132.5, 132.6, 135.0, 143.0, 150.0, 153.0, 154.2.

Anal. Calcd. for $\text{C}_{17}\text{H}_{13}\text{BrN}_4\text{O}_2$ ($M = 385.23$): C, 53.00; H, 3.40; N, 14.54. Found: C, 52.8; H, 3.3; N, 14.4.

5-(2-Azidophenyl)-7,8-dimethoxyquinoline (**8c**).

The reaction of **7c** (0.28 g, 1 mmole) according to the general procedure gave after purification by column chromatography with ethyl acetate as an eluent 0.31 g (100%) of **8c** as a yellow oil; ir: ν 3395, 2934, 2123, 1604, 1473, 1336, 1155, 1078 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 4.01 (s, 3H, OCH_3), 4.18 (s, 3H, OCH_3), 7.0 (m, 6H, $\text{H}_{3-6,3'-4'-5'-6'}$), 7.71 (dd, $J = 8.5\text{--}1.6$ Hz, 1H, H_4), 8.87 (dd, $J = 4.1\text{--}1.6$ Hz, 1H, H_2); ^{13}C nmr (deuteriochloroform): δ 56.7, 61.7, 116.7, 118.3, 119.1, 122.8, 124.7, 129.5, 130.4, 131.9, 132.1, 134.3, 138.4, 142.6, 143.1, 150.2, 150.6.

Anal. Calcd. for $\text{C}_{17}\text{H}_{14}\text{N}_4\text{O}_2$ ($M = 306.33$): C, 66.66; H, 4.61; N, 18.29. Found: C, 66.4; H, 4.7; N, 18.4.

5-(2-Azido-5-methoxyphenyl)-7,8-dimethoxyquinoline (**8d**).

The reaction of **7d** (0.31 g, 1 mmole) according to the general procedure gave after purification by column chromatography with ethyl acetate as an eluent 0.25 g (75%) of **8d** as a yellow oil; ir: ν 2936, 2836, 2112, 1600, 1494, 1473, 1336, 1244, 1157 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 3.64 (s, 3H, OCH_3), 3.99 (s, 3H, OCH_3), 4.13 (s, 3H, OCH_3), 6.92 (d, $J = 2.6$ Hz, 1H, H_6), 6.97 (d, $J = 8.7$ Hz, 1H, H_3), 7.05 (dd, $J = 8.7\text{--}2.6$ Hz, 1H, H_4), 7.16 (dd, $J = 8.5\text{--}4.1$ Hz, 1H, H_3), 7.25 (s, 1H, H_6), 7.74 (dd, $J = 8.5\text{--}1.5$ Hz, 1H, H_4), 8.87 (dd, $J = 4.1\text{--}1.5$ Hz, 1H, H_2); ^{13}C nmr (deuteriochloroform): δ 55.7, 56.7, 61.6, 112.1, 116.5, 119.0, 119.5, 122.3, 122.8, 129.2, 131.6, 132.3, 134.5, 142.5, 143.1, 150.1, 150.7, 154.3.

Anal. Calcd. for $\text{C}_{18}\text{H}_{16}\text{N}_4\text{O}_3$ ($M = 336.35$): C, 64.28; H, 4.79; N, 16.66. Found: C, 64.0; H, 4.6; N, 16.5.

5-(2-Azidophenyl)-8-methoxyquinoline (**8e**).

The reaction of **7e** (0.25 g, 1 mmole) according to the general

procedure gave after purification by column chromatography with ethyl acetate as an eluent 0.28 g (100%) of **8e** as a yellow oil; ^1H nmr (deuteriochloroform): δ 4.10 (s, 3H, OCH_3), 7.09 (d, $J = 8.0$ Hz, 1H, H_7), 7.4 (m, 6H, $\text{H}_{3-6,3'-4'-5'-6'}$), 7.80 (dd, $J = 8.5\text{--}1.6$ Hz, 1H, H_4), 8.92 (dd, $J = 4.1\text{--}1.6$ Hz, 1H, H_2); ^{13}C nmr (deuteriochloroform): δ 55.9, 106.8, 118.4, 121.6, 124.7, 127.8, 128.3, 129.1, 130.0, 130.8, 132.4, 134.2, 138.7, 139.7, 148.9, 155.1.

Anal. Calcd. for $\text{C}_{16}\text{H}_{12}\text{N}_4\text{O}$ ($M = 276.30$): C, 69.55; H, 4.38; N, 20.28. Found: C, 69.4; H, 4.4; N, 20.1.

General Procedure for the Synthesis of 7H-Pyrido[2,3-*c*]carbazoles **9a-d** from Azides **8a-c,e**.

The required azide (1 mmole) in 1,2-dichlorobenzene (7 ml) was slowly heated to 170°. Stirring was continued for 2 hours at 170°, before solvent removal under vacuum. The crude solid was purified by preparative flash chromatography on a silica gel column.

6-Bromo-5-methoxy-7H-pyrido[2,3-*c*]carbazole (**9a**).

The reaction of **8a** (0.36 g, 1 mmole) according to the general procedure gave after purification by column chromatography with ethyl acetate as an eluent 0.27 g (81%) of **9a** as a beige solid, mp >250°; ir: ν 3084, 1523, 1455, 1352, 1319, 1277, 1229, 1087 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 4.28 (s, 3H, OCH_3), 7.5 (m, 4H, $\text{H}_{2-8,9-10}$), 8.42 (m, 1H, H_{11}), 8.78 (bs, 1H, NH), 8.97 (dd, 1H, H_3), 9.05 (dd, 1H, H_1); ms: (electron impact) m/z 326/328 (M^+).

Anal. Calcd. for $\text{C}_{16}\text{H}_{11}\text{BrN}_2\text{O}$ ($M = 327.19$): C, 58.74; H, 3.39; N, 8.56. Found: C, 58.6; H, 3.2; N, 8.7.

6-Bromo-5,10-dimethoxy-7H-pyrido[2,3-*c*]carbazole (**9b**).

The reaction of **8b** (0.39 g, 1 mmole) according to the general procedure gave after purification by column chromatography with dichloromethane and ethyl acetate (75/25) as an eluent 0.046 g (13%) of **9b** as a yellow solid, mp >250°; ir: ν 3126, 2931, 1554, 1487, 1464, 1352, 1300, 1215, 1158, 1083 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 4.02 (s, 3H, OCH_3), 4.26 (s, 3H, OCH_3), 7.15 (dd, 1H, H_9), 7.56 (d, 1H, H_8), 7.65 (dd, 1H, H_2), 7.85 (d, 1H, H_{11}), 8.66 (s, 1H, NH), 8.9 (m, 2H, H_{1-3}); ms: (chemical ionization) m/z 357/359 ($\text{M}^+ + 1$).

Anal. Calcd. for $\text{C}_{17}\text{H}_{13}\text{BrN}_2\text{O}_2$ ($M = 357.21$): C, 57.16; H, 3.67; N, 7.84. Found: C, 57.0; H, 3.5; N, 7.7.

5,6-Dimethoxy-7H-pyrido[2,3-*c*]carbazole (**9c**).

The reaction of **8c** (0.31 g, 1 mmole) according to the general procedure gave after purification by column chromatography with ethyl acetate as an eluent 0.23 g (81%) of **9c** as a beige solid, mp 179°; ir: ν 2934, 1577, 1529, 1456, 1347, 1294, 1192, 1090 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 4.22 (s, 3H, OCH_3), 4.29 (s, 3H, OCH_3), 7.5 (m, 4H, $\text{H}_{2-8,9-10}$), 8.41 (m, 1H, H_{11}), 8.93 (dd, $J = 4.3\text{--}1.6$ Hz, 1H, H_3), 8.98 (dd, $J = 8.3\text{--}1.6$ Hz, 1H, H_1), 9.12 (bs, 1H, NH); ms: (electron impact) m/z 278 (M^+).

Anal. Calcd. for $\text{C}_{17}\text{H}_{14}\text{N}_2\text{O}_2$ ($M = 278.31$): C, 73.37; H, 5.07; N, 10.07. Found: C, 73.1; H, 4.9; N, 9.9.

5-Methoxy-7H-pyrido[2,3-*c*]carbazole (**9e**).

The reaction of **8e** (0.28 g, 1 mmole) according to the general procedure gave after purification by column chromatography with dichloromethane and ethyl acetate (1:1) as an eluent 0.17 g (70%) of **9e** as a beige solid, mp >250°; ir: ν 3046, 1605, 1530, 1458, 1353, 1326, 1278, 1209 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 4.17 (s, 3H, OCH_3), 7.20 (s, 1H, H_6), 7.4 (m, 3H, H_{8-9}).

δ 10), 7.63 (dd, $J = 8.4$ -4.2 Hz, 1H, H_2), 8.37 (m, 1H, H_{11}), 8.65 (bs, 1H, NH), 8.93 (dd, $J = 4.2$ -1.6 Hz, 1H, H_3), 9.01 (dd, $J = 8.4$ -1.6 Hz, 1H, H_1).

Anal. Calcd. for $C_{16}H_{12}N_2O$ ($M = 248.29$): C, 77.40; H, 4.87; N, 11.28. Found: C, 77.3; H, 4.9; N, 11.1.

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