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Substituted 8-Methoxyquinolines: Regioselective Bromination, Coupling Reactions and Cyclization to an 11H-Indolo[3,2-C]quinoline

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SUBSTITUTED 8-METHOXYQUINOLINES: REGIOSELECTIVE BROMINATION, COUPLING REACTIONS AND CYCLIZATION TO AN 11*H*-INDOLO[3,2-c]QUINOLINE.

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Abstract: 5,7-Disubstituted 8-methoxyquinolines were brominated at C-3 position. The palladium-catalyzed cross-coupling of obtained 3-bromoquinolines with phenylboric acids gave corresponding 3-arylquinolines from which a substituted 11*H*-indolo[3,2-c]quinoline could be synthesized.

Bromination at C-3 position of quinoline has been largely studied by Eisch[1] and a mechanism explaining the regioselectivity of the reaction has been suggested by Kress and Costantino.[2] Considering the smooth reaction conditions, we thought it was possible to extend this technique to substituted quinolines and we chosed easily available 8-methoxyquinolines[3] for this purpose.

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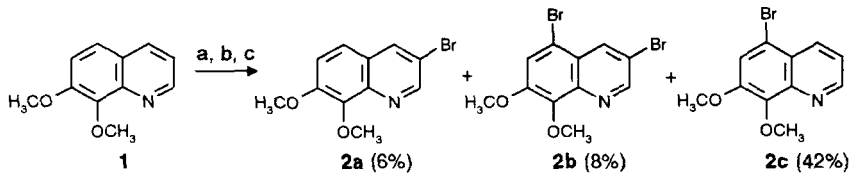
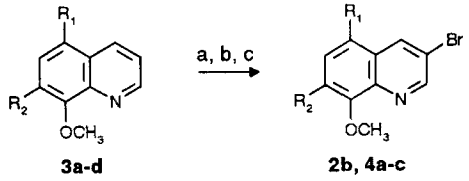


Scheme 1. a) Br_2 / CCl_4 / 20°C; b) 77°C / 1 h; c) Pyridine / 77°C / 20 h.

First tested 7,8-dimethoxyquinoline[3] (**1**) mainly underwent bromination at C-5 position together with the expected compound **2a** (Scheme 1).

Reaction was then tested on 5,7-dibromo-8-methoxyquinoline[3] (**3a**) and its 5,7-disubstituted derivatives **3b-d**, easily synthesized from **3a**: a regioselective bromine-lithium exchange reaction at C-7[3] gave **3b**, a regioselective coupling reaction at C-5[4] gave **3c** and a coupling reaction[4] from **3b** led to **3d**. In this case, bromination in the Eisch's conditions[1] occurred regioselectively at C-3 position. Competitive bromination was observed neither at C-6 nor on the C-5 phenyl ring in the case **3c-d** (Scheme 2 and Table 1).

Catalyzed coupling reaction from 3-bromoquinoline has been largely developped to prepare either 3,3'-biquinoline[5] or 3-substituted quinolines[6] but it was not extended to more substituted quinolines. Moreover, a survey of the literature revealed that few efficient general methods are available to give access to therapeutic[7] substituted 3-arylquinolines, excepted those using ring closures.[7] Consequently, we investigated the synthesis of 3-aryl-5,7-disubstituted-8-methoxyquinolines from corresponding 3-bromo derivatives, using cross-coupling reaction. Under Suzuki's conditions,[8] reaction of **4c** with (2-pivaloylaminophenyl)boric acid[9] afforded **5** with a good yield (81%) (Scheme 3).

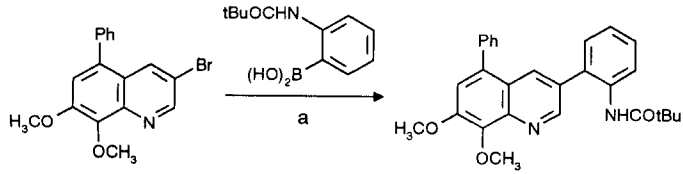


3a-d **2b, 4a-c**

Scheme 2. a) Br_2 / CCl_4 / 20°C; b) 77°C / 1 h; c) Pyridine / 77°C / 20 h.

Table 1. Bromination on 5,7-Disubstituted 8-Methoxyquinolines

Starting material	**3a**	**3b**	**3c**	**3d**
R_1	Br	Br	Ph	Ph
R_2	Br	OCH_3	Br	OCH_3
Product	**4a**	**2b**	**4b**	**4c**
Yield	73 %	55 %	58 %	68 %



4c 81% **5**

Scheme 3. a) cat. $Pd(PPh_3)_4$ / aq. K_2CO_3 / EtOH / N_2 / toluene / 95°C / 3 d

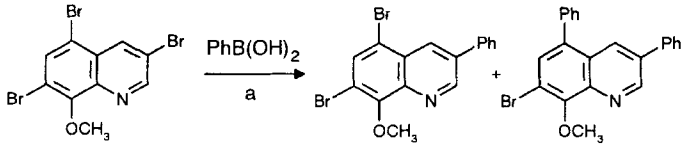
From 8-methoxy-3,5,7-tribromoquinoline (**4a**), coupling reaction tested in Suzuki's conditions[8] with 1.2 eq of commercial phenylboric acid afforded the expected substituted 3-phenylquinoline **6a** and the substituted 3,5-diphenylquinoline **6b**, which were easily separated (Scheme 4).

Products resulting from reaction at C-7 position could not be detected, so we tested the reaction on the 3,7-dibromo derivative **4b** with 1.2 eq of (2-pivaloylaminophenyl)boric acid. By using sodium carbonate-methanol pair, we obtained compound **7a**, resulting from a regioselective reaction at C-3 position. If sodium carbonate-methanol is replaced by potassium carbonate-ethanol, compound **7b** is formed; it probably results from a second palladium insertion, followed by the hydrolysis of this intermediate. When there is no arylboric acid in the reaction mixture, this is sometimes observed[10] (Scheme 5 and Table 2).

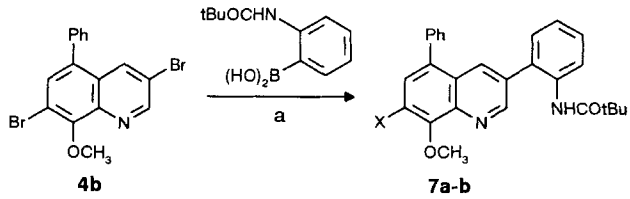
From compound **7b**, a new 11*H*-indolo[3,2-c]quinoline, which series have been shown to possess antitumor activity,[11] could be prepared. Thus, hydrolysis of **7b** with hot diluted sulphuric acid, diazotation[12] of the amino derivative **8** and reaction with sodium azide[12] afforded compound **9**. Finally, a regioselective thermocyclization[12] at C-4 position led to the substituted 11*H*-indolo[3,2-c] quinoline **10** (Scheme 6). This result is particularly interesting as far as thermal cyclization of azides is not usually regioselective in the pyridine series.[13]

EXPERIMENTAL SECTION

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 $CDCl_3$. IR spectra were taken on a Perkin Elmer FT IR 205 spectrometer, and main IR absorptions are given in



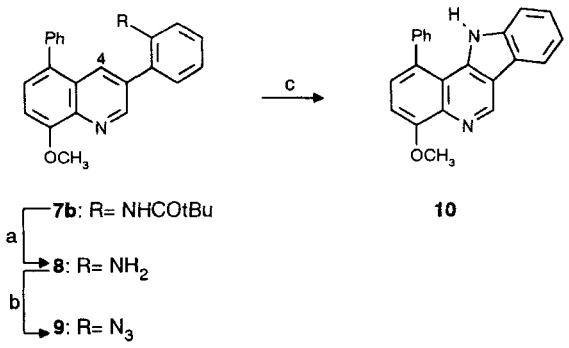
Scheme 4. a) cat. $Pd(PPh_3)_4$ / aq. Na_2CO_3 / MeOH / N_2 / toluene / 95°C / 3 d



Scheme 5. a) cat. $Pd(PPh_3)_4$ / base / alcohol / N_2 / toluene / 95°C / 3 d

Table 2.

base	alcohol	X	Yield
Na_2CO_3	MeOH	Br	**7a** (76%)
K_2CO_3	EtOH	H	**7b** (52%)



Scheme 6. a) 20% H_2SO_4, 115°C, 10 h, (90%); b) H_2SO_4, 20°C, 10 min; $NaNO_2$, 5°C, 45 min; NaN_3, 5°C, 45 min, (79%); c) 1,2-dichlorobenzene, 180°C, (73%)

cm^{-1}. Mass spectra were obtained on a JEOL D700 instrument, and elemental analyses were performed on a Carlo Erba 1106 apparatus.

General procedure for the synthesis of 3-bromoquinolines.

The required quinoline (47.3 mmol) was dispersed in tetrachloromethane (40 mL). Bromine (15.2 g, 94.6 mmol) was slowly added. The mixture was refluxed for an hour after which pyridine (7.7 mL, 94.6 mmol) was introduced. Stirring was continued at reflux temperature for 15 hours. Aqueous 2 *M* sodium hydroxyde (50 mL) was then added. Extraction with dichloromethane (3 x 50 mL), drying over magnesium sulphate and solvents removal afforded a crude product which was purified by flash chromatography on a silica gel column (eluent).

3-Bromo-7,8-dimethoxyquinoline (2a)

7,8-Dimethoxyquinoline (**1**) (8.95 g, 47.3 mmol) was allowed to react according to the procedure described above. Compound **2a** was obtained in 6 % yield (0.76 g) after chromatography (dichloromethane / ether: 95/5) as a yellow oil; ^{1}H-NMR ($CDCl_3$): 4.04 (s, 3H, OCH_3), 4.12 (s, 3H, OCH_3), 7.39 (d, J = 9.1 Hz, 1H, H_6),

7.50 (d, J = 9.1 Hz, 1H, H_5), 8.25 (d, J = 2.2 Hz, 1H, H_4), 8.90 (d, J = 2.2 Hz, 1H, H_2). Anal. Calc. for $C_{11}H_{10}BrNO_2$ (M = 268.12): C, 49.28; H, 3.76; N, 5.22. Found: C, 49.11; H, 3.62; N, 5.09.

3,5-Dibromo-7,8-dimethoxyquinoline (2b)

7,8-Dimethoxyquinoline (**1**) (8.95 g, 47.3 mmol) was allowed to react according to the procedure described above. Compound **2b** was obtained in 8 % yield (1.31 g) after chromatography (dichloromethane / ether: 95/5) as a beige solid; mp 113°C; IR ν_{max} 2930, 1600, 1580, 1475, 1440, 1355, 1310 and 1090 cm^{-1}; ^{1}H-NMR ($CDCl_3$): 4.03 (s, 3H, OCH_3), 4.09 (s, 3H, OCH_3), 7.67 (s, 1H, H_6), 8.59 (d, J = 2.0 Hz, 1H, H_4), 8.92 (d, J = 2.0 Hz, 1H, H_2); ^{13}C-NMR ($CDCl_3$): 57.1, 61.9, 114.5, 116.6, 120.4, 124.2, 135.0, 136.8, 141.7, 151.6, 151.8. Anal. Calc. for $C_{11}H_9Br_2NO_2$ (M = 347.02): C, 38.07; H, 2.61; N, 4.04. Found: C, 38.25; H, 2.75; N, 3.94.

5-Bromo-7,8-dimethoxyquinoline (2c)

7,8-Dimethoxyquinoline (**1**) (8.95 g, 47.3 mmol) was allowed to react according to the procedure described above. Compound **2c** was obtained in 42 % yield (5.33 g) after chromatography (dichloromethane / ether: 95/5) as a yellow solid; mp 103°C; IR ν_{max} 2920, 1600, 1490, 1475, 1310, 1255, 1150 and 1075 cm^{-1}; ^{1}H-NMR ($CDCl_3$): 3.66 (s, 3H, OCH_3), 3.74 (s, 3H, OCH_3), 7.33 (dd, J = 8.5-4.2 Hz, 1H, H_3), 7.61 (s, 1H, H_6), 8.36 (dd, J = 8.5-1.5 Hz, 1H, H_4), 8.89 (dd, J = 4.2-1.5 Hz, 1H, H_2); ^{13}C-NMR ($CDCl_3$): 57.0, 61.8, 115.9, 119.4, 120.2, 123.3, 135.5, 142.9, 143.5, 150.8, 151.3. Anal. Calc. for $C_{11}H_{10}BrNO_2$ (M = 268.12): C, 49.28; H, 3.76; N, 5.22. Found: C, 49.34; H, 3.73; N, 5.22.

8-Methoxy-3,5,7-tribromoquinoline (4a)

5,7-Dibromo-8-methoxyquinoline (**3a**) (15 g, 47.3 mmol) was allowed to react according to the procedure described above. Compound **4a** was obtained in 73 %

yield (13.67 g) after chromatography (dichloromethane) as a white solid; mp 151°C; IR ν_{max} 2940, 1570, 1470, 1450, 1380, 1350, 1340 and 1075 cm^{-1}; ^{1}H-NMR ($CDCl_3$): 4.18 (s, 3H, OCH_3), 8.02 (s, 1H, H_6), 8.65 (d, J = 2.4 Hz, 1H, H_4), 8.98 (d, J = 2.4 Hz, 1H, H_2); ^{13}C-NMR ($CDCl_3$): 62.3, 114.8, 116.5, 119.2, 128.9, 134.7, 137.3, 141.6, 151.7, 153.6. Anal. Calc. for $C_{10}H_6Br_3NO$ (M = 395.89): C, 30.34; H, 1.53; N, 3.54. Found: C, 30.04; H, 1.36; N, 3.55.

3,7-Dibromo-8-methoxy-5-phenylquinoline (4b)

7-Bromo-8-methoxy-5-phenylquinoline (**3c**) (14.86 g, 47.3 mmol) was allowed to react according to the procedure described above. Compound **4b** was obtained in 58 % yield (10.78 g) after chromatography (dichloromethane) as a yellow solid; mp 152°C; IR ν_{max} 2920, 1550, 1465, 1420, 1370, 1340, 1220 and 1070 cm^{-1}; ^{1}H-NMR ($CDCl_3$): 4.20 (s, 3H, OCH_3), 7.4 (m, 5H, phenyl), 7.68 (s, 1H, H_6), 8.30 (d, J = 2.2 Hz, 1H, H_4), 8.94 (d, J = 2.2 Hz, 1H, H_2); ^{13}C-NMR ($CDCl_3$): 62.1, 116.4, 118.0, 128.1, 128.3, 128.7, 129.7, 132.2, 136.1, 136.1, 137.1, 141.4, 150.9, 152.9. Anal. Calc. for $C_{16}H_{11}Br_2NO$ (M = 393.09): C, 48.89; H, 2.82; N, 3.56. Found: C, 48.99; H, 2.85; N, 3.57.

3-Bromo-7,8-dimethoxy-5-phenylquinoline (4c)

7,8-Dimethoxy-5-phenylquinoline (**3d**) (12.55 g, 47.3 mmol) was allowed to react according to the procedure described above. Compound **4c** was obtained in 68 % yield (11.07 g) after chromatography (dichloromethane / ether: 95/5) as a yellow oil; IR ν_{max} 2900, 1594, 1471, 1352, 1335, 1157, 1096 and 1066 cm^{-1}; ^{1}H-NMR ($CDCl_3$): 4.02 (s, 3H, OCH_3), 4.13 (s, 3H, OCH_3),7.31 (s, 1H, H_6), 7.4 (m, 5H, phenyl), 8.22 (d, J = 2.2 Hz, 1H, H_4), 8.88 (d, J = 2.2 Hz, 1H, H_2); ^{13}C-NMR ($CDCl_3$): 56.8, 61.8, 115.4, 117.3, 123.5, 127.9, 128.6, 129.8, 135.5, 135.7, 138.4, 141.5, 142.6, 151.0, 151.0. Anal. Calc. for $C_{17}H_{14}BrNO_2$ (M = 344.22): C, 59.32; H, 4.10; N, 4.07. Found: C, 59.02; H, 3.95; N, 3.91.

General Procedure for the coupling of 3-Bromoquinolines.

Required 5-bromoquinoline (1.0 mmol) and arylboric acid (1.2 mmol) were added to a solution of base (2 *M*, 1 mL) and alcohol (0.5 mL) in deoxygenated toluene (10 mL). The resulting mixture was stirred for 30 minutes under an argon atmosphere. Tetrakis(triphenylphosphine)palladium(0) (35 mg, 0.03 mmol) 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 flash chromatography on a silica gel column (eluent).

2,2-Dimethyl-N-(2-(7,8-dimethoxy-5-phenyl-3-quinolyl)phenyl)propanamide (5)

3-Bromo-7,8-dimethoxy-5-phenylquinoline (**4c**) (344 mg, 1.0 mmol) and (2-pivaloylaminophenyl)boric acid (265 mg, 1.2 mmol) were allowed to react according to the procedure described above and using potassium carbonate and ethanol. Compound **5** was obtained in 81 % yield (357 mg) after chromatography (hexane / ethyl acetate: 1/1) as a beige solid; mp 178°C; IR ν_{max} 3296, 2928, 1649, 1595, 1514, 1480, 1339 and 1156 cm^{-1}; ^{1}H-NMR ($CDCl_3$): 0.96 (s, 9H, $C(CH_3)_3$), 4.06 (s, 3H, OCH_3), 4.19 (s, 3H, OCH_3), 7.3 (m, 10H, phenyl, $H_{3\text{-}4\text{-}5\text{-}6'}$, NH), 8.17 (d, J = 1.4 Hz, 1H, $H_{4'}$), 8.22 (m, 1H, H_6), 8.95 (d, J = 1.4 Hz, 1H, $H_{2'}$); ^{13}C-NMR ($CDCl_3$): 27.1, 39.4, 56.7, 61.8, 116.9, 121.6, 122.0, 124.5, 127.8, 128.6, 128.9, 129.0, 129.2, 129.8, 130.3, 134.0, 135.2, 136.1, 138.5, 142.5, 142.6, 150.9, 151.2, 176.1. Anal. Calc. for $C_{28}H_{28}N_2O_3$ (M = 440.55): C, 76.34; H, 6.41; N, 6.36. Found: C, 76.63; H, 6.22; N, 6.14.

5,7-Dibromo-8-methoxy-3-phenylquinoline (6a)

8-Methoxy-3,5,7-tribromoquinoline (**4a**) (396 mg, 1.0 mmol) and phenylboric acid (146 mg, 1.2 mmol) were allowed to react according to the procedure described

above, using sodium carbonate and methanol. Compound **6a** was obtained in 40 % yield (157 mg) after chromatography (trichloromethane) as a white solid; mp 121°C; IR ν_{max} 2920, 1580, 1570, 1470, 1450, 1380 and 1355 cm^{-1}; ^{1}H-NMR ($CDCl_3$): 4.19 (s, 3H, OCH_3), 7.5 (m, 5H, phenyl), 7.96 (s, 1H, H_6), 8.55 (d, J = 2.5 Hz, 1H, H_4), 9.20 (d, J = 2.5 Hz, 1H, H_2); ^{13}C-NMR ($CDCl_3$): 62.2, 115.9, 116.4, 127.3, 127.8, 128.5, 129.2, 132.9, 133.8, 135.1, 136.7, 142.4, 150.1, 153.4. Anal. Calc. for $C_{16}H_{11}Br_2NO$ (M = 393.09): C, 48.89; H, 2.82; N, 3.56. Found: C, 48.94; H, 2.87; N, 3.37.

7-Bromo-3,5-diphenyl-8-methoxyquinoline (6b)

8-Methoxy-3,5,7-tribromoquinoline (**4a**) (396 mg, 1.0 mmol) and phenylboric acid (146 mg, 1.2 mmol) were allowed to react according to the procedure described above, using sodium carbonate and methanol. Compound **6b** was obtained in 30 % yield (117 mg) after chromatography (trichloromethane) as a yellow oil; ^{1}H-NMR ($CDCl_3$): 4.25 (s, 3H, OCH_3), 7.5 (m, 10H, phenyl), 7.70 (s, 1H, H_6), 8.34 (d, J = 2.6 Hz, 1H, H_4), 9.23 (d, J = 2.6 Hz, 1H, H_2); ^{13}C-NMR ($CDCl_3$): 62.1, 115.9, 127.1, 127.3, 127.9, 128.1, 128.6, 129.0, 129.8, 131.5, 131.9, 134.0, 137.1, 137.4, 137.8, 142.3, 149.6, 152.7. Anal. Calc. for $C_{22}H_{16}BrNO$ (M = 390.29): C, 67.71; H, 4.13; N, 3.59. Found: C, 67.52; H, 3.97; N, 3.41.

2,2-Dimethyl-N-(2-(7-bromo-8-methoxy-5-phenyl-3-quinolyl)phenyl) propanamide (7a)

3,7-Dibromo-8-methoxy-5-phenylquinoline (**4b**) (393 mg, 1.0 mmol) and (2-pivaloylaminophenyl)boric acid (265 mg, 1.2 mmol) were allowed to react according to the procedure described above, using sodium carbonate and methanol. Compound **7a** was obtained in 76 % yield (372 mg) after chromatography (dichloromethane / ethyl acetate: 9/1) as a beige solid; mp 192°C; IR ν_{max} 3285, 2960, 1652, 1514, 1364 and 1088 cm^{-1}; ^{1}H-NMR ($CDCl_3$): 0.99

(s, 9H, $C(CH_3)_3$), 4.25 (s, 3H, OCH_3), 7.25 (m, 3H, H_{3-4-5}), 7.4 (m, 6H, phenyl, NH), 7.72 (s, 1H, $H_{6'}$), 8.16 (m, 1H, H_6), 8.24 (d, J = 2.2 Hz, 1H, $H_{4'}$), 8.99 (d, J = 2.2 Hz, 1H, $H_{2'}$); ^{13}C-NMR ($CDCl_3$): 27.2, 39.4, 62.1, 116.6, 122.8, 124.8, 126.6, 128.1, 128.7, 129.2, 129.3, 129.7, 130.3, 131.6, 131.9, 134.2, 135.0, 136.9, 137.3, 142.4, 150.8, 152.9, 176.1. Anal. Calc. for $C_{27}H_{25}BrN_2O_2$ (M = 489.42): C, 66.26; H, 5.15; N, 5.72. Found: C, 66.18; H, 5.23; N, 5.66.

2,2-Dimethyl-N-(2-(8-methoxy-5-phenyl-3-quinolyl)phenyl)propanamide (7b)

3,7-Dibromo-8-methoxy-5-phenylquinoline (**4b**) (393 mg, 1.0 mmol) and (2-pivaloylaminophenyl)boric acid (265 mg, 1.2 mmol) were allowed to react according to the procedure described above, using potassium carbonate and ethanol. Compound **7b** was obtained in 52 % yield (213 mg) after chromatography (dichloromethane / ethyl acetate: 9/1) as a yellow oil; ^{1}H-NMR ($CDCl_3$): 0.86 (s, 9H, $C(CH_3)_3$), 4.03 (s, 3H, OCH_3), 7.2 (m, 11H, NH, phenyl, $H_{3-4-5-6'-7'}$), 8.09 (m, 1H, H_6), 8.18 (d, J = 1.7 Hz, 1H, $H_{4'}$), 8.87 (d, J = 1.7 Hz, 1H, $H_{2'}$); ^{13}C-NMR ($CDCl_3$): 27.1, 39.3, 55.9, 107.5, 122.3, 124.5, 126.6, 127.3, 128.1, 128.4, 128.9, 129.2, 129.8, 130.3, 131.6, 132.0, 133.7, 135.1, 138.6, 139.0, 149.4, 154.7, 176.1. Anal. Calc. for $C_{27}H_{26}N_2O_2$ (M = 410.52): C, 79.00; H, 6.38; N, 6.82. Found: C, 78.89; H, 6.58; N, 6.71.

3-(2-Aminophenyl)-8-methoxy-5-phenylquinoline (8)

Amide **7b** (410 mg, 1.0 mmol) 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 silica gel, using dichloromethane / ethyl acetate (4/1) as eluent. Amine **8** was obtained in 90 % yield (294 mg) as a viscous white solid; ^{1}H-NMR ($CDCl_3$): 3.72 (bs, 2H, NH_2), 4.06 (s, 3H, OCH_3),

7.1 (m, 11H, phenyl, $H_{6\text{-}7\text{-}3'\text{-}4'\text{-}5'\text{-}6'}$), 8.27 (d, J = 2.2 Hz, 1H, H_4), 9.05 (d, J = 2.2 Hz, 1H, H_2); ^{13}C-NMR ($CDCl_3$): 55.6, 106.7, 115.4, 118.3, 123.2, 126.8, 126.9, 127.4, 128.1, 128.9, 129.6, 130.3, 131.8, 132.7, 133.2, 138.5, 138.7, 143.6, 149.5, 154.3. Anal. Calc. for $C_{22}H_{18}N_2O$ (M = 326.40): C, 80.96; H, 5.56; N, 8.58. Found: C, 80.80; H, 5.42; N, 8.61.

3-(2-Azidophenyl)-8-methoxy-5-phenylquinoline (9)

Amine **8** (326 mg, 1.0 mmol) was added to a solution of water (1 mL) and concentrated sulphuric acid (0.3 mL). The resulting solution was stirred for 10 minutes and ice-cooled before addition of sodium nitrite (74 mg, 1.05 mmol) in water (0.4 mL). After stirring for 45 minutes, sodium azide (84 mg, 1.2 mmol) in water (0.5 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 silica gel, using dichloromethane / ethyl acetate (7/3) as eluent. Azide **9** was obtained in 79 % yield (278 mg) as a yellow oil; IR ν_{max} 2962, 2126, 2090, 1576, 1489, 1321 and 1122 cm^{-1}; ^{1}H-NMR ($CDCl_3$): 4.10 (s, 3H, OCH_3), 7.3 (m, 11H, phenyl, $H_{6\text{-}7\text{-}3'\text{-}4'\text{-}5'\text{-}6'}$), 8.29 (d, J = 2.2 Hz, 1H, H_4), 9.04 (d, J = 2.2 Hz, 1H, H_2); ^{13}C-NMR ($CDCl_3$): 55.8, 107.1, 118.6, 124.9, 126.6, 127.0, 127.4, 128.2, 129.3, 129.8, 129.9, 130.9, 131.3, 132.1, 134.1, 137.4, 138.7, 139.0, 149.5, 154.5. Anal. Calc. for $C_{22}H_{16}N_4O$ (M = 352.40): C, 74.98; H, 4.58; N, 15.90. Found: C, 74.89; H, 4.54; N, 16.02.

4-Methoxy-1-phenyl-11*H*-indoloquinoline (10)

Azide **9** (352 mg, 1 mmol) in 1,2-dichlorobenzene (7 mL) was slowly heated to 180°C. Stirring was continued for 2 hours at 180°C, before solvent removal under vacuum. The crude solid was purified by preparative flash chromatography, using dichloromethane / ethyl acetate (3/2) as eluent. Compound **10** was obtained in 73

% yield (237 mg) as a white solid; mp 230°C; IR ν_{max} 1594, 1525, 1490, 1425, 1329, 1250, 1130 and 1045 cm^{-1}; ^{1}H-NMR ($CDCl_3$): 4.20 (s, 3H, OCH_3), 7.4 (m, 10H, phenyl, $H_{2\text{-}3\text{-}8\text{-}9\text{-}10}$), 7.79 (bs, 1H, NH), 8.21 (dd, J = 8.4-1.4 Hz, 1H, H_7), 9.61 (s, 1H, H_6); ^{13}C-NMR ($CDCl_3$): 56.0, 106.1, 111.1, 116.3, 119.9, 121.0, 121.3, 125.7, 127.2, 128.3, 128.9, 129.1, 129.9, 130.0, 137.6, 139.4, 141.4, 143.4, 155.6. Anal. Calc for $C_{22}H_{16}N_2O$ (324.39): C, 81.46; H, 4.97; N, 8.64. Found: C, 81.32; H, 4.91; N, 8.42. Mass Calc for $C_{22}H_{16}N_2O$: 324. Found (CI): 325 (M+1).

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