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Synthesis of 11*H*-Pyrido[2,3-a]carbazoles and 6*H*-Pyrido[3,2-b]carbazoles from 8-Methoxy Bromoquinolines

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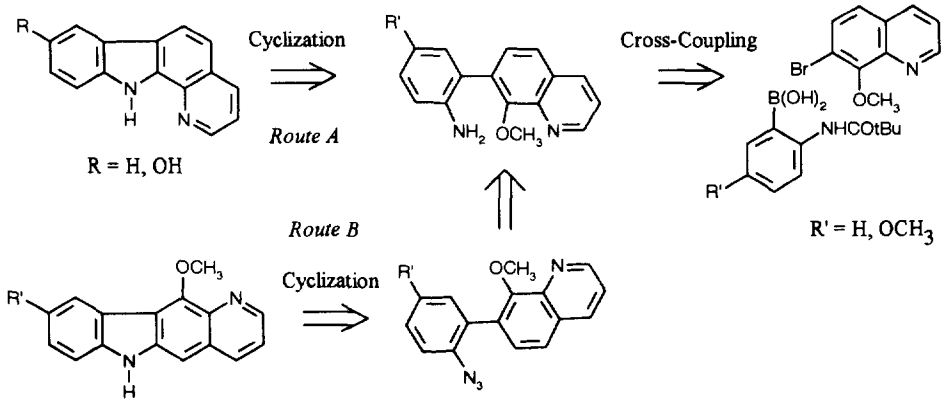
Abstract: Cross-coupling reaction *via* substituted 7-bromoquinolines **1**, **8** and (2-aminophenyl)boric acids afforded substituted 7-(2-aminophenyl)quinolines **3a-b**, **10** from which synthesis of either 11*H*-pyrido[2,3-a]carbazoles **4a-b**, **11** *via* C-8 cyclization or 6*H*-pyrido[3,2-b]carbazoles **6a-b**, **13** *via* C-6 cyclization could be achieved.

INTRODUCTION

It is well established that the pyridocarbazole ring is an appropriate skeleton to design DNA intercaling drugs.[1] Some compounds such as ellipticines and olivacines elicit high antitumor properties.[1-3] Since the discovery of the potent activity of 11*H*-pyrido[2,3-a]carbazoles[1] and 6*H*-pyrido[3,2-b]carbazoles,[3] numerous syntheses have been reported;[1,4] indoles,[4a-e] but also 3-aminocarbazoles,[4h] stilbenes,[4e] substituted benzenes[4g] or quinolines[1,4f] were often used as starting materials. Moreover, these methods often have low yields due either to the large number of steps[4g] or to the presence of several isomers.[4c-d,4i]

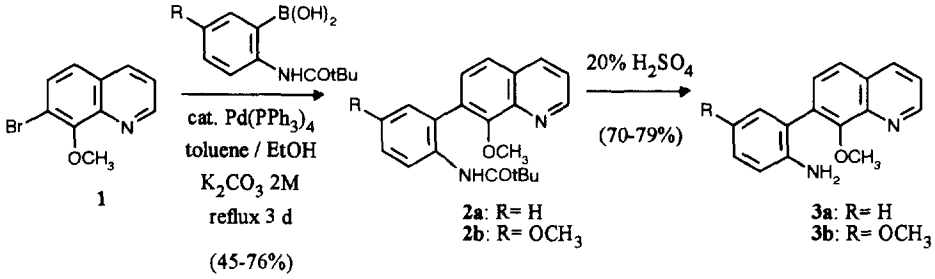
We here describe an efficient route to 11*H*-pyrido[2,3-a]carbazoles from quinoline and benzene building blocks (Scheme 1, *Route A*). A slight modification of the methodology also gave an interesting route to substituted 6*H*-pyrido[3,2-b]carbazoles (Scheme 1, *Route B*).



Scheme 1

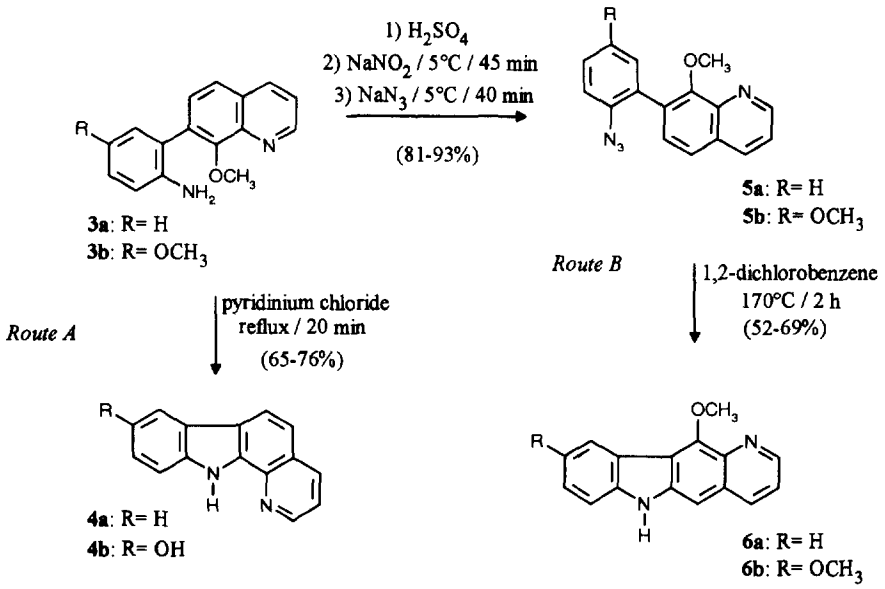
RESULTS AND DISCUSSION

The palladium catalyzed cross-coupling reaction[5] between 7-bromo-8-methoxyquinoline[6] (**1**) and phenylboric acids[7f] was achieved by the Suzuki's procedure[5a] to give 7-(2-aminophenyl)-8-methoxyquinolines **2a-b**, which were hydrolyzed under acidic conditions to the corresponding amino derivatives **3a-b** (Scheme 2).



Scheme 2

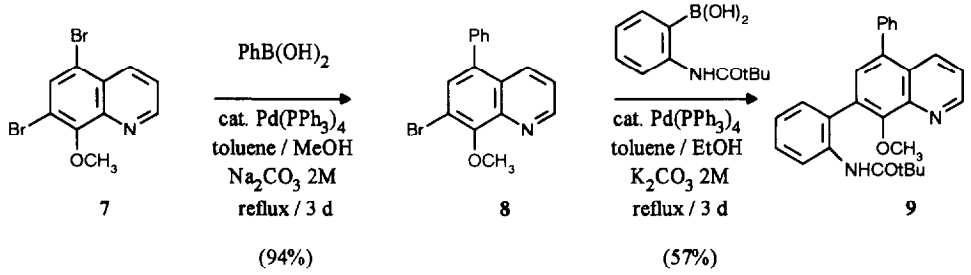
Cyclization of the 7-(2-aminophenyl)-8-methoxyquinolines **3a-b** with boiling pyridinium chloride[7] gave the 11*H*-pyrido[2,3-a]carbazoles **4a-b** (Scheme 3, *Route A*). The ^{1}H NMR spectra and melting points were found to be identical with those reported.[4f-g,1] Besides, diazotation of amino compounds **3a-b**,[8] followed by the treatment of the diazonium salts with sodium azide[8] afforded azides **5a-b** from which thermal cyclization[8] at C-6 gave 11-methoxy-6*H*-pyrido[3,2-b]carbazoles **6a-b** (Scheme 3, *Route B*). In the case of **3b**, the cleavage of the methoxy group to an hydroxy group was observed as expected during the cyclization step.



Scheme 3

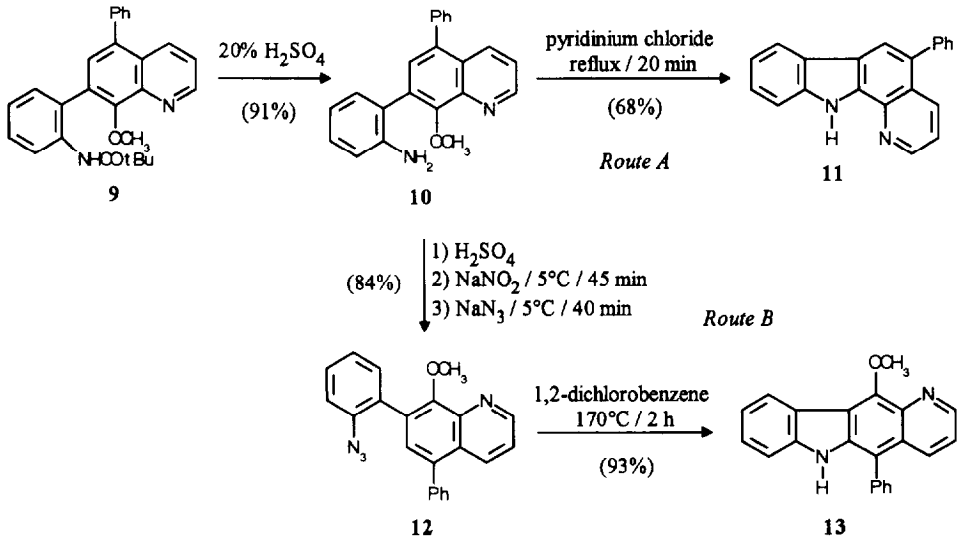
From 7-bromo-8-methoxyquinoline (**1**), pyridocarbazoles **4a-b** and **6a-b** could be prepared with good yields.

In order to synthesize more substituted pyridocarbazoles, our methodology has been tested on another starting material: 5,7-dibromo-8-methoxyquinoline[6] (**7**). The palladium catalyzed cross-coupling reaction between the 5,7-dibromoquinoline (**7**) and commercial phenylboric acid was achieved under Suzuki's conditions.[5a] The total regioselectivity observed at C-5 when using sodium carbonate-methanol tandem afforded, with an excellent yield of 94%, compound **8** on which a second coupling reaction at C-7 gave the biaryl derivative **9** (Scheme 4).



Scheme 4

From **9**, a C-8 cyclization[7] of the amine **10** gave the 5-substituted 11*H*-pyrido[2,3-a]carbazole **11** (Scheme 5, *Route A*). Besides, a C-6 cyclization *via* formation of azide **12** afforded the 5-substituted 6*H*-pyrido[3,2-b]carbazole **13** (Scheme 5, *Route B*).



Scheme 5

CONCLUSION

Starting from 7-bromo-8-methoxyquinoline (**1**), the 11*H*-pyrido[2,3-a]carbazole (**4a**) and the 8-hydroxy derivative (**4b**) were prepared in 3 steps with respectively 40% and 23% overall yield whereas, in the previous syntheses, they were prepared with respectively 7% overall yield in 5 steps from gramine[4d] and 4% overall yield in 3 steps from 8-quinolylhydrazine dihydrochloride.[1] On the other hand, amines **3a-b** could also be used for the synthesis of 6*H*-pyrido[3,2-b]carbazoles **6a-b**. The strategy thus developed was also suitable for 5-substituted 11*H*-pyrido[2,3-a]carbazoles and 6*H*-pyrido[3,2-b]carbazoles.

EXPERIMENTAL

General data. Melting points were measured on a Kofler apparatus. ^1H and ^{13}C NMR spectra were obtained on a 200 MHz Bruker AM 200 spectrometer and were recorded in ppm downfield from an internal standard, TMS in $CDCl_3$ or HMDS in DMSO-d_6. IR spectra were taken on a Perkin Elmer FT IR 205 spectrometer, and main IR absorptions are given in cm^{-1}. Mass spectra were obtained on a JEOL D700 instrument, and elemental analyses were performed on a Carlo Erba 1106 apparatus.

Starting materials. (2-Pivaloylaminophenyl)boric acid was prepared from pivaloylaminobenzene.[7f] 7-Bromo-8-methoxyquinoline (**1**) and 5,7-dibromo-8-methoxyquinoline (**7**) were prepared from corresponding 8-hydroxyquinolines.[6] Tetrakis(triphenylphosphine)palladium(0) was synthesized by literature method.[9]

General procedure for the cross-coupling reaction between 7-bromo-8-methoxyquinoline (1) or 7-bromo-5-phenyl-8-methoxyquinoline (8) and arylboric acids. Required 7-bromoquinoline (1.0 mmol) and arylboric acid (1.2 mmol) were added to a solution of potassium carbonate (2M, 1.0 mL) and ethanol (0.5 mL) in deoxygenated toluene (10 mL). The resulting mixture was stirred for 0.5h under an argon atmosphere. Tetrakis(triphenylphosphine)palladium(0) (35 mg, 0.03 mmol) was added and this mixture was refluxed for 3 d. Cooling, filtration, extraction with toluene, drying over $MgSO_4$, and solvent removal afforded a crude product which was purified by preparative flash chromatography on silica (eluent).

2,2-Dimethyl-N-(2-(8-methoxy-7-quinolyl)phenyl)propanamide (2a). The foregoing procedure, used with 7-bromo-8-methoxyquinoline (**1**) and (2-pivaloylaminophenyl)boric acid, gave 76% (CH_2Cl_2/Et_2O: 9/1) of **2a** (oil): ^1H NMR ($CDCl_3$) δ 0.88 (s, 9H, tBu), 3.71 (s, 3H, OCH_3), 7.2 (m, 5H, $H_{3\text{-}4\text{-}5\text{-}6\text{-}3'}$), 7.49 (d, 1H, *J= 8.5 Hz*, $H_{5'}$), 7.91 (d, 1H, *J= 8.5 Hz*, $H_{6'}$), 8.03 (dd, 1H, *J= 8.3-1.7 Hz*, $H_{4'}$), 8.27 (s, 1H, NH), 8.86 (dd, 1H, *J= 4.2-1.7 Hz*, $H_{2'}$); ^{13}C NMR ($CDCl_3$) δ 26.9, 38.9, 62.1, 121.3, 123.6, 123.7, 124.3, 128.1, 128.9, 129.6, 130.3, 130.3, 130.6, 135.1, 135.7, 141.9, 149.9, 151.6, 176.5; IR (neat): 3430, 2962, 1681, 1516, 1444, 1359, 1095. Anal. Calcd for $C_{21}H_{22}N_2O_2$ (334.42): C, 75.42; H, 6.63; N, 8.38. Found: C, 75.13; H, 6.61; N, 8.26.

2,2-Dimethyl-N-(4-methoxy-2-(8-methoxy-7-quinolyl)phenyl)propanamide (2b). The foregoing procedure, used with 7-bromo-8-methoxyquinoline (**1**) and (5-methoxy-2-pivaloylaminophenyl)boric acid, gave 45% (CH_2Cl_2/Et_2O: 8/2) of **2b** (oil): ^1H NMR ($CDCl_3$) δ 1.19 (s, 9H, tBu), 3.65 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3), 6.83 (d, 1H, *J= 8.9 Hz*, H_6), 7.4 (m, 5H, $H_{3\text{-}5\text{-}3'\text{-}5'\text{-}6'}$), 7.79 (s, 1H, NH), 8.03 (dd, 1H, *J= 8.3-1.6 Hz*, $H_{4'}$), 8.85 (dd, 1H, *J= 4.2-1.6*, $H_{2'}$); ^{13}C NMR ($CDCl_3$) δ 27.4, 39.2, 55.7, 61.8, 111.1, 121.0, 121.5, 122.1, 123.9, 127.3, 129.0, 130.0, 130.3, 131.0, 131.7, 131.8, 136.0, 142.6, 153.3, 176.7; IR (neat): 3342,

2962, 1654, 1498, 1459, 1437, 1357, 1227, 1099. Anal. Calcd for $C_{22}H_{24}N_2O_3$ (364.45): C, 72.51; H, 6.64; N, 7.69. Found: C, 72.23; H, 6.61; N, 7.46.

2,2-Dimethyl-N-(2-(8-methoxy-5-phenyl-7-quinolyl)phenyl)propanamide (9). The foregoing procedure, used with 7-bromo-5-phenyl-8-methoxyquinoline (**8**) and (2-pivaloylaminophenyl)boric acid, gave 57% (CH_2Cl_2/Et_2O: 95/5) of **9** (oil): ^1H NMR ($CDCl_3$) δ 1.06 (s, 9H, tBu), 3.87 (s, 3H, OCH_3), 7.3 (m, 10H, C_6H_5, $H_{3\text{-}4\text{-}5\text{-}3'\text{-}6'}$), 8.03 (dd, 1H, *J= 8.8-1.4 Hz*, H_6), 8.23 (dd, 1H, *J= 8.6-1.7 Hz*, $H_{4'}$), 8.53 (s, 1H, NH), 8.98 (dd, 1H, *J= 4.1-1.7 Hz*, $H_{2'}$); ^{13}C NMR ($CDCl_3$) δ 27.2, 39.2, 62.5, 121.4, 124.2, 124.7, 125.1, 127.4, 127.6, 128.0, 128.4, 128.8, 129.8, 130.5, 130.5, 134.5, 135.4, 136.7, 138.4, 142.4, 150.0, 151.1, 176.9. Anal. Calcd for $C_{27}H_{26}N_2O_2$ (410.52): C, 79.00; H, 6.38; N, 6.82. Found: C, 78.81; H, 6.21; N, 6.56.

7-Bromo-5-phenyl-8-methoxyquinoline (8). 5,7-Dibromo-8-methoxyquinoline (**7**) (1.0 mmol) and phenylboric acid (1.2 mmol) were added to a solution of sodium carbonate (2M, 1.0 mL) and methanol (0.5 mL) in deoxygenated toluene (10 mL). The resulting mixture was stirred for 0.5 h under an argon atmosphere. Tetrakis(triphenylphosphine)palladium(0) (35 mg, 0.03 mmol) was added and this mixture was refluxed for 3 d. Cooling, filtration, extraction with toluene, drying over $MgSO_4$, and solvent removal afforded a crude product which was purified by preparative flash chromatography on silica (CH_2Cl_2 as eluent). The procedure gave 94% of **8** (oil): ^1H NMR ($CDCl_3$) δ 4.33 (s, 3H, OCH_3), 7.47 (dd, 1H, *J= 8.4-3.6 Hz*, H_3), 7.55 (m, 5H, C_6H_5), 7.68 (s, 1H, H_6), 8.19 (dd, 1H, *J= 8.4-1.8 Hz*, H_4), 8.97 (dd, 1H, *J= 3.6-1.8 Hz*, H_2); ^{13}C NMR ($CDCl_3$) δ 61.9, 116.0, 121.2, 127.1, 127.8, 128.4, 129.7, 129.8, 134.1, 136.8, 137.5, 143.2, 149.9, 152.6; IR (neat): 3060, 3030, 3000, 2930, 1735, 1580, 1500, 1460, 1390, 1370, 1085. Anal. Calcd for $C_{16}H_{12}BrNO$ (314.19): C, 61.17; H, 3.85; N, 4.46. Found: C, 60.99; H, 3.9; N, 4.14.

General procedure for the hydrolysis of pivalamides (2a-b) and (9). The required pivaloylamino compound (1.0 mmol) was added to a 20% solution of sulfuric acid (10 mL) and refluxed for 6 h. The resulting cold solution was poured into a mixture of ice and concentrated ammonia. Extraction with ethyl acetate, drying over $MgSO_4$ and solvent removal afforded a crude product which was purified by preparative flash chromatography on silica (eluent).

7-(2-Aminophenyl)-8-methoxyquinoline (3a). The foregoing procedure applied to **2a** gave 70% (CH_2Cl_2/Et_2O: 4/1) of **3a**: mp 194°C; ^1H NMR ($CDCl_3$) 3.86 (s, 3H, OCH_3), 4.95 (s, 2H, NH_2), 6.9 (m, 4H, $H_{3'\text{-}4'\text{-}5'\text{-}6'}$), 7.43 (dd, 1H, *J= 8.3-4.2 Hz*, H_3), 7.48 (d, 1H, *J= 8.5 Hz*, H_5), 7.63 (d, 1H, *J= 8.5 Hz*, H_6), 8.18 (dd, 1H, *J= 8.3-1.7 Hz*, H_4), 8.99 (dd, 1H, *J= 4.2-1.7 Hz*, H_2); ^{13}C NMR ($CDCl_3$) δ 62.1, 116.1, 118.4, 121.1, 123.3, 124.5, 128.7, 129.0, 130.3, 130.9, 131.5, 135.9, 142.8, 144.5, 149.9, 152.9; IR (KBr): 3450, 3302, 1628, 1487, 1466, 1361, 1101. Anal. Calcd for $C_{16}H_{14}N_2O$ (250.30): C, 76.78; H, 5.64; N, 11.19. Found: C, 76.67; H, 5.45; N, 11.00.

7-(2-Amino-5-methoxyphenyl)-8-methoxyquinoline (3b). The foregoing procedure applied to **2b** gave 79% (CH_2Cl_2/Et_2O: 7/3) of **3b**: mp 139°C; ^1H NMR ($CDCl_3$) δ 3.73 (s, 3H, OCH_3), 3.79 (s, 2H, NH_2), 3.84 (s, 3H, OCH_3), 6.7 (m, 3H, $H_{3'\text{-}4'\text{-}6'}$), 7.36 (dd, 1H, *J= 8.3-4.2 Hz*, H_3), 7.43 (d, 1H, *J= 8.5 Hz*, H_5), 7.57 (d, 1H, *J= 8.5 Hz*, H_6), 8.11 (dd, 1H, *J= 8.3-1.6 Hz*, H_4), 8.94 (dd, 1H, *J= 4.2-1.6 Hz*, H_2); ^{13}C NMR ($CDCl_3$) δ 55.5, 62.1, 114.6, 116.0, 117.5, 121.3, 123.3, 125.6, 129.0, 130.0, 131.4, 135.9, 138.3, 142.7, 149.9, 152.4,

152.8; IR (KBr): 3345, 2931, 2825, 1609, 1492, 1460, 1356, 1230, 1098. Anal. Calcd for $C_{17}H_{16}N_2O_2$ (280.33): C, 72.84; H, 5.75; N, 9.99. Found: C, 72.76; H, 6.01; N, 9.81.

7-(2-Aminophenyl)-5-phenyl-8-methoxyquinoline (10). The foregoing procedure applied to **9** gave 91% (CH_2Cl_2/Et_2O: 9/1) of **10** (oil): ^1H NMR ($CDCl_3$) δ 3.91 (s, 3H, OCH_3), 4.08 (s, 2H, NH_2), 8.85 (m, 2H, C_6H_4), 7.2 (m, 3H, H_3, C_6H_4), 7.47 (s, 5H, C_6H_5), 7.49 (s, 1H, H_6), 8.28 (dd, 1H, *J= 8.6-1.7 Hz*, H_4), 9.01 (dd, 1H, *J= 4.1-1.7 Hz*, H_2); ^{13}C NMR ($CDCl_3$) δ 62.2, 116.3, 118.5, 121.1, 124.4, 127.2, 127.5, 128.4, 128.8, 129.9, 130.9, 130.9, 131.0, 134.5, 136.1, 138.8, 142.9, 144.6, 149.8, 152.0. Anal. Calcd for $C_{22}H_{18}N_2O$ (326.40): C, 80.96; H, 5.56; N, 8.58. Found: C, 80.73; H, 5.49; N, 8.31.

General procedure for the synthesis of azides (5a-b) and (12) from amines (3a-b) and (10). The required amino compound (2.0 mmol) was added to a solution of water (2.0 mL) and concentrated sulfuric acid (0.6 mL). The resulting solution was stirred for 10 min and ice-cooled before addition of sodium nitrite (147 mg) in water (0.4 mL). After stirring for 45 min, sodium azide (167 mg) in water (0.53 mL) was added and stirring was continued for 40 min. Treatment with $NaHCO_3$, extraction by CH_2Cl_2, drying over $MgSO_4$ and solvent removal afforded a crude product which was purified by preparative flash chromatography on silica (eluent).

7-(2-Azidophenyl)-8-methoxyquinoline (5a). The foregoing procedure applied to **3a** gave 93% (ethyl acetate) of **5a**: mp 113°C; ^1H NMR ($CDCl_3$) δ 3.91 (s, 3H, OCH_3), 7.3 (m, 6H, $H_{3\text{-}5\text{-}3'\text{-}4'\text{-}5'\text{-}6'}$), 7.56 (d, 1H, *J= 8.4 Hz*, H_6), 8.12 (dd, 1H, *J= 8.3-1.7 Hz*, H_4), 8.96 (dd, 1H, *J= 4.2-1.7 Hz*, H_2); ^{13}C NMR ($CDCl_3$) δ 61.9, 118.3, 121.2, 122.2, 124.4, 128.9, 129.2, 129.3, 129.9, 130.1, 131.6, 135.8, 137.8, 142.6, 149.5, 153.3; IR (KBr): 2934, 2126, 1488, 1459, 1357, 1302, 1094, 1066. Anal. Calcd for $C_{16}H_{12}N_4O$ (276.30): C, 69.55; H, 4.38; N, 20.28. Found: C, 69.21; H, 4.29; N, 19.96.

7-(2-Azido-5-methoxyphenyl)-8-methoxyquinoline (5b). The foregoing procedure applied to **3b** gave 81% (CH_2Cl_2/Et_2O: 7/3) of **5b** (oil): ^1H NMR ($CDCl_3$) δ 3.83 (s, 3H, OCH_3), 3.94 (s, 3H, OCH_3), 7.2 (m, 3H, $H_{3'\text{-}4'\text{-}6'}$), 7.42 (d, 1H, *J= 8.4 Hz*, H_5), 7.44 (dd, 1H, *J= 8.3-4.2 Hz*, H_3), 7.61 (d, 1H, *J= 8.4 Hz*, H_6), 8.19 (dd, 1H, *J= 8.3-1.7 Hz*, H_4), 8.98 (dd, 1H, *J= 4.2-1.7 Hz*, H_2); IR (KBr): 3379, 2929, 2834, 2359, 1600, 1579, 1484, 1460, 1357, 1105. Anal. Calcd for $C_{17}H_{14}N_4O_2$ (306.33): C, 66.66; H, 4.61; N, 18.29. Found: C, 66.41; H, 4.47; N, 18.03.

7-(2-Azidophenyl)-8-methoxy-5-phenylquinoline (12). The foregoing procedure applied to **10** gave 84% (CH_2Cl_2/Et_2O: 1/1) of **12** (oil): ^1H NMR ($CDCl_3$) δ 3.97 (s, 3H, OCH_3), 7.4 (m, 11H, $H_{3\text{-}6\text{-}3'\text{-}4'\text{-}5'\text{-}6'}$, C_6H_5), 8.28 (dd, 1H, *J= 8.5-1.7 Hz*, H_4), 8.99 (dd, 1H, *J= 4.1-1.7 Hz*, H_2). Anal. Calcd for $C_{22}H_{16}N_4O$ (352.40): C, 74.98; H, 4.58; N, 15.90. Found: C, 74.87; H, 4.47; N, 15.52.

General procedure for the synthesis of 11*H*-pyrido[2,3-a]carbazoles (4a-b) and (11) from amines (3a-b) and (10). Anhydrous pyridinium chloride (5g) at the boiling point was added to the required amine (0.35 mmol) and the mixture was refluxed for 20 min. The resulting hot solution was poured into a mixture of ice and concentrated ammonia. Extraction of the aqueous layer by ethyl acetate, drying over $MgSO_4$ and solvent removal afforded a crude product which was purified by preparative flash chromatography on silica (eluent).

11*H*-Pyrido[2,3-a]carbazole (4a). The foregoing procedure applied to **3a** gave 76% (hexane/ethyl acetate: 7/3) of **4a**: mp 172°C, lit[10] 172-173°C, lit[11] 169°C; ^{1}H NMR ($CDCl_3$) δ 7.54 (dd, 1H, *J= 8.2-4.4 Hz*, H_3), 7.3-8.22 (m, 4H, $H_{7\text{-}8\text{-}9\text{-}10}$), 7.64 (d, 1H, *J= 8.5 Hz*, H_5), 8.29 (d, 1H, *J= 8.5 Hz*, H_6), 8.39 (dd, 1H, *J= 8.2-1.6 Hz*, H_4), 9.02 (dd, 1H, *J= 4.4-1.6 Hz*, H_2), 11.78 (s, 1H, NH); ^{13}C NMR ($CDCl_3$) δ 111.5, 118.4, 119.7, 120.1, 120.4, 120.4, 121.3, 123.6, 125.4, 127.0, 135.4, 136.8, 137.4, 139.3, 148.1; IR (KBr): 3300, 1524, 1458, 1372, 1329, 1296, 1228, 1148. Anal. Calcd for $C_{15}H_{10}N_2$ (218.26): C, 82.55; H, 4.62; N, 12.83. Found: C, 82.81; H, 4.53; N, 12.81.

8-Hydroxy-11*H*-pyrido[2,3-a]carbazole (4b). The foregoing procedure applied to **3b** gave 65% (ethyl acetate) of **4b**: mp > 260°C, lit[1] > 270°C; ^{1}H NMR (DMSO-d_6) δ 6.94 (dd, 1H, *J= 8.7-2.3 Hz*, H_9), 7.5 (m, 4H, $H_{3\text{-}5\text{-}7\text{-}10}$), 8.18 (d, 1H, *J= 8.5 Hz*, H_6), 8.43 (dd, 1H, *J= 8.2-1.6 Hz*, H_4), 8.91 (dd, 1H, *J= 4.3-1.6 Hz*, H_2), 9.02 (s, 1H, OH), 10.82 (s, 1H, NH); IR (KBr): 3332, 2355, 1578, 1526, 1372, 1320, 1235, 1184. Anal. Calcd for $C_{15}H_{10}N_2O$ (234.26): C, 76.91; H, 4.30; N, 11.96. Found: C, 76.55; H, 4.07; N, 11.42.

5-Phenyl-11*H*-pyrido[2,3-a]carbazole (11). The foregoing procedure applied to **10** gave 68% (CH_2Cl_2/Et_2O: 9/1) of **11**: mp 219°C; ^{1}H NMR ($CDCl_3$) δ 7.5 (m, 10H, $H_{3\text{-}7\text{-}8\text{-}9\text{-}10}$, C_6H_5), 8.25 (s, 1H, H_6), 8.45 (dd, 1H, *J= 8.2-1.6 Hz*, H_4), 8.99 (dd, 1H, *J= 4.3-1.6 Hz*, H_2), 11.16 (s, 1H, NH); IR (KBr): 3175, 1592, 1560, 1512, 1496, 1458, 1440, 1360, 1345. Anal. Calcd for $C_{21}H_{14}N_2$ (294.36): C, 85.69; H, 4.79; N, 9.52. Found: C, 85.43; H, 4.53; N, 9.38. Mass Calcd for $C_{21}H_{14}N_2$: 294. Found (CI): 295 (M+1).

General procedure for the synthesis of 6*H*-pyrido[3,2-b]carbazoles (6a-b) and (13) from azides (5a-b) and (12). The required azide (1.98 mmol) in 1,2-dichlorobenzenze (13 mL) was slowly heated to 170°C. Stirring was continued for 2 h at 170°C, before solvent removal under vacuum. The crude solid was purified by preparative flash chromatography on silica (eluent).

11-Methoxy-6*H*-pyrido[3,2-b]carbazole (6a). The foregoing procedure applied to **5a** gave 69% (ethyl acetate) of **6a**: mp 238°C; ^{1}H NMR ($CDCl_3$) δ 4.44 (s, 3H, OCH_3), 7.4 (m, 5H, $H_{3\text{-}5\text{-}7\text{-}8\text{-}9}$), 8.17 (s, 1H, NH), 8.24 (dd, 1H, *J= 8.5-1.7 Hz*, H_4), 8.54 (d, 1H, *J= 7.1 Hz*, H_{10}), 8.92 (dd, 1H, *J= 4.1-1.7 Hz*, H_2); ^{13}C NMR (DMSO-d_6) δ 61.6, 100.5, 110.4, 118.8, 119.1, 120.0, 121.2, 123.5, 127.4, 128.3, 135.3, 135.5, 140.3, 142.1, 145.8, 150.4; IR (KBr): 3000, 1637, 1612, 1488, 1453, 1410, 1364, 1263, 1094. Anal. Calcd for $C_{16}H_{12}N_2O$ (248.29): C, 77.40; H, 4.87; N, 11.28. Found: C, 77.17; H, 4.56; N, 11.06. Mass Calcd for $C_{16}H_{12}N_2O$: 248. Found (CI): 249 (M+1).

9,11-Dimethoxy-6*H*-pyrido[3,2-b]carbazole (6b). The foregoing procedure applied to **5b** gave 52% (CH_2Cl_2/Et_2O: 7/3) of **6b**: mp 226°C; ^{1}H NMR ($CDCl_3$) δ 4.00 (s, 3H, OCH_3), 4.44 (s, 3H, OCH_3), 7.16 (dd, 1H, *J= 8.4-2.1 Hz*, H_8), 7.34 (d, 1H, *J= 8.9 Hz*, H_7), 7.38 (dd, 1H, *J= 8.4-4.1 Hz*, H_3), 7.46 (s, 1H, H_5), 7.99 (s, 1H, NH), 8.06 (d, 1H, *J= 2.4 Hz*, H_{10}), 8.22 (dd, 1H, *J= 8.4-1.7 Hz*, H_4), 8.89 (dd, 1H, *J= 4.1-1.7 Hz*, H_2); IR (KBr): 3058, 2990, 2931, 1624, 1490, 1464, 1364, 1206, 1098. Anal. Calcd for $C_{17}H_{14}N_2O_2$ (278.31): C, 73.37; H, 5.07; N, 10.07. Found: C, 73.19; H, 4.94; N, 9.74.

11-Methoxy-5-phenyl-6*H*-pyrido[3,2-b]carbazole (13). The foregoing procedure applied to **12** gave 93% (CH_2Cl_2/ethyl acetate: 1/1) of **13**: mp 194°C; ^{1}H NMR ($CDCl_3$) δ 4.46 (s, 3H, OCH_3), 7.4 (m, 9H, $H_{3\text{-}7\text{-}8\text{-}9}$, C_6H_5), 8.15 (s, 1H, NH), 8.18 (dd, 1H, *J= 8.7-1.6 Hz*, H_4), 8.56 (d, 1H, *J= 7.6 Hz*, H_{10}), 8.91 (dd, 1H, *J=*

3.9, 1.6 Hz, H_2); ^{13}C NMR ($CDCl_3$) δ 61.9, 109.9, 113.5, 119.1, 119.9, 119.9, 122.1, 124.3, 126.6, 127.4, 127.8, 129.2, 130.7, 132.8, 135.6, 136.8, 138.2, 141.4, 146.2, 150.4; IR (KBr): 3061, 1612, 1489, 1452, 1396, 1378, 1240, 1094. Anal. Calcd for $C_{22}H_{16}N_2O$ (324.39): C, 81.46; H, 4.97; N, 8.64. Found: C, 81.19; H, 4.94; N, 8.34.

REFERENCES AND NOTES

1. Lescot, E.; Muzard, G.; Markovits, J.; Belleney, J.; Roques, B.P.; Le Pecq, J.B. *J. Med. Chem.* **1986**, *29*, 1731-1737 and references cited therein.
2. Dalton, L.K.; Demerac, S.; Teitei, T. *Aust. J. Chem.* **1969**, *22*, 185-195. Perche, J.-C.; Saint-Ruf, G.; Buu-Hoï, N.P. *J. Chem. Soc., Perkin Trans 1* **1972**, *2*, 260-262. Pelaprat, D.; Oberlin, R.; Le Guen, I.; Roques, B.P. *J. Med. Chem.* **1980**, *23*, 1330-1335. Lesca, P.; Lecointe, P.; Pelaprat, D.; Paoletti, C.; Mansuy, D. *Biochem. Pharmacol.* **1980**, *29*, 3231-3237. Léon, P.; Garbay-Jaureguiberry, C.; Barsi, M.C.; Le Pecq, J.B.; Roques, B.P. *J. Med. Chem.* **1987**, *30*, 2074-2080. Moron, J.; Huel, C.; Bisagni, E. *Heterocycles* **1993**, *36*, 2753-2764.
3. Robba, M.; Gauduchon, P.; Lancelot, J.-C.; Le Talaer, J.Y.; Rault, S. Fr. Demande FR 2,665,162 31 Jan 1992; *Chem. Abstr.* **1992**, *117*, 233999g.
4. a) Beccali, E.M.; Marchesini, A. *Tetrahedron* **1993**, *49*, 4741-4758. b) Galvez, C.; Fernandez, I.; Segura, R.; Vazquez, J. *J. Chem. Res. (S)* **1987**, 16-17. c) Dieng, C.; Thal, C.; Husson, H.-P.; Potier, P. *J. Heterocycl. Chem.* **1975**, *12*, 455-460. d) De Silva, S.O.; Snieckus, V. *Can. J. Chem.* **1974**, *52*, 1294-1306. e) Lancelot, J.-C.; Rault, S.; Robba, M.; Huy Dung, N. *Chem. Pharm. Bull.* **1987**, *35*, 425-428. f) Danieli, B.; Palmisano, G. *J. Heterocycl. Chem.* **1977**, *14*, 839-844. g) Alunni-Bistocchi, G.; Orvietani, P.; Mauffret, O.; El Antri, S.; Deroussent, A.; Jacquignon, P.C.; Fermandjian, S.; Ricci, A.; Lescot, E. *J. Chem. Soc., Perkin Trans 1* **1992**, *21*, 2935-2941. h) Perche, J.-C.; Saint-Ruf, G. *J. Heterocycl. Chem.* **1974**, *11*, 93-96. i) Minot, C.; Roland-Gosselin, P.; Thal, C. *Tetrahedron* **1980**, *36*, 1209-1214. j) Alunni-Bistocchi, G.; Orvietani, P.; Bittoun, P.; Ricci, A.; Lescot, E. *Pharmazie* **1993**, *48*, 817-820.
5. a) Miyaura, N.; Yanagi, T.; Suzuki, A. *Synth. Commun.* **1981**, *11*, 513-519. b) Widdowson, D.A.; Zhang, Y.Z. *Tetrahedron* **1986**, *42*, 2111-2116. c) Fu, J.-M.; Sharp, M.J.; Snieckus, V. *Tetrahedron Lett.* **1988**, *29*, 5459-5462.e) Godard, A.; Rocca, P.; Fourquez, J.-M.; Rovera, J.-C.; Marsais, F.; Quéguiner, G. *Tetrahedron Lett.* **1993**, *34*, 7919-7922.
6. For a convenient preparation of 8-methoxyquinolines: Trécourt, F.; Mallet, M.; Mongin, F.; Quéguiner, G. *Synthesis*, submitted.
7. a) Royer, R.; Bodo, B.; Demerseman, P.; Clavel, J.-M. *Bull. Chem. Soc. Fr.* **1971**, 2929-2933. b) Kuroki, M.; Tsunashima, Y. *J. Heterocycl. Chem.* **1981**, *18*, 709-714. c) Aiello, E.; Dattolo, G.; Cirrincione, G.; Almerico, A.M. *J. Heterocyclic Chem.* **1984**, *21*, 721-724. d) Stadlbauer, W.; Pfaffenschlager, A.; Kappe, Th. *Synthesis* **1989**, 781-783. e) Trécourt, F.; Marsais, F.; Güngor, T.; Quéguiner, G. *J. Chem. Soc., Perkin Trans 1* **1990**, 2409-2415. f) Rocca, P.; Marsais, F.; Godard, A.; Quéguiner, G. *Tetrahedron* **1993**, *49*, 49-64.
8. Mendenhall, G.D.; Smith, P.A.S. *Org. Synth.* **1973**, *5*, 829-833.
9. Coulson, D.R. *Inorganic Syntheses* **1972**, *13*, 121-124.
10. Manske, R.H.F.; Kulka, M. *Can. J. Chem.* **1952**, *30*, 712-715.
11. Clemo, E.; Felton, D.G.I. *J. Chem. Soc.* **1951**, 671-677.

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