A general, versatile synthesis of 2*H*-pyrrolo[3,4-*c*]quinolines *via* tosylmethylisocyanide reaction

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Abstract
A new synthetic procedure for obtaining 2*H*-pyrrolo[3,4-*c*]quinolines is reported. The synthetic pathway utilizes TosMIC reaction to prepare appropriate nitroarylpyrrylcarboxylic esters, which on treatment with Fe-AcOH undergo reduction of nitro group with concomitant intramolecular cyclization to give title derivatives. The procedure proved general and more profitable than those previously reported in the literature. The synthesis of still unknown parent compound **4** *via* TosMIC is described. 2*H*-Pyrrolo[3,4-*c*]quinolines substituted at 1 and 3 positions have been obtained by making use of methyl-TosMIC.

Keywords: Pyrroloquinolines, TosMIC, synthesis

Introduction

The presence of heterocyclic structures in many natural and synthetic products endowed with biological activities makes account for the large amount of searches devoted in the past years to the synthesis of novel polycyclic systems containing one or more heteroatoms.

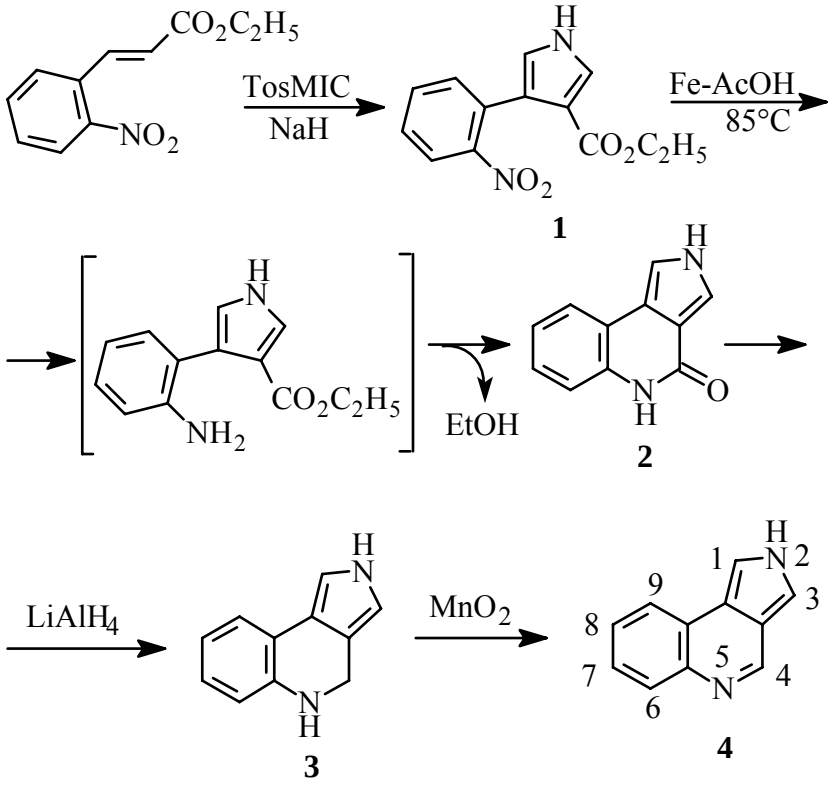
Various 5,6,6 tricyclic pyrrole annulated rings, including pyrroloquinoxalines and pyrroloquinolines, have been used as lead chemical structures for developing chemotherapeutic agents and drugs acting on Central Nervous System. Pyrrolo[1,2-*a*]quinoxaline parent nucleus and its derivatives have been thoroughly investigated,[1] whereas only few reports are available in the literature concerning the synthesis of 2*H*-pyrrolo[3,4-*c*]quinoline derivatives.[2-4]

Our decennial interest in the chemistry of pyrrole annulated heterocyclic systems[5-9]and our recent involvement in a work project on potential ligands of 5-HT receptors led us to explore new routes for obtaining 2*H*-pyrrolo[3,4-*c*]quinoline derivatives.

Results and Discussion

As a first approach, we describe a smooth two steps synthesis of 2*H*-pyrrolo[3,4-*c*]quinolin-4(5*H*)-one **2** (Scheme 1) starting from ethyl 2-nitrocinnamate, which was treated with toluene-4-sulfonylmethylisocyanide (TosMIC)[10,11] in the presence of sodium hydride, to afford pyrrole **1**.[12] Powdered iron-acetic acid reduction of the last compound gave directly the quinolinone **2** by intramolecular cyclization of the intermediate amino ester.

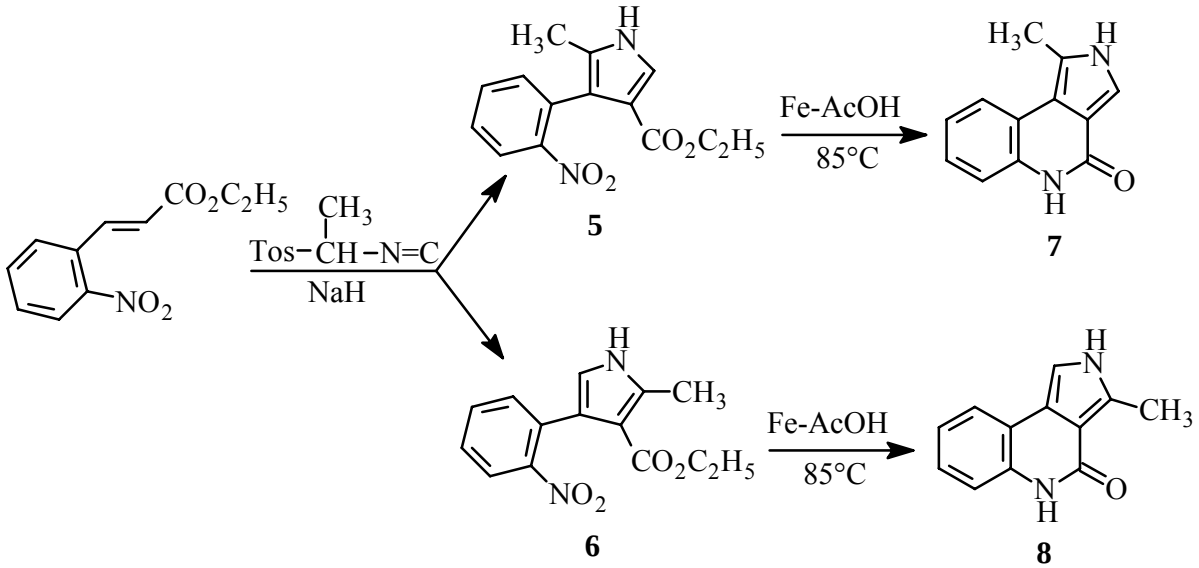
Preparation of the parent tricyclic system **4** was promptly achieved from **2** by lithium aluminum hydride reduction of carbonyl to methylene with formation of 4,5-dihydro-2*H*-pyrrolo[3,4-*c*]quinoline **3**, which partially oxidizes in presence of air to the parent heterocycle **4**. The total oxidation of **3** to pyrroloquinoline **4** was performed with activated MnO_2.



Scheme 1

The herein described synthetic approach was employed to prepare a number of novel 2*H*-pyrrolo[4,5-*c*]quinolines bearing substituents in the benzene ring as well as at positions 1, 2, 3 and 4 in the pyrrolopyridine moiety.

The use of methyl-TosMIC[13] made available 1-methyl-2*H*-pyrrolo[3,4-*c*]quinolin-4(5*H*)-one **7** (Scheme 2), together with the 3-methyl-*2H*-pyrrolo[3,4-c]quinolin-4(5*H*)-one **8**[14] counterpart, *via* the intermediates **5** and **6**,[14] respectively.



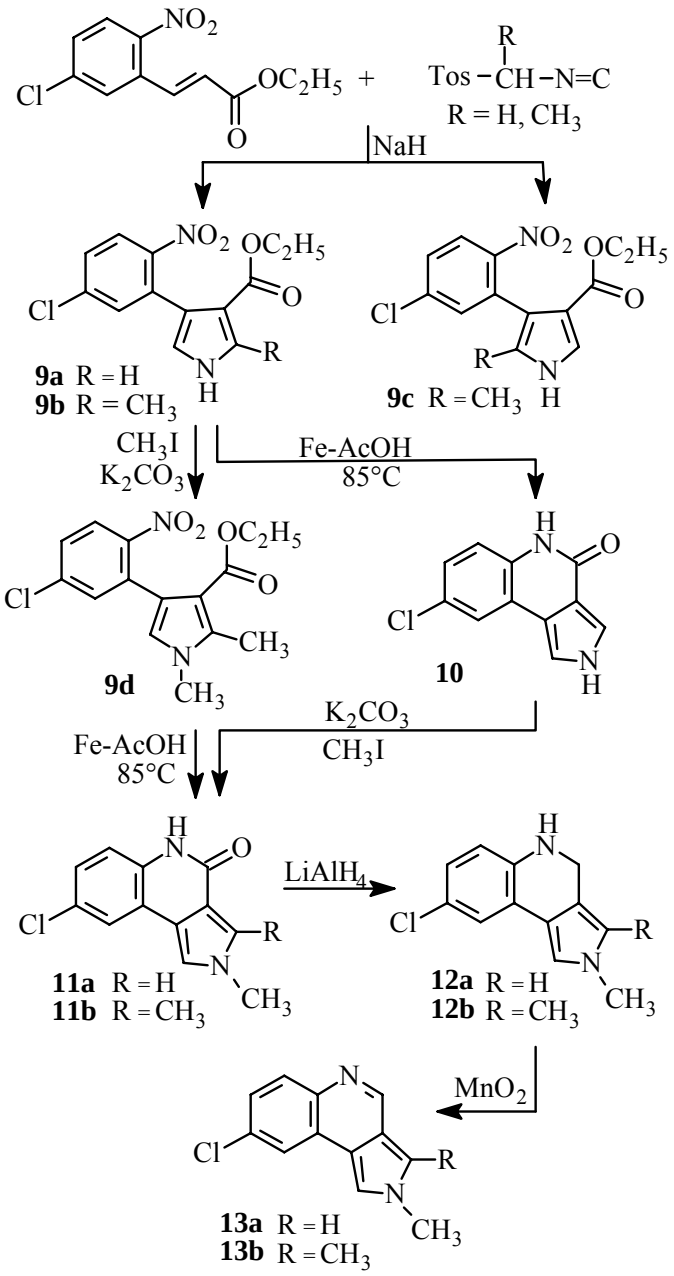
Scheme 2

Properly substituted 2-nitrocinnamates, as exemplified by the synthesis of 8-chloro-2*H*-pyrrolo[3,4-c]quinolin-4(5*H*)-one **10**, can be employed as starting materials in the synthesis of pyrroloquinolines substituted at benzene ring (Scheme 3).

Alkylation at 2-position of pyrroloquinolinone **10** with methyl iodide in the presence of anhydrous potassium carbonate, followed by lithium aluminum hydride reduction and manganese dioxide oxidation, afforded 2-substituted derivatives **11a**, **12a** and **13a**.

2,3-Substituted pyrroloquinolines **11b**, **12b** and **13b** were synthesized by a similar pathway starting from pyrrole derivative **9d**, obtained by reaction of methylTosMIC on 5-chloro-2-nitro-cinnamate, followed by alkylation with methyl iodide in alkaline medium.

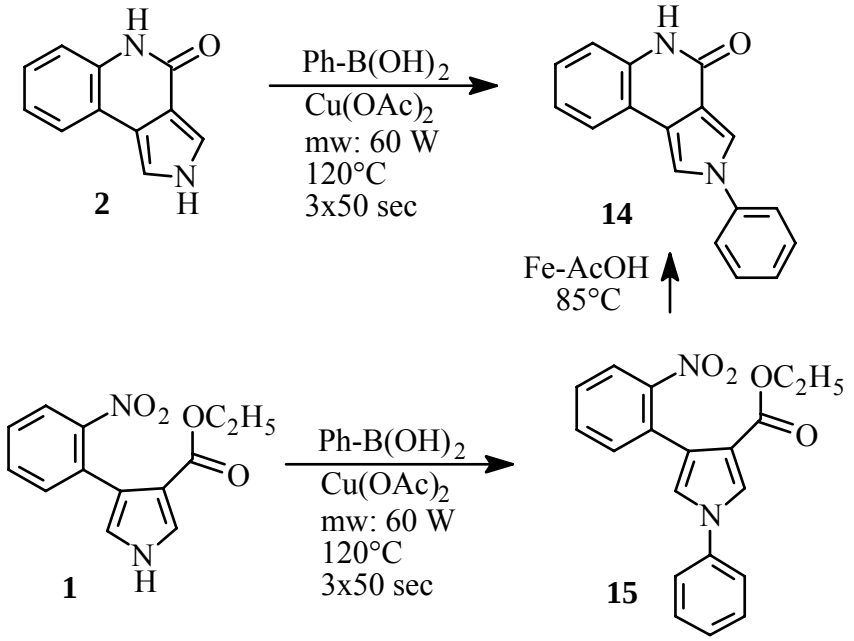
Introduction of a phenyl group in 2-position of the pyrroloquinoline system can be obtained by direct arylation of **2** with phenylboronic acid in the presence of Cu(II) in typical Suzuki reaction conditions to obtain **14**. However, the yields of the above phenylation were not satisfactory neither when the traditional conditions (21%) were used or when the microwave-assisted reactions were performed (14%).



Scheme 3

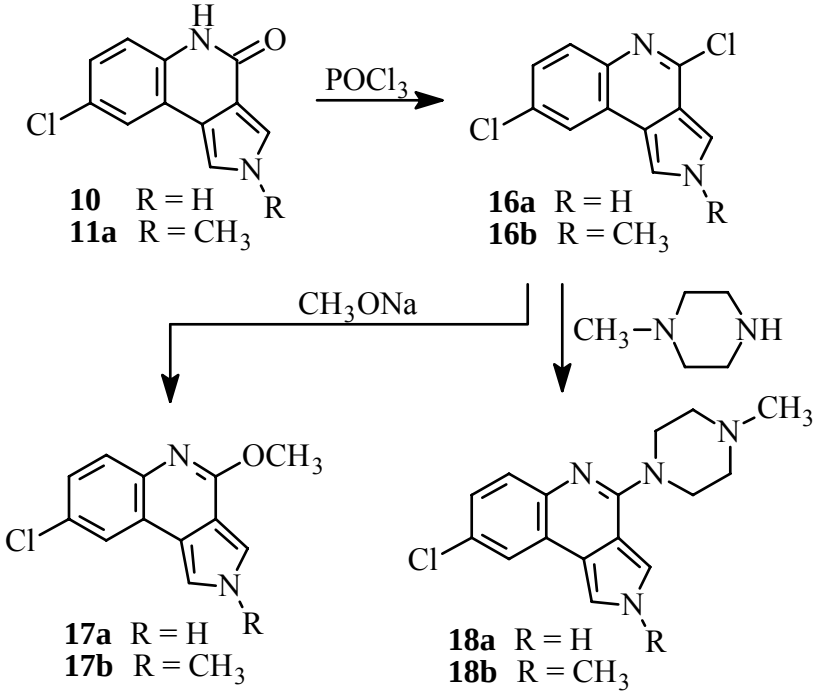
In any case, **14** was obtained with better yields by *N*-arylation of **1** with microwave heating (60 W, 120°C; 3 x 50 sec) (94% yield) followed by cyclization of 1-phenylpyrrole derivative **15** in Fe/AcOH system (69% yield) (Scheme 4).

4-Chloroderivatives **16a** and **16b**, obtained by chlorination with phosphorus oxychloride of intermediate lactams **10** and **11a**, respectively, were easily transformed into 4-methoxy and



Scheme 4

4-methyl-1-piperazinyl derivatives **17a**,**b** and **18a**,**b** by reaction with sodium methoxide and *N*-methylpiperazine, respectively (Scheme 5).



Scheme 5

In conclusion, the examples here reported, although not exhaustive, point out the utility of TosMIC and its methyl derivative in the simple and profitable new approach to 2*H*-pyrrolo[3,4-*c*]quinoline derivatives, which are undoubtedly useful for the design of new drugs acting on central nervous system.

Experimental Section

General Procedures. Melting points were determined on a Büchi 530 melting point apparatus and are uncorrected. Infrared (IR) spectra (Nujol mulls) were recorded on a Perkin-Elmer Spectrum-one spectrophotometer. ^{1}H NMR spectra were recorded at 400 MHz on a Bruker AC 400 Ultrashield spectrophotometer using tetramethylsilane (Me_4Si) as the internal reference standard. Microwave reactions were conducted using a CEM Discover Synthesis Unit. The machine consists of a continuous focused microwave power delivery system with operator-selectable power output from 0 to 300 W. Reactions were performed in glass vessels (capacity 5 mL) sealed with a septum. The pressure is controlled by a load cell connected to the vessel via a 14-gauge needle, wich penetrates just below the septum surface. The temperature of the contents of the vessel was monitored using a calibrated infrared temperature control mounted under the reaction vessel. All experiments were performed using a stirring option whereby the contents of the vessel are stirred by means of a rotating magnetic plate located below the floor of the microwave cavity and a Teflon-coated magnetic stir bar in the vessel. Column chromatographies were performed on alumina (Merck; 70-230 mesh) or silica gel (Merck; 70-230 mesh) column. All compounds were routinely checked by TLC using aluminium-baked silica gel plates (Fluka DC-Alufolien Kieselgel 60 F_{254}). Developed plates were visualized by UV light. Solvents were reagent grade and, when necessary, were purified and dried by standard methods. Concentration of solutions after reactions and extractions involved the use of rotary evaporator (Büchi) operating at a reduced pressure (ca. 20 Torr). Organic solutions were dried over anhydrous sodium sulfate. Analytical results agreed to within ±0.40% of the theoretical values. All compounds were analysed for C, H, N, and, when present Cl.

4-(2-Nitrophenyl)-1*H*-pyrrole-3-carboxylic acid ethyl ester (1). A solution of ethyl 2-nitrocinnamate (120 mmol, 26.0 g) and TosMIC (130 mmol, 25.4 g) in anhydrous DMSO-Et_2O mixture (150:300 mL) was added, by dropping, into a well-stirred suspension of sodium hydride (260 mmol, 10.4 g of 60% suspension in white oil) in anhydrous Et_2O (300 mL) under argon stream. When addition stopped, the mixture was stirred at room temperature for 25 min, then treated with water (500 mL) and extracted with ethyl acetate (3 x 600 mL). The organic extracts were collected, washed with brine (3 x 300 mL), dried, and the solvent was evaporated under reduced pressure. The residue was chromatographed on aluminum oxide column (chloroform/ethyl acetate 1:1 as eluent) to furnish pure **1** (12.8 g, 41%), mp 159-161°C (from ethanol). ^{1}H NMR ($CDCl_3$): δ 1.13 (t, 3H, CH_3), 4.12 (q, 2H, CH_2), 6.77 (m, 1H, pyrrole C5-H), 7.38-7.58 (m, 4H, pyrrole C2-H and benzene H), 8.00 (m, 1H, benzene C3-H), 8.73 (broad s, 1H,

NH). IR: ν 3290 cm^{-1} (NH), 1675 cm^{-1} (CO). Anal. Calcd. for $C_{13}H_{12}N_2O_4$ (260.25): C, 60.00; H, 4.65; N, 10.76. Found: C, 59.98; H, 4.60; N, 10.89.

2*H*-Pyrrolo[3,4-*c*]quinolin-4(5*H*)-one (2). Iron powder (120 mmol, 6.7 g) was added portionwise into a well-stirred solution of **1** (7.7 mmol, 2.0 g) in glacial acetic acid (100 mL) heated at 85°C. The mixture was stirred at the same temperature for 45 min, then the precipitate was filtered off and washed with tetrahydrofuran. The filtrate was evaporated under reduced pressure and the crude product was chromatographed on aluminum oxide column (ethyl acetate as eluent) to furnish pure **2** (1.0 g, 74%), sublimes at 280°C (from ethanol). ^{1}H NMR (DMSO-d_6): δ 7.05-7.28 (m, 3H, pyrroloquinoline C6-H, C7-H and C8-H), 7.57 and 7.64 (2 m, 2H, pyrroloquinoline C1-H and C3-H), 7.87 (dd, 1H, J_o = 7.8 Hz, pyrroloquinoline C9-H), 10.70 and 12.10 (2 broad s, 2H, NH). IR: ν 3150 cm^{-1} (NH), 1640 cm^{-1} (CO). Anal. Calcd. for $C_{11}H_8N_2O$ (184.20): C, 71.73; H, 4.38; N, 15.21. Found: C, 71.61; H, 4.33; N, 15.16.

4,5-Dihydro-2*H*-pyrrolo[3,4-*c*]quinoline (3) and 2*H*-pyrrolo[3,4-*c*]quinoline (4). A solution of **2** (2.7 mmol, 500 mg) in dry tetrahydrofuran (70 mL) was added dropwise under argon stream into a well-stirred suspension of lithium aluminium hydride (47 mmol, 1.8 g) in the same solvent (10 mL), cooled at 0°C. After the addition, the mixture was refluxed for 28 h while stirring, then cooled and carefully treated with crushed ice. The inorganic precipitate which formed was removed, and the solution was concentrated and extracted with ethyl acetate (3 x 100 mL). The collected organic extracts were washed with brine (3x50 mL), dried, and evaporated under reduced pressure. The mixture was chromatographed on aluminum oxide column (ethyl acetate as eluent) and the first eluates afforded 4,5-dihydro-2*H*-pyrrolo[3,4-*c*]quinoline (**3**) as an oil, (280 mg, 60%). ^{1}H NMR (acetone-d_6): δ 4.10 (broad s, 1H, NH), 4.43 (s, 2H, pyrroloquinoline C4-H), 6.53-6.65 (m, 3H, pyrroloquinoline H), 6.80-6.88 (m, 1H, pyrroloquinoline H), 7.06 (m, 1H, pyrroloquinoline C1-H), 7.29 (dd, 1H, J_o = 7.5 Hz, J_m = 1.5 Hz, pyrroloquinoline C9-H), 10.00 (broad s, 1H, pyrrole NH). IR: ν 3400 cm^{-1} (NH). Anal. Calcd. For $C_{11}H_{10}N_2$ (170.21): C, 77.62; H, 5.92; N, 16.46. Found: C, 77.47; H, 5.88; N, 16.39.

Further elution afforded 2*H*-pyrrolo[3,4-*c*]quinoline (**4**), (140 mg, 30%), mp 210-212°C (from toluene). ^{1}H NMR (acetone-d_6): δ 7.46-7.52 (m, 2H, pyrroloquinoline C7-H and C8-H), 7.72 and 7.87 (2 m, 2H, pyrroloquinoline C1-H and C3-H), 7.93 (m, 1H, pyrroloquinoline C6-H), 8.20 (m, 1H, pyrroloquinoline C9-H), 9.10 (s, 1H, pyrroloquinoline C4-H), 11.85 (broad s, 1H, NH). IR: ν 3200 cm^{-1} (NH). Anal. Calcd. For $C_{11}H_8N_2$ (168.20): C, 78.55; H, 4.79; N, 16.66. Found: C, 78.43; H, 4.78; N, 16.46.

2*H*-Pyrrolo[3,4-*c*]quinoline (4) by oxidation with MnO_2 of 4,5-dihydro-2*H*-pyrrolo[3,4-*c*]quinoline (3). A well stirred suspension of **3** (0.5 mmol, 90 mg) and manganese dioxide (10.6 mmol, 920 mg) in dioxane (25 mL) was heated at 80°C for 1 h. The precipitate was filtered off and washed with chloroform. The filtrate was evaporated and the crude product was chromatographed on aluminum oxide column (ethyl acetate as eluent) to furnish pure **4** (30 mg, 34%), chemico-physical and spectroscopic data were identical to those of the product obtained with the above reaction.

5-Methyl-4-(2-nitrophenyl)-1*H*-pyrrole-3-carboxylic acid ethyl ester (5) and 2-methyl-4-(2-nitrophenyl)-1*H*-pyrrole-3-carboxylic acid ethyl ester (6). A solution of ethyl 2-nitrocinnamate (10 mmol, 2.2 g) and methyl-TosMIC (12 mmol, 2.5 g) in anhydrous DMSO-Et_2O mixture (15:30 mL) was added, by dropping, into a well-stirred suspension of sodium hydride (22 mmol, 0.9 g of 60% suspension in white oil) in anhydrous Et_2O (30 mL) under argon stream. When addition stopped, the mixture was stirred at room temperature for 15 h, then treated with water (30 mL) and extracted with ethyl acetate (3 x 50 mL). The organic extracts were collected, washed with brine (3 x 30 mL), dried, and the solvent was evaporated under reduced pressure. The isomers were separated by chromatography on aluminum oxide column (chloroform as eluent). First eluates afforded 5 as an oil, (500 mg, 20%). ^{1}H NMR ($CDCl_3$): δ 1.10 (t, 3H, CH_2CH_3), 2.10 (s, 3H, CH_3), 4.10 (q, 2H, CH_2), 7.30-7.36 (m, 2H, pyrrole C2-H and benzene C6-H), 7.45 and 7.58 (2 m, 2H, J_o = 7.6 Hz, J_m = 1.8 Hz, benzene C4-H and C5-H), 8.00 (dd, 1H, J_o = 7.6 Hz, J_m = 1.8 Hz, benzene C3-H), 8.85 (broad s, 1H, NH). IR: ν 3310 cm^{-1} (NH), 1685 cm^{-1} (CO). Anal. Calcd. For $C_{14}H_{14}N_2O_4$ (274.28): C, 61.31; H, 5.14; N, 10.22. Found: C, 61.29; H, 5.15; N, 10.17.

Further elution afforded **6** (500 mg, 20%), mp 152-154°C (from benzene/cyclohexane). ^{1}H NMR ($CDCl_3$): δ 0.98 (t, 3H, CH_2CH_3), 2.48 (s, 3H, CH_3), 3.97 (q, 2H, CH_2), 6.65 (d, 1H, $J_{1,5}$ = 2.6 Hz, pyrrole C5-H), 7.37 (dd, 1H, J_o = 7.7 Hz, J_m = 2.3 Hz, benzene C6-H) 7.42 and 7.54 (2 m, 2H, J_o = 7.7 Hz, J_m = 2.3 Hz, benzene C4-H and C5-H), 7.98 (dd, 1H, J_o = 7.7 Hz, J_m = 2.3 Hz, benzene C3-H), 8.30 (broad s, 1H, NH). IR: ν 3310 cm^{-1} (NH), 1680 cm^{-1} (CO). Anal. Calcd. For $C_{14}H_{14}N_2O_4$ (274.28): C, 61.31; H, 5.14; N, 10.22. Found: C, 61.8; H, 5.26; N, 10.4.

1-Methyl-2*H*-pyrrolo[3,4-*c*]quinolin-4(5*H*)-one (7). Iron powder (750 mmol, 5.8 g) was added portionwise into a well-stirred solution of **5** (4.5 mmol, 1.2 g) in glacial acetic acid (60 mL), heated at 85°C. The mixture was stirred at the same temperature for 3 h. The inorganic compounds were filtered off and washed with tetrahydrofuran. The filtrate was evaporated under reduced pressure and the crude product was chromatographed on aluminum oxide column (ethyl acetate as eluent) to furnish pure **7** (240 mg, 27%), mp >300°C (from ethanol). ^{1}H NMR (DMSO-d_6): δ 2.54 (s, 3H, CH_3), 6.98-7.15 (m, 3H, pyrroloquinoline C6-H and C7-H and C8-H), 7.30 (d, 1H, $J_{2,3}$ = 2.9 Hz, pyrroloquinoline C3-H), 7.71 (dd, 1H, J_o = 7.9 Hz, pyrroloquinoline C9-H), 10.52 and 11.84 (2 broad s, 2H, NH). IR: ν 3200 cm^{-1} (NH), 1650 cm^{-1} (CO). Anal. Calcd. For $C_{12}H_{10}N_2O$ (198.22): C, 72.70; H, 5.09; N, 14.14. Found: C, 72.65; H, 4.98; N, 14.2.

3-Methyl-2*H*-pyrrolo[3,4-*c*]quinolin-4(5*H*)-one (8). Iron powder (225 mmol, 12.4 g) was added portionwise into a well-stirred solution of **5** (9.5 mmol, 2.6 g) in glacial acetic acid (120 mL) heated at 85°C. The suspension was stirred at the same temperature for 6 h. The inorganic compounds were filtered off and washed with tetrahydrofuran. The filtrate was evaporated under reduced pressure and the crude product was chromatographed on aluminum oxide column (ethyl acetate as eluent) to furnish pure **8** (600 mg, 30%), mp 238-240 °C (from ethanol/water). 1H NMR (DMSO-d_6): δ 2.61 (s, 3H, CH_3), 7.02 (m, 1H, pyrroloquinoline C8-H), 7.13 (m, 2H, pyrroloquinoline C6-H and C7-H), 7.39 (d, 1H, $J_{1,2}$ = 2.5 Hz, pyrroloquinoline C1-H), 7.84 (m, 1H, pyrroloquinoline C9-H), 10.47 and 11.82 (2 broad s, 2H, NH). IR: ν 3300 and

3200 cm^{-1} (NH), 1640 cm^{-1} (CO). Anal. Calcd. For $C_{12}H_{10}N_2O$ (198.22): C, 72.70; H, 5.09; N, 14.14. Found: C, 72.57; H, 5.08; N, 14.12.

4-(5-Chloro-2-nitrophenyl)-1*H*-pyrrole-3-carboxylic acid ethyl ester (9a). A solution of ethyl 2-nitrocinnamate (42 mmol, 10.8 g) and TosMIC (46 mmol, 9.0 g) in anhydrous DMSO-Et_2O mixture (50:100 mL) was added, by dropping, into a well-stirred suspension of sodium hydride (92 mmol, 3.7 g of 60% suspension in white oil) in anhydrous Et_2O (100 mL) under argon stream. When addition stopped, the mixture was stirred at room temperature for 25 min, then treated with water (200 mL) and extracted with ethyl acetate (3 x 300 mL). The organic extracts were collected, washed with brine (3 x 150 mL), dried, and the solvent was evaporated under reduced pressure. The residue was chromatographed on aluminum oxide column (chloroform/ethyl acetate 1:1 as eluent) to furnish pure **9a** (7.8 g, 63%), mp 193-195°C (from ethanol). ^{1}H NMR ($CDCl_3$): δ 1.10 (t, 3H, CH_3), 4.06 (q, 2H, CH_2), 6.73 (m, 1H, pyrrole C5-H), 7.33-7.43 (m, 3H, pyrrole C2-H and benzene C4-H and C6-H), 7.91 (d, 1H, J_o = 8.4 Hz, benzene C3-H), 8.58 (broad s, 1H, NH). IR: ν 3250 cm^{-1} (NH), 1660 cm^{-1} (CO). Anal. Calcd. For $C_{13}H_{11}ClN_2O_4$ (294.69): C, 52.98; H, 3.76; Cl, 12.03; N, 9.52. Found: C, 53.05; H, 3.77; Cl, 11.89; N, 9.52.

4-(5-Chloro-2-nitrophenyl)-2-methyl-1*H*-pyrrole-3-carboxylic acid ethyl ester (9b) and 4-(5-chloro-2-nitrophenyl)-5-methyl-1*H*-pyrrole-3-carboxylic acid ethyl ester (9c). A solution of ethyl 5-chloro-2-nitrocinnamate (31 mmol, 7.9 g) and methyl-TosMIC (34 mmol, 7.1 g) in anhydrous DMSO-Et_2O mixture (40:80 mL) was added, by dropping, to a well-stirred suspension of sodium hydride (68 mmol, 2.7 g of 60% suspension in white oil) in anhydrous Et_2O (80 mL) under argon stream. When addition stopped, the mixture was stirred at room temperature for 3 h, then treated with water (50 mL) and extracted with ethyl acetate (3 x 100 mL). The organic extracts were collected, washed with brine (3 x 50 mL), dried, and the solvent was evaporated under reduced pressure. The mixed isomers were separated by aluminum oxide column (chloroform/ethyl acetate 1:1 as eluent). First eluates afforded 4-(5-chloro-2-nitrophenyl)-2-methyl-1*H*-pyrrole-3-carboxylic acid ethyl ester (9b), (4.1 g, 42%), mp 158-160°C (from benzene). ^{1}H NMR ($CDCl_3$): δ 1.08 (t, 3H, CH_2CH_3), 2.53 (s, 3H, CH_3), 4.07 (q, 2H, CH_2), 6.61 (d, 1H, $J_{1,5}$ = 2.5 Hz, pyrrole C5-H), 7.36-7.39 (m, 2H, benzene C4-H and C6-H), 7.93 (d, 1H, J_o = 8.5 Hz, benzene C3-H), 8.44 (broad s, 1H, NH). IR: ν 3320 cm^{-1} (NH), 1665 cm^{-1} (CO). Anal. Calcd. For $C_{14}H_{13}ClN_2O_4$ (308.72): C, 54.47; H, 4.24; Cl, 11.48; N, 9.07. Found: C, 54.54; H, 4.25; Cl, 11.35; N, 9.09.

Further elution afforded 4-(5-chloro-2nitro-phenyl)-5-methyl-1*H*-pyrrole-3-carboxylic acid ethyl ester (**9c**),[15] (700 mg, 8%), mp 129-132°C (from benzene/cyclohexane). ^{1}H NMR ($CDCl_3$): δ 1.11 (t, 3H, CH_2CH_3), 2.06 (s, 3H, CH_3), 4.12 (q, 2H, CH_2), 7.25-7.35 (m, 2H, pyrrole C2-H and benzene C6-H), 7.40 (dd, 1H, J_o = 8.5 Hz, J_m = 2.0 Hz, benzene C4-H), 7.96 (d, 1H, J_o = 8.5 Hz, benzene C3-H), 8.48 (broad s, 1H, NH). IR: ν 3280 cm^{-1} (NH), 1675 cm^{-1} (CO). Anal. Calcd. For $C_{14}H_{13}ClN_2O_4$ (308.72): C, 54.47; H, 4.24; Cl, 11.48; N, 9.07. Found: C, 54.46; H, 4.11; Cl, 11.39; N, 9.13.

4-(5-Chloro-2-nitrophenyl)-1,2-dimethyl-1*H*-pyrrole-3-carboxylic acid ethyl ester (9d). A well-stirred suspension of **9b** (8.1 mmol, 2.5 g), methyl iodide (8.1 mmol, 1.2 g) and anhydrous

potassium carbonate (8.1 mmol, 1.1 g) in dry *N,N*-dimethylformamide (10 mL) was heated at 90°C for 62 h. After cooling, the mixture was treated with water (50 mL) and extracted with ethyl acetate (3 x 100 mL). The organic extracted were collected, washed with brine (3 x 50 mL), dried, and the solvent was evaporated under reduced pressure. The residue was chromatographed on aluminun oxide column (chloroform as eluent) to furnish pure **9d** (3.0 g, 79%), mp 127-129°C (from cyclohexane). ^{1}H NMR ($CDCl_3$): δ 1.05 (t, 3H, CH_2CH_3), 2.52 (s, 3H, CH_3), 3.58 (s, 3H, NCH_3), 4.03 (q, 2H, CH_2), 6.54 (s, 1H, pyrrole H), 7.33 (d, 1H, J_m = 2,3 Hz, benzene C6-H), 7.36 (dd, 1H, J_o = 8.5 Hz, J_m = 2.3 Hz, benzene C4-H), 7.91 (d, 1H, J_o = 8.5 Hz, benzene C3-H). IR: ν 1670 cm^{-1} (CO). Anal. Calcd. For $C_{15}H_{15}ClN_2O_4$ (322.75): C, 55.82; H, 4.68; Cl, 10.98; N, 8.68. Found: C, 55.67; H, 4.49; Cl, 10.75; N, 8.66.

8-Chloro-2*H*-pyrrolo[3,4-*c*]quinolin-4(5*H*)-one (10). Iron powder (100 mmol, 5.8 g) was added portionwise into a well-stirred solution of **9a** (6.8 mmol, 2.0 g) in glacial acetic acid (90 mL), heated at 85°C. The mixture was stirred at the same temperature for 2 h. The precipitate was filtered off and washed with tetrahydrofuran. The filtrate was evaporated under reduced pressure and the crude product was chromatographed on silica gel column (ethyl acetate as eluent) to furnish pure **10** (900 mg, 60%), mp >300°C (from ethanol). ^{1}H NMR (DMF-d_7): δ 7.30 (dd, 1H, J_o = 8.5 Hz, J_m = 2.3 Hz, pyrroloquinoline C7-H), 7.43 (d, 1H, J_o = 8.5 Hz, pyrroloquinoline C6-H), 7.72 and 7.90 (2 m, 2H, pyrroloquinoline C1-H and C3-H), 8.04 (d, 1H, J_m = 2.3 Hz, pyrroloquinoline C9-H), 10.80 and 12.40 (2 broad s, 2H, NH). IR: ν 3300 cm^{-1} (NH), 1680 cm^{-1} (CO). Anal. Calcd. For $C_{11}H_7ClN_2O$ (218.64): C, 60.43; H, 3.23; Cl, 16.22; N, 12.85. Found: C, 60.54; H, 3.11; Cl, 16.04; N, 12.66.

8-Chloro-2-methyl-2*H*-pyrrolo[3,4-*c*]quinolin-4(5*H*)-one (11a). A well-stirred suspension of **10** (2.3 mmol, 500 mg), methyl iodide (2.3 mmol, 300 mg) and anhydrous potassium carbonate (2.3 mmol, 300 mg) in dry *N,N*-dimethylformamide (10 mL) was heated at 90°C for 26 h. After cooling, the mixture was treated with water (50 mL) and extracted with ethyl acetate (3 x 100 mL). The organic extracted were collected, washed with brine (3 x 50 mL), dried, and the solvent was evaporated under reduced pressure. The residue was chromatographed on silica gel column (ethyl acetate/ethanol 9:1 as eluent) to furnish pure **11a** (250 mg, 45%), mp >300°C (from *N,N*-dimethylformamide/water). ^{1}H NMR (DMSO-d_6): δ 3.88 (s, 3H, CH_3), 7.22-7.24 (m, 2H, pyrroloquinoline C6-H and C7-H), 7.56 and 7.67 (2 m, 2H, pyrroloquinoline C1-H and C3-H), 7.88 (d, 1H, J_m = 1.7 Hz, pyrroloquinoline C9-H), 10.84 (broad s, 1H, NH). IR: ν 3200 cm^{-1} (NH), 1650 cm^{-1} (CO).). Anal. Calcd. For $C_{12}H_9ClN_2O$ (232.67): C, 61.95; H, 3.90; Cl, 15.24; N, 12.04. Found: C, 61.88; H, 3.71; Cl, 15.26; N, 12.00.

8-Chloro-2,3-dimethyl-2*H*-pyrrolo[3,4-*c*]quinolin-4(5*H*)-one (11b). Iron powder (73 mmol, 4.0 g) was added portionwise into a well-stirred solution of **9d** (4.7 mmol, 1.5 g) in glacial acetic acid (60 mL), heated at 85°C. The mixture was stirred at the same temperature for 30 min. The precipitate was filtered off and washed with tetrahydrofuran. The filtrate was evaporated under reduced pressure and the crude product was chromatographed on aluminum oxide column (ethyl acetate as eluent) to furnish pure **11b** (390 mg, 35%), mp >300°C (from toluene). ^{1}H NMR (DMSO-d_6): δ 2.86 (s, 3H, CH_3), 3.32 (s, 3H, NCH_3), 6.25 (s, 1H, pyrroloquinoline C1-H), 7.40 (d, 1H, J_o = 8.9 Hz, pyrroloquinoline C6-H), 7.62 (dd, 1H, J_o = 8.9 Hz, J_m = 2.4 Hz,

pyrroloquinoline C7-H), 8.56 (d, 1H, J_m = 2.4 Hz, pyrroloquinoline C9-H), 12.27 (broad s, 1H, NH). IR: ν 3340 cm^{-1} (NH), 1645 cm^{-1} (CO). Anal. Calcd. For $C_{13}H_{11}ClN_2O$ (246.70): C, 63.29; H, 4.49; Cl, 14.37; N, 11.36. Found: C, 63.40; H, 4.51; Cl, 14.21; N, 11.38.

8-Chloro-4,5-dihydro-2-methyl-2*H*-pyrrolo[3,4-*c*]quinoline (12a) and 8-chloro-2-methyl-2*H*-pyrrolo[3,4-*c*]quinoline (13a). A solution of **11a** (1.7 mmol, 400 mg) in dry tetrahydrofuran (55 mL) was added dropwise under argon stream into a well-stirred suspension of lithium aluminium hydride (8.5 mmol, 300 mg) in the same solvent (7 mL) cooled at 0°C. After adding, the mixture was refluxed for 6 h then was cooled and carefully treated with crushed ice. The inorganic precipitate which formed was removed, the solution was concentrated under reduced pressure and the residue was extracted with ethyl acetate (3 x 50 mL). The collected organic extracts were washed with brine (3 x 30 mL), dried, and evaporated under reduced pressure. The mixture was chromatographed on aluminum oxide column (ethyl acetate as eluent). First eluates afforded **12a** as an oil, (180 mg, 48%). ^{1}H NMR (acetone-d_6): δ 3.56 (s, 3H, CH_3), 4.27 (s, 2H, pyrroloquinoline C4-H), 4.60 (broad s, 1H, NH), 6.35 (m, 1H, pyrroloquinoline C3-H), 6.48 (d, 1H, J_o = 8.7 Hz, pyrroloquinoline C6-H), 6.68 (dd, 1H, J_o = 8.7 Hz, J_m = 2.4 Hz, pyrroloquinoline C7-H), 6.88 (d, 1H, $J_{1,3}$ = 2.1 Hz, pyrroloquinoline C1-H), 7.09 (d, 1H, J_m = 2.4 Hz, pyrroloquinoline C9-H). IR: ν 3380 cm^{-1} (NH). Anal. Calcd. For $C_{12}H_{11}ClN_2$ (218.69): C, 65.91; H, 5.07; Cl, 16.21; N, 12.81. Found: C, 66.04; H, 5.08; Cl, 16.04; N, 12.84.

Further elution afforded **13a** as an oil, (180 mg, 50%).^{1}H NMR (acetone-d_6): δ 3.99 (s, 3H, CH_3), 7.30 (dd, 1H, J_o = 8.9 Hz, J_m = 2.4 Hz, pyrroloquinoline C7-H), 7.48 and 7.67 (2 d, 2H, $J_{1,3}$ = 1.8 Hz, pyrroloquinoline C1-H and C3-H), 7.75 (d, 1H, J_o = 8.9 Hz, pyrroloquinoline C6-H), 7.98 (d, 1H, J_m = 2.4 Hz, pyrroloquinoline C9-H), 8.84 (s, 1H, pyrroloquinoline C4-H). Anal. Calcd. For $C_{12}H_9ClN_2$ (216.67): C, 66.52; H, 4.19; Cl, 16.36; N, 12.96. Found: C, 66.65; H, 4.36; Cl, 16.19; N, 12.81.

8-Chloro-2-methyl-2*H*-pyrrolo[3,4-*c*]quinoline (13a) by oxidation with MnO_2 of 8-chloro-4,5-dihydro-2-methyl-2*H*-pyrrolo[3,4-*c*]quinoline (12a). A mixture of 12a (0.4 mmol, 90 mg) and manganese dioxide (8.5 mmol, 740 mg) in dioxane (20 mL) was heated at 80°C for 1 h while stirring. The precipitate was filtered off and washed with chloroform. The filtrate was evaporated under reduced pressure and the crude product was chromatographed on aluminum oxide column (ethyl acetate as eluent) to furnish pure 13a (40 mg, 45%) which shared chemico-physical and spectral properties identical to those of the product obtained in the above reaction.

8-Chloro-4,5-dihydro-2,3-dimethyl-2*H*-pyrrolo[3,4-*c*]quinoline (12b) and 8-chloro-2,3-dimethyl-2*H*-pyrrolo[3,4-*c*]quinoline (13b). A solution of **11b** (1.1 mmol, 270 mg) in dry tetrahydrofuran (30 mL) was added dropwise under argon stream into a well-stirred suspension of lithium aluminium hydride (5.5 mmol, 210 mg) in the same solvent (5 mL) cooled at 0°C. After adding, the mixture was refluxed for 2 h then was cooled and carefully treated with crushed ice. The inorganic precipitate which formed was removed, the solution was concentrated under reduced pressure and the residue was extracted with ethyl acetate (3 x 50 mL). The collected organic extracts were washed with brine (3 x 30 mL), dried, and evaporated under reduced pressure. The mixture was chromatographed on aluminum oxide column (ethyl acetate as eluent). First eluates afforded **12b** as an oil, (30 mg, 12%). ^{1}H NMR (acetone-d_6): δ 2.04 (s,

3H, CH_3), 3.61 (s, 3H, NCH_3), 4.05 (broad s, 1H, NH), 4.15 (s, 2H, pyrroloquinoline C4-H), 6.54 (d, 1H, J_o = 8.6 Hz, pyrroloquinoline C6-H), 6.65 (s, 1H, pyrroloquinoline C1-H), 6.89 (dd, 1H, J_o = 8.6 Hz, J_m = 2.5 Hz, pyrroloquinoline C7-H), 7.28 (d, 1H, J_m = 2.5 Hz, pyrroloquinoline C9-H). IR: ν 3380 cm^{-1} (NH). Anal. Calcd. For $C_{13}H_{13}ClN_2$ (232.71): C, 67.10; H, 5.63; Cl, 15.23; N, 12.04. Found: C, 67.22; H, 5.55; Cl, 15.07; N, 12.27.

Further elution afforded **13b** as an oil, (40 mg, 16%).^{1}H NMR (acetone-d_6): δ 2.64 (s, 3H, CH_3), 3.96 (s, 3H, NCH_3), 7.37 (dd, 1H, J_o = 8.6 Hz, J_m = 2.4 Hz, pyrroloquinoline C7-H), 7.69 (s, 1H, pyrroloquinoline C1-H), 7.82 (d, 1H, J_o = 8.6 Hz, pyrroloquinoline C6-H), 8.03 (d, 1H, J_m = 2.4 Hz, pyrroloquinoline C9-H), 8.95 (s, 1H, pyrroloquinoline C4-H). Anal. Calcd. For $C_{13}H_{11}ClN_2$ (230.70): C, 67.68; H, 4.81; Cl, 15.37; N, 12.14. Found: C, 67.81; H, 4.86; Cl, 15.20; N, 12.06.

8-Chloro-2,3-dimethyl-2*H*-pyrrolo[3,4-*c*]quinoline (13b) by oxidation with MnO_2 of 8-chloro-4,5-dihydro-2,3-dimethyl-2*H*-pyrrolo[3,4-*c*]quinoline (12b). A mixture of 12b (0.5 mmol, 120 mg) and manganese dioxide (10.6 mmol, 920 mg) in dioxane (25 mL) was heated at 80°C for 1 h while stirring. The precipitate was filtered off and washed with chloroform. The filtrate was evaporated under reduced pressure and the crude product was chromatographed on aluminum oxide column (ethyl acetate as eluent) to furnish pure 13a (60 mg, 55%) which shared chemico-physical and spectral properties identical to those of the product obtained in the above reaction.

2-Phenyl-2*H*-pyrrolo[3,4-*c*]quinolin-4(5*H*)-one (14). Method A. To a flask was added **2** (2.7 mmol, 500 mg), cupric acetate (4.0 mmol, 740 mg), phenylboronic acid (5.4 mmol, 660 mg), and pyridine (5.4 mmol, 430 mg) in that order, followed by 1,2-dimethoxyethane (60 mL). The flask fitted with a male gas inlet and the mixture was allowed to stir at reflux, open to air, for 14 h. After cooling, the mixture was diluted with tetrahydrofuran (90 mL), filtered off, and the solvent was evaporated under reduced pressure. The residue was chromatographed on silica gel column (ethyl acetate as eluent) to furnish **14** (150 mg, 21%), mp 190-192°C (from toluene). ^{1}H NMR (acetone-d_6): δ 7.14-8.13 (m, 11H, pyrroloquinoline H and benzene H), 10.10 (broad s, 1H, NH). IR: ν 3200 cm^{-1} (NH), 1660 cm^{-1} (CO). Anal. Calcd. For $C_{17}H_{12}N_2O$ (260.29): C, 78.43; H, 4.65; N, 10.77. Found: C, 78.32; H, 4.79; N, 10.91.

Method B. In a 5-mL glass tube were placed **2** (0.54 mmol, 100 mg), cupric acetate (2.7 mmol, 490 mg), phenylboronic acid (1.9 mmol, 230 mg), NMP-pyridine mixture (0.7:0.7 mL), and a magnetic stir bar. The vessel was sealed with a septum and placed into the microwave cavity. Microwave irradiation of 60 W was used, the temperature being ramped from room temperature to 120 °C. Once 120 °C was reached, the reaction mixture was held at this temperature for 3 x 50 sec (after each cycle, the reaction vessel was cooled and cupric acetate (2.7 mmol), phenylboronic acid (1.9 mmol), and NMP-pyridine (0.7:0.7 mL) were added). The reaction vessel was opened and the mixture was diluted with tetrahydrofuran (10 mL), filtered off, and the solvent was evaporated under reduced pressure. The residue was dissolved in ethyl acetate (50 mL), washed with HCl 1N (2 x 20 mL) then with brine (3 x 20 mL), dried, and evaporated. The crude product was chromatographed on silica gel column (ethyl acetate as eluent) to furnish

14 (20 mg, 14%), chemico-physical and spectral properties were identical to those obtained for the product synthesized by Method A.

Method C. Iron powder (31 mmol, 1.8 g) was added portionwise into a well stirred solution of **15** (1.4 mmol, 500 mg) in glacial acetic acid (30 mL) heated at 85°C. The mixture was stirred at the same temperature for 4 h. The precipitate was filtered off and washed with tetrahydrofuran. The filtrate was evaporated under reduced pressure and the crude product was chromatographed on silica gel column (ethyl acetate as eluent) to furnish pure **14** (250 mg, 69%), having chemico-physical and spectral properties identical to those reported for **14** prepared by Method A.

4-(2-Nitrophenyl)-1-phenyl-1*H*-pyrrole-3-carboxylic acid ethyl ester (15). Method A. To a flask was added **1** (1.9 mmol, 500 mg), cupric acetate (2.9 mmol, 520 mg), phenylboronic acid (3.8 mmol, 460 mg), and pyridine (3.8 mmol, 300 mg) in that order, followed by 1,2-dimethoxiethane (50 mL). The flask fitted with a male gas inlet and the mixture was allow to stir at reflux, open to air, for 72 h. After cooling, the mixture was diluted with tetrahydrofuran (70 mL), filtered off, and the solvent was evaporated under reduced pressure. The residue was chromatographed on silica gel column (ethyl acetate/*n*-hexane 1:2 as eluent) to furnish **15** (140 mg, 22%) as oil. ^{1}H NMR (DMSO-d_6): δ 1.11 (t, 3H, CH_3), 4.03 (q, 2H, CH_2), 7.35-8.12 (m, 11H, pyrrole H and benzene H). IR: ν 1700 cm^{-1} (CO). Anal. Calcd. For $C_{19}H_{16}N_2O_4$ (336.35): C, 67.85; H, 4.79; N, 8.33. Found: C, 67.66; H, 4.62; N, 8.50.

Method B. In a 5-mL glass tube were placed **1** (0.38 mmol, 100 mg), cupric acetate (1.9 mmol, 350 mg), phenylboronic acid (1.4 mmol, 140 mg) NMP-pyridine mixture (0.5:0.5 mL), and a magnetic stir bar. The vessel was sealed with a septum and placed into the microwave cavity. Microwave irradiation of 60 W was used, the temperature being ramped from room temperature to 120 °C. Once 120 °C was reached, the reaction mixture was held at this temperature for 3 x 50 sec (after each cycle, the reaction vessel was cooled and cupric acetate (1.9 mmol), phenylboronic acid (1.4 mmol), and NMP-pyridine (0.5:0.5 mL) were added). The reaction vessel was opened and the mixture was diluted with tetrahydrofuran (5 mL), filtered off, and the solvent was evaporated under reduced pressure. The residue was dissolved in ethyl acetate (20 mL), washed with 1N HCl (2 x 10 mL) then with brine (3 x 10 mL), dried, and evaporated. The crude product was chromatographed on silica gel column (ethyl acetate/*n*-hexane 1:2 as eluent) to furnish pure **15** (120 mg, 94%), with the same chemico-physical and spectral properties showed by the product obtained by method A.

4,8-Dichloro-2*H*-pyrrolo[3,4-*c*]quinoline (16a). A mixture of **10** (1.8 mmol, 400 mg), *N*,*N*-dimethylaniline (0.5 mL), and phosphorus oxychloride (6 mL) was heated at reflux for 5 h. After cooling, the mixture was concentrated at reduced pressure and treated with chloroform and water. The organic layer was separated, washed with brine and dried. Removal of the solvent gave a residue which was chromatographed on silica gel (chloroform/ethyl acetate 4:1 as eluent) to afford pure **16a** (100 mg, 22 %) which was used for the next reaction without characterization because of its instability.

4,8-Dichloro-2-methyl-2*H*-pyrrolo[3,4-*c*]quinoline (16b). A mixture of **11a** (4.3 mmol, 1.0 g), triethylamine (1.1 mL), and phosphorus oxychloride (14 mL) was heated at reflux for 45 min.

After cooling and quenching with ice water, the mixture was extracted with ethyl acetate (3 x 100 mL). The organic extracted were collected, washed with saturated sodium hydrogen carbonate (3 x 50 mL), and with brine (3 x 50 mL). The organic solution was dried, and the solvent was evaporated under reduced pressure. The residue was chromatographed on silica gel column (ethyl acetate/*n*-hexane 1:2 as eluent) to furnish pure **16b** (480 mg, 42%), which was used for the next reaction without characterization because of its instability.

8-Chloro-4-methoxy-2*H*-pyrrolo[3,4-*c*]quinoline (17a). A suspension of **16a** (0.84 mmol, 200 mg) in toluene (10 mL) was added into a solution of sodium methoxide prepared by addition of sodium (2.9 mmol, 70 mg) in methanol (1 mL). The mixture was refluxed for 5 h, then cooled, treated with water, and extracted with ethyl acetate (3 x 20 mL). The collected organic extracts were washed with brine (3 x 10 mL), dried, and concentrated. The crude product was chromatographed on silica gel column (chloroform/methanol 100: 1 as eluent) to give pure **17a** (140 mg, 69%), mp 133-135°C (from toluene/cyclohexane). ^{1}H NMR (DMSO-d_6): δ 4.03 (s, 3H, CH_3), 7.33 (dd, 1H, J_o = 8.6 Hz, J_m = 2.4 Hz, pyrroloquinoline C7-H), 7.59 (d, 1H, J_o = 8.6 Hz, pyrroloquinoline C6-H), 7.52 and 7.87 (2 m, 2H, pyrroloquinoline C1-H and C3-H), 8.14 (d, 1H, J_m = 2.4 Hz, pyrroloquinoline C9-H), 12.42 (broad s, 1H, NH). IR: ν 3160 cm^{-1} (NH). Anal. Calcd. For $C_{12}H_9ClN_2O$ (232.67): C, 61.95; H, 3.90; Cl, 15.24; N, 12.04. Found: C, 62.06; H, 3.81; Cl, 15.27; N, 11.97.

8-Chloro-4-methoxy-2-methyl-2*H*-pyrrolo[3,4-*c*]quinoline (17b). A suspension of **16b** (0.75 mmol, 200 mg) in toluene (6 mL) was added into a solution of sodium methoxide prepared by addition of sodium (2.6 mmol, 60 mg) in methanol (1 mL). The mixture was refluxed for 15 h, then cooled, treated with water, and extracted with ethyl acetate (3 x 20 mL). The collected organic extracts were washed with brine (3 x 10 mL), dried, and concentrated. The crude product was chromatographed on silica gel column (ethyl acetate/*n*-hexane 1:2 as eluent) to give pure **17b** as an oil (100 mg, 54%). ^{1}H NMR ($CDCl_3$): δ 3.98 (s, 3H, NCH_3), 4.19 (s, 3H, OCH_3), 7.24-7.27 (m, 1H, pyrroloquinoline C6-H), 7.26 and 7.30 (2 d, 2H, $J_{1,3}$ = 2.0 Hz, pyrroloquinoline C1-H and C3-H), 7.33 (dd, 1H, J_o = 8.7 Hz, J_m = 2.4 Hz, pyrroloquinoline C7-H), 7.81 (d, 1H, J_m = 2.4 Hz, pyrroloquinoline C9-H). Anal. Calcd. For $C_{13}H_{11}ClN_2O$ (246.70): C, 63.29; H, 4.49; Cl, 14.37; N, 11.36. Found: C, 63.40; H, 4.51; Cl, 14.21; N, 11.38.

8-Chloro-4-(4-methylpiperazin-1-yl)-2*H*-pyrrolo[3,4-*c*]quinoline (18a). A mixture of **16a** (0.84 mmol, 200 mg) and *N*-methylpiperazine (2.5 mL) was heated at 130°C for 55 min. After cooling the solution was poured in water, and extracted with ethyl acetate (3 x 20 mL). The collected organic extracts were washed with brine (3 x 10 mL), dried, and concentrated. The residue which was obtained was chromatographed on aluminum oxide column (ethyl acetate/ethanol 9:1 as eluent) to give pure **18a** (100 mg, 41 %), mp 164-166°C (from toluene/*n*-hexane). ^{1}H NMR (DMSO-d_6): δ 2.22 (s, 3H, CH_3), 2.51 (m, 4H, piperazine C2-H and C6-H), 3.77 (m, 4H, piperazine C3-H and C5-H), 7.21 (dd, 1H, J_o = 8.7 Hz, J_m = 2.4 Hz, pyrroloquinoline C7-H), 7.42 (d, 1H, J_o = 8.7 Hz, pyrroloquinoline C6-H), 7.64 and 7.85 (2 m, 2H, pyrroloquinoline C1-H and C3-H), 8.00 (d, 1H, J_m = 2.4 Hz, pyrroloquinoline C9-H), 12.36 (broad s, 1H, NH). IR: ν 3140 cm^{-1} (NH). Anal. Calcd. For $C_{16}H_{17}ClN_4$ (300.79): C, 63.89; H, 5.70; Cl, 11.79; N, 18.63. Found: C, 63.99; H, 5.71; Cl, 11.65; N, 18.66.

8-Chloro-2-methyl-4-(4-methylpiperazin-1-yl)-2*H*-pyrrolo[3,4-*c*]quinoline (18b). A mixture of **16b** (0.7 mmol, 180 mg) and *N*-methylpiperazine (2 mL) was heated at 130°C for 1 h. After cooling the solution was poured in water, and extracted with ethyl acetate (3 x 20 mL). The collected organic extracts were washed with brine (3 x 10 mL), dried, and concentrated. The residue whiuch was obtained was chromatographed on aluminum oxide column (ethyl acetate as eluent) to give pure **18b** (180 mg, 80 %) as an oil. ^{1}H NMR ($CDCl_3$): δ 2.41 (s, 3H, piperazine N-CH_3), 2.64 (t, 4H, $J_{2,3}$ = 8.0 Hz, piperazine C2-H and C6-H), 3.90 (t, 4H, $J_{2,3}$ = 8.0 Hz, piperazine C3-H and C5-H), 3.96 (s, 3H, pyrroloquinoline N-CH_3), 7.19-7.33 (m, 3H, pyrroloquinoline C1-H, C3-H and C7-H), 7.61 (d, 1H, J_o = 8.7 Hz, pyrroloquinoline C6-H), 7.77 (d, 1H, J_m = 2.4 Hz, pyrroloquinoline C9-H). Anal. Calcd. For $C_{17}H_{19}ClN_4$ (314.82): C, 64.86; H, 6.08; Cl, 11.26; N, 17.80. Found: C, 64.94; H, 6.10; Cl, 11.13; N, 17.83.

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