

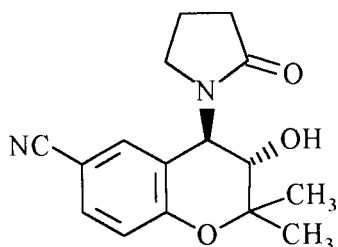
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3,4-Dihydro-2*H*-pyrano[2,3-*b*]quinolines **5a-e** and 2*H*-pyrano[2,3-*b*]quinolines **10a-c** were synthesised starting from the appropriate  $\omega$ -chloro-*n*-valeroylanilides **2a-e**. Compounds **10a-c** were transformed to analogs of the novel antihypertensive agent Cromakalim (**1**).

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Since the first synthesis of Cromakalim (**1**) [1,2], a novel potassium-channel activator antihypertensive [3] benzopyran derivative (Figure 1), numerous modifications of the benzopyran ring have been carried out [4,5].



**1**  
Figure 1

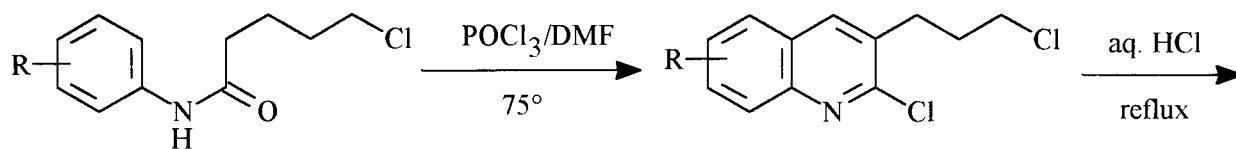
Change of the benzene moiety to pyridine was executed by Evans and Stemp [6]. These pyranopyridines, where the position of the nitrogen atom was varied, showed good blood pressure lowering activity [7]. However, substitution of the homoaromatic ring by quinoline ring has not been

reported yet.

In this paper we wish to report on the synthesis of 2*H*-pyrano[2,3-*b*]quinolines and their transformations to Cromakalim analogs. Only one example is known for preparation of 3,4-dihydro-2*H*-pyrano[2,3-*b*]quinolines [8]. This method consists of three steps: the first step is the esterification of 1,2-dihydro-2-oxo-3-quinolinepropionic acid by ethanol, followed by the reduction of the ester with lithium aluminium hydride and cyclisation of the obtained quinolinepropanol in polyphosphoric acid. Our method is a new, efficient synthesis of 3,4-dihydro-2*H*-pyrano[2,3-*b*]quinolines **5a-e** (Scheme 1).

$\omega$ -Chloro-*n*-valeroylanilides **2a-e** were transformed to 2-chloro-3-(3-chloro)propylquinolines **3a-e** according to the procedure of Meth-Cohn [9] in 60-70% yields. Treatment of propylquinolines **3a-e** with aqueous hydrochloric acid at reflux temperature gave 3,4-dihydro-2*H*-pyrano[2,3-*b*]quinolines **5a-e** in 50-80% yields except for the 3,4-dihydro-7-methoxy-2*H*-pyrano[2,3-*b*]quinoline (**5d**, 21%). The lower yield of **5d** is probably caused by the de-

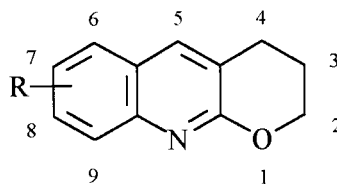
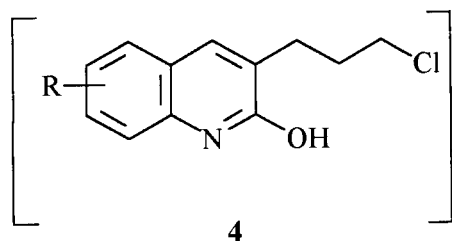
Scheme 1



**2a-e**

- a: R=H
- b: R=3-Cl
- c: R=3-Me
- d: R=4-OMe
- e: R=3-OMe

**3a-e**



**5a-e**

- a: R=H
- b: R=8-Cl
- c: R=8-Me
- d: R=7-OMe
- e: R=8-OMe

Scheme 2

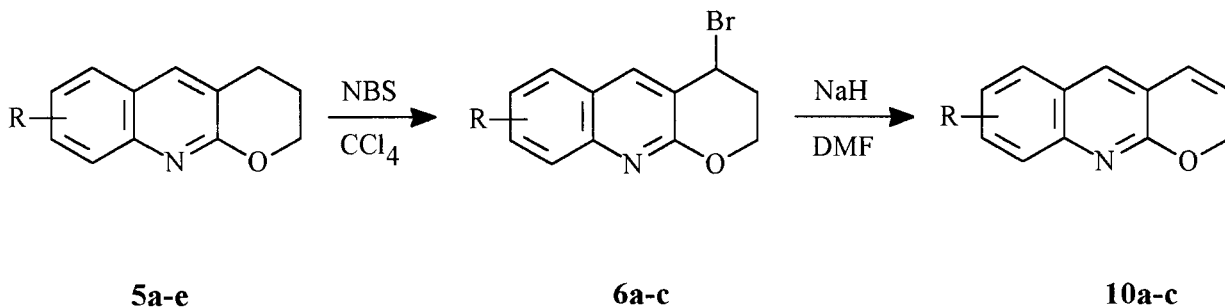
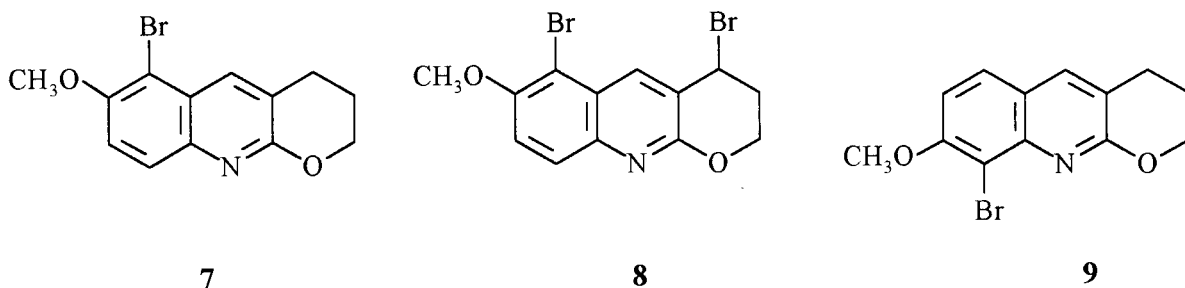


Figure 2



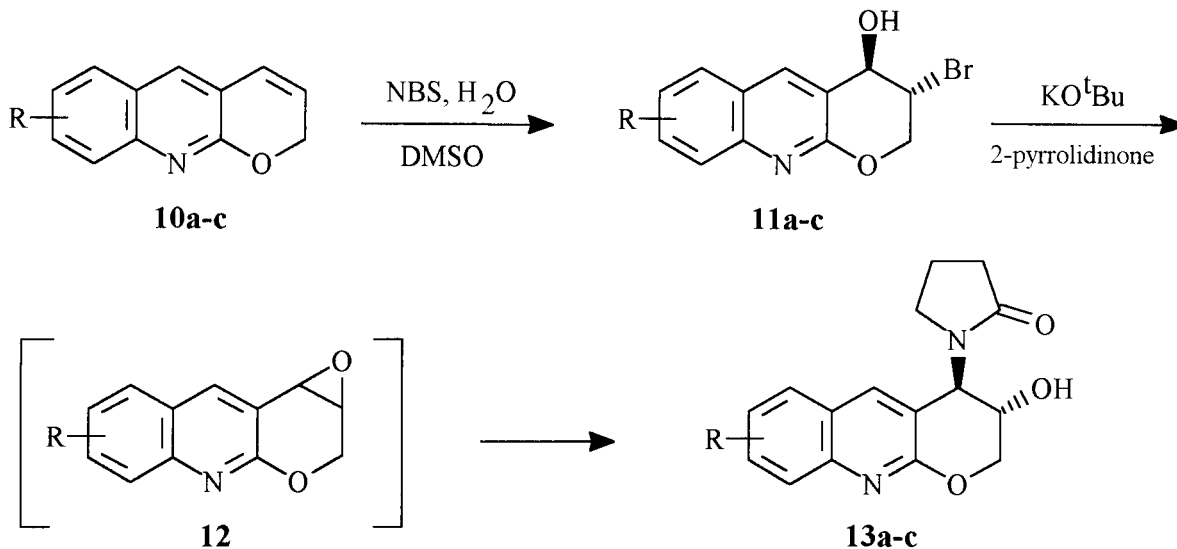
activation effect of the methoxy group. To determine the structure of the intermediate **4**, in the case of compound **3b** the reaction was interrupted after 2 hours reflux and the prepared compound was assigned as 7-chloro-2-hydroxy-3-(3-chloro)propylquinoline (**4b**). Thus, the first step of the formation of the pyranoquinoline ring is the hydrolysis of the 2-chloro group which is followed by an intramolecular ring-closure.

The synthesis of the 2*H*-pyrano[2,3-*b*]quinolines **10a-c** is shown in Scheme 2.

Bromination of the pyranoquinolines **5a-e** with *N*-bro-

mosuccinimide (NBS) was carried out in carbon tetrachloride at reflux temperature. The products **6a-c** were prepared in 50-65% yields. In the case of 7- and 8-methoxy-2*H*-pyrano[2,3-*b*]quinolines **5d** and **5e** - similarly to the 2-chloro-6- and 7-methoxyquinoline-3-carboxaldehydes [10] - the starting materials underwent bromination at positions 6 and 9 giving compounds **7** and **9**, respectively (Figure 2). In addition to the formation of compound **7**, bromination at the 4-position was also observed and the dibromo derivative **8** was isolated as a by-product. Dehy-

Scheme 3



drobromination of the 4-bromo-2*H*-pyrano[2,3-*b*]quinolines **6a-c** was performed by sodium hydride in *N,N*-dimethylformamide at room temperature. After column chromatography, 2*H*-pyrano[2,3-*b*]quinolines **10a-c** were obtained in 40-80% yields. These compounds were transformed to analogs of Cromakalim (**1**) in the usual way (Scheme 3).

*trans*-Bromohydrines **11a-c**, obtained from the reaction of pyranoquinolines **10a-c** with NBS and water, were treated with potassium *tert*-butoxide in 2-pyrrolidinone as solvent giving the compounds **13a-c** in 58-90% yields in one-pot reaction. Antihypertensive activities of these compounds are under investigation and the results will be published later.

## EXPERIMENTAL

Melting points were determined in open capillary tubes on a Büchi apparatus and are uncorrected. The <sup>1</sup>H-nmr spectra were recorded on a Varian Gemini-200 instrument at 200 MHz in deuteriochloroform unless otherwise stated. Tetramethylsilane was used as the internal standard and chemical shifts are expressed in ppm. Mass spectra were scanned on a VG Trio-2 spectrometer in EI mode at 70 eV.

### 2-Chloro-3-(3-chloro)propylquinoline **3a**.

*N,N*-dimethylformamide (12 ml, 155 mmoles) was dropped to a cold solution (0-5°) of phosphorus oxychloride (66.4 ml, 730 mmoles).  $\omega$ -Chloro-*n*-valeroylanilide (**2a**) (21.1 g, 100 mmoles) was added to this solution and the reaction mixture was stirred at 75° for 12 hours. The reaction mixture was poured into ice-water (500 ml) and the solution was extracted 3 times with chloroform (250 ml). The organic layer was dried with sodium sulfate, evaporated in vacuum and the residue was crystallized from ethanol to give **3a**, yield 16.8 g (70%), mp 74-76°; <sup>1</sup>H-nmr:  $\delta$  2.22 (m, 2H), 3.06 (t, J = 7.5 Hz, 2H), 3.61 (t, J = 7 Hz, 2H), 7.55 (m, 1H), 7.70 (m, 1H), 7.79 (m, 1H), 8.00 (m, 1H), 8.02 (s, 1H); ms: *m/z* 239 (M<sup>+</sup>, 25), 176 (100), 140 (32).

*Anal.* Calcd. for C<sub>12</sub>H<sub>11</sub>Cl<sub>2</sub>N: C, 60.02; H, 4.62; N, 5.83. Found: C, 59.88; H, 4.71; N, 5.85.

### 2,7-Dichloro-3-(3-chloro)propylquinoline (**3b**).

This compound was produced from **2b** (24.6 g, 100 mmoles) just as **3a** was produced from **2a**, yield 15.6 g (57%), mp 66-67° (ethanol); <sup>1</sup>H-nmr:  $\delta$  2.21 (m, 2H), 3.06 (t, J = 7.5 Hz, 2H), 3.62 (t, J = 7 Hz, 2H), 7.49 (dd, J<sub>1</sub> = 8.5 Hz, J<sub>2</sub> = 2 Hz, 1H), 7.72 (d, J = 8.5 Hz, 1H), 7.98 (d, J = 2 Hz, 1H), 8.01 (s, 1H); ms: *m/z* 273 (M<sup>+</sup>, 23), 210 (100), 174 (25).

*Anal.* Calcd. for C<sub>12</sub>H<sub>10</sub>Cl<sub>3</sub>N: C, 52.49; H, 3.67; N, 5.10. Found: C, 52.58; H, 3.55; N, 5.21.

### 2-Chloro-7-methyl-3-(3-chloro)propylquinoline (**3c**).

Compound **2c** (22.6 g, 100 mmoles) was subjected to the same procedure as described above for the preparation of **3a**, yield 17.0 g (67%), mp 59-60° (ethanol); <sup>1</sup>H-nmr:  $\delta$  2.20 (m, 2H), 2.56 (s, 3H), 3.02 (t, J = 7.5 Hz, 2H), 3.60 (t, J = 7 Hz, 2H), 7.38 (dd, J<sub>1</sub> = 8 Hz, J<sub>2</sub> = 1.5 Hz, 1H), 7.67 (d, J = 8 Hz, 1H), 7.78 (d, J = 1.5 Hz, 1H), 7.95 (s, 1H); ms: *m/z* 253 (M<sup>+</sup>, 27), 190 (100), 154 (17).

*Anal.* Calcd. for C<sub>13</sub>H<sub>13</sub>Cl<sub>2</sub>N: C, 61.43; H, 5.16; N, 5.51. Found: C, 61.58; H, 5.28; N, 5.40.

### 2-Chloro-6-methoxy-3-(3-chloro)propylquinoline (**3d**).

Compound **2d** (24.2 g, 100 mmoles) was treated in a manner similar to that described above for the preparation of **3a**, yield 16.5 g (61%), mp 117-119° (ethanol); <sup>1</sup>H-nmr:  $\delta$  2.21 (m, 2H), 3.03 (t, J = 7.5 Hz, 2H), 3.60 (t, J = 7 Hz, 2H), 3.92 (s, 3H), 7.04 (d, J = 2 Hz, 1H), 7.33 (dd, J<sub>1</sub> = 8.5 Hz, J<sub>2</sub> = 2 Hz, 1H), 7.89 (d, J = 8.5 Hz, 1H), 7.91 (s, 1H); ms: *m/z* 269 (M<sup>+</sup>, 72), 206 (100), 170 (12).

*Anal.* Calcd. for C<sub>13</sub>H<sub>13</sub>Cl<sub>2</sub>NO: C, 57.80; H, 4.85; N, 5.19. Found: C, 58.01; H, 4.86; N, 5.10.

### 2-Chloro-7-methoxy-3-(3-chloro)propylquinoline (**3e**).

Using the same treatment described in the foregoing preparation of **3a**, **2e** (24.2 g, 100 mmoles) gave **3e**, yield 16.8 g (62%), mp 79-81° (ethanol); <sup>1</sup>H-nmr:  $\delta$  2.19 (m, 2H), 3.02 (t, J = 7.5 Hz, 2H), 3.59 (t, J = 7 Hz, 2H), 3.91 (s, 3H), 7.19 (dd, J<sub>1</sub> = 8.5 Hz, J<sub>2</sub> = 2 Hz, 1H), 7.32 (d, J = 2 Hz, 1H), 7.66 (d, J = 8.5 Hz, 1H), 7.93 (s, 1H); ms: *m/z* 269 (M<sup>+</sup>, 25), 206 (100), 163 (8).

*Anal.* Calcd. for C<sub>13</sub>H<sub>13</sub>Cl<sub>2</sub>NO: C, 57.80; H, 4.85; N, 5.19. Found: C, 57.93; H, 4.72; N, 5.00.

### 3,4-Dihydro-2*H*-pyrano[2,3-*b*]quinoline (**5a**).

Quinoline **3a** (12.0 g, 50 mmoles), concentrated hydrochloric acid (60 ml) and water (60 ml) were heated at reflux temperature for 10 hours. Water (50 ml) was added to the reaction mixture and the pH was adjusted to 7 with concentrated ammonia solution. The solid material was filtered off, washed with water, dried and crystallized from ethanol, yield 6.3 g (68%), mp 137-139° (lit [8] mp 133-134°); <sup>1</sup>H-nmr:  $\delta$  2.06 (m, 2H), 2.95 (t, J = 7.5 Hz, 2H), 4.42 (t, J = 7 Hz, 2H), 7.32 (m, 1H), 7.55 (m, 1H), 7.62 (m, 1H), 7.75 (s, 1H), 7.81 (m, 1H); ms: *m/z* 185 (M<sup>+</sup>, 100), 170 (31), 129 (63).

*Anal.* Calcd. for C<sub>12</sub>H<sub>11</sub>NO: C, 77.81; H, 5.99; N, 7.56. Found: C, 77.70; H, 6.13; N, 7.71.

### 8-Chloro-3,4-dihydro-2*H*-pyrano[2,3-*b*]quinoline (**5b**).

Compound **3b** (13.7 g, 50 mmoles), treated for 30 hours in the same way described above for the preparation of **5a**, afforded **5b**, yield 5.9 g (54%), mp 165-168° (ethanol); <sup>1</sup>H-nmr:  $\delta$  2.06 (m, 2H), 2.94 (t, J = 7.5 Hz, 2H), 4.42 (t, J = 7 Hz, 2H), 7.25 (dd, J<sub>1</sub> = 8.5 Hz, J<sub>2</sub> = 2 Hz, 1H), 7.52 (d, J = 8.5 Hz, 1H), 7.72 (s, 1H), 7.78 (d, J = 2 Hz, 1H); ms: *m/z* 219 (M<sup>+</sup>, 100), 204 (19), 184 (21).

*Anal.* Calcd. for C<sub>12</sub>H<sub>10</sub>ClNO: C, 65.61; H, 4.59; N, 6.38. Found: C, 65.80; H, 4.53; N, 6.28.

### 3,4-Dihydro-8-methyl-2*H*-pyrano[2,3-*b*]quinoline (**5c**).

Compound **3c** (12.7 g, 50 mmoles) was subjected to the same procedure for 20 hours as described above for the preparation of **5a**, yield 7.8 g (78%), mp 126-128° (ethanol); <sup>1</sup>H-nmr:  $\delta$  2.08 (m, 2H), 2.50 (s, 3H), 2.96 (t, J = 7.5 Hz, 2H), 4.44 (t, J = 7 Hz, 2H), 7.17 (dd, J<sub>1</sub> = 8 Hz, J<sub>2</sub> = 1.5 Hz, 1H), 7.53 (d, J = 8 Hz, 1H), 7.59 (d, J = 1.5 Hz, 1H), 7.73 (s, 1H); ms: *m/z* 199 (M<sup>+</sup>, 100), 184 (33), 143 (48).

*Anal.* Calcd. for C<sub>13</sub>H<sub>13</sub>NO: C, 78.36; H, 6.58; N, 7.03. Found: C, 78.17; H, 6.67; N, 7.01.

### 3,4-Dihydro-7-methoxy-2*H*-pyrano[2,3-*b*]quinoline (**5d**).

This compound was prepared from **3d** (13.5 g, 50 mmoles) just as **5a** was prepared from **3a**, reaction time, 50 hours, yield 2.3 g (21%), mp 106-108° (ethanol); <sup>1</sup>H-nmr:  $\delta$  2.07 (m, 2H), 2.98 (t, J = 7.5 Hz, 2H), 3.88 (s, 3H), 4.42 (t, J = 7 Hz, 2H), 6.94 (d, J = 2 Hz, 1H), 7.23 (dd, J<sub>1</sub> = 8.5 Hz, J<sub>2</sub> = 2 Hz, 1H), 7.70 (s, 1H), 7.73 (d, J = 8.5 Hz, 1H); ms: *m/z* 215 (M<sup>+</sup>, 100), 200 (48), 172 (23).

*Anal.* Calcd. for C<sub>13</sub>H<sub>13</sub>NO<sub>2</sub>: C, 72.54; H, 6.09; N, 6.51. Found:

C, 72.57; H, 6.00; N, 6.67.

### 3,4-Dihydro-8-methoxy-2H-pyrano[2,3-*b*]quinoline (5e).

Using the same treatment described in the foregoing preparation of **5a**, **3e** (13.5 g, 50 mmoles) gave **5e**, reaction time, 40 hours, yield 8.1 g (74%), mp 119-121° (DMSO-ethanol); <sup>1</sup>H-nmr: δ 2.06 (m, 2H), 2.93 (t, J = 7.5 Hz, 2H), 3.88 (s, 3H), 4.42 (t, J = 7 Hz, 2H), 6.98 (dd, J<sub>1</sub> = 8.5 Hz, J<sub>2</sub> = 2 Hz, 1H), 7.17 (d, J = 2 Hz, 1H), 7.52 (d, J = 8.5 Hz, 1H), 7.71 (s, 1H); ms: m/z 215 (M<sup>+</sup>, 100), 206 (25), 200 (20).

Anal. Calcd. for C<sub>13</sub>H<sub>13</sub>NO<sub>2</sub>: C, 72.54; H, 6.09; N, 6.51. Found: C, 72.72; H, 5.92; N, 6.68.

### 7-Chloro-2-hydroxy-3-(3-chloro)propylquinoline (4b).

The previously described procedure for the preparation of **5a** was used, but the reaction was interrupted after 2 hours, yield 10.4 g (81%), mp 165-167° (ethanol); <sup>1</sup>H-nmr: δ 2.20 (m, 2H), 2.85 (t, J = 7.5 Hz, 2H), 3.63 (t, J = 7 Hz, 2H), 7.17 (dd, J<sub>1</sub> = 8.5 Hz, J<sub>2</sub> = 2 Hz, 1H), 7.41 (d, J = 2 Hz, 1H), 7.43 (d, J = 8.5 Hz, 1H), 7.64 (s, 1H), 12.45 (s, 1H); ms: m/z 255 (M<sup>+</sup>, 10), 219 (100), 193 (83).

Anal. Calcd. for C<sub>12</sub>H<sub>11</sub>Cl<sub>2</sub>NO: C, 56.27; H, 4.33; N, 5.47. Found: C, 56.03; H, 4.21; N, 5.59.

### 4-Bromo-3,4-dihydro-2H-pyrano[2,3-*b*]quinoline (6a).

Compound **5a** (3.7 g, 20 mmoles), NBS (3.8 g, 22 mmoles), benzoyl peroxide (0.25 g, 1 mmole) and carbon tetrachloride (50 ml) were refluxed for 2 hours. The hot reaction mixture was filtered and the solution was evaporated under vacuum. The residue was crystallized from benzene, yield 3.4 g (65%), mp 141-142°; <sup>1</sup>H-nmr: δ 2.38-2.70 (m, 2H), 4.62 (m, 1H), 4.88 (m, 1H), 5.64 (m, 1H), 7.39 (m, 1H), 7.64 (m, 1H), 7.71 (m, 1H), 7.84 (m, 1H), 8.12 (s, 1H); ms: m/z 263 (M<sup>+</sup>, 5), 185 (93), 154 (100).

Anal. Calcd. for C<sub>12</sub>H<sub>10</sub>BrNO: C, 54.57; H, 3.82; N, 5.30. Found: C, 54.57; H, 3.71; N, 5.16.

### 4-Bromo-8-chloro-3,4-dihydro-2H-pyrano[2,3-*b*]quinoline (6b).

Compound **5b** (4.4 g, 20 mmoles) was treated in a manner similar to that described above for the preparation of **6a**, yield 3.0 g (51%), mp 144-146° (toluene); <sup>1</sup>H-nmr: δ 2.37-2.70 (m, 2H), 4.62 (m, 1H), 4.87 (m, 1H), 5.60 (m, 1H), 7.33 (dd, J<sub>1</sub> = 8.5 Hz, J<sub>2</sub> = 2 Hz, 1H), 7.63 (d, J = 8.5 Hz, 1H), 7.81 (d, J = 2 Hz, 1H), 8.09 (s, 1H); ms: m/z 297 (M<sup>+</sup>, 2), 218 (100), 154 (49).

Anal. Calcd. for C<sub>12</sub>H<sub>9</sub>BrClNO: C, 48.27; H, 3.04; N, 4.69. Found: C, 48.43; H, 3.19; N, 4.63.

### 4-Bromo-3,4-dihydro-8-methyl-2H-pyrano[2,3-*b*]quinoline (6c).

This compound was produced from **5c** (4.0 g, 20 mmoles) just as **6a** was produced from **5a**, yield 2.8 g (51%), mp 122-124° (benzene); <sup>1</sup>H-nmr: δ 2.35-2.69 (m, 2H), 2.50 (s, 3H), 4.60 (m, 1H), 4.86 (m, 1H), 5.62 (m, 1H), 7.20 (dd, J<sub>1</sub> = 8 Hz, J<sub>2</sub> = 1.5 Hz, 1H), 7.59 (d, J = 8 Hz, 1H), 7.61 (d, J = 1.5 Hz, 1H), 8.07 (s, 1H); ms: m/z 277 (M<sup>+</sup>, 3), 196 (100), 168 (52).

Anal. Calcd. for C<sub>13</sub>H<sub>12</sub>BrNO: C, 56.14; H, 4.35; N, 5.04. Found: C, 56.30; H, 4.33; N, 5.08.

### 6-Bromo-3,4-dihydro-7-methoxy-2H-pyrano[2,3-*b*]quinoline (7) and 4,6-Dibromo-3,4-dihydro-7-methoxy-2H-pyrano[2,3-*b*]quinoline (8).

Using the same treatment described in the foregoing preparation of **6a**, **5d** (4.3 g, 20 mmoles) gave, after silica gel column chromatography (eluent:chloroform-acetone 9:1), 1.8 g of compound **7** (31%) and 1.3 g of compound **8** (17%).

Compound **7** had mp 171-173° (ethanol); <sup>1</sup>H-nmr: δ 2.10 (m, 2H), 3.05 (t, J = 7.5 Hz, 2H), 3.99 (s, 3H), 4.46 (t, J = 7 Hz, 2H), 7.33 (d, J = 8.5 Hz, 1H), 7.80 (d, J = 8.5 Hz, 1H), 8.18 (s, 1H); ms: m/z 293 (M<sup>+</sup>, 100), 278 (59), 215 (43).

Anal. Calcd. for C<sub>13</sub>H<sub>12</sub>BrNO<sub>2</sub>: C, 53.08; H, 4.11; N, 4.76. Found: C, 53.28; H, 4.06; N, 4.70.

Compound **8** had mp 156-158° dec (DMSO-ethanol); <sup>1</sup>H-nmr: δ 2.37-2.71 (m, 2H), 4.00 (s, 3H), 4.62 (m, 1H), 4.88 (m, 1H), 5.67 (m, 1H), 7.41 (d, J = 7.5 Hz, 1H), 7.80 (d, J = 7.5 Hz, 1H), 8.48 (s, 1H); ms: m/z 373 (M<sup>+</sup> + 2, 8), 293 (100), 278 (42).

Anal. Calcd. for C<sub>13</sub>H<sub>11</sub>Br<sub>2</sub>NO<sub>2</sub>: C, 41.86; H, 2.97; N, 3.76. Found: C, 41.85; H, 2.88; N, 3.89.

### 9-Bromo-3,4-dihydro-8-methoxy-2H-pyrano[2,3-*b*]quinoline (9).

Compound **5e** (4.3 g, 20 mmoles) was subjected to the same procedure as described above for the preparation of **6a**, yield 2.4 g (40%), mp 212-214° dec (DMSO-ethanol); <sup>1</sup>H-nmr (DMSO-d<sub>6</sub>): δ 1.99 (m, 2H), 2.94 (t, J = 7.5 Hz, 2H), 3.98 (s, 3H), 4.40 (t, J = 7 Hz, 2H), 7.33 (d, J = 7.5 Hz, 1H), 7.81 (d, J = 7.5 Hz, 1H), 8.02 (s, 1H); ms: m/z 293 (M<sup>+</sup>, 100), 250 (20), 199 (21).

Anal. Calcd. for C<sub>13</sub>H<sub>12</sub>BrNO<sub>2</sub>: C, 53.08; H, 4.11; N, 4.76. Found: C, 53.19; H, 4.15; N, 4.70.

### 2H-Pyrano[2,3-*b*]quinoline (10a).

Compound **6a** (2.6 g, 10 mmoles), sodium hydride (0.33 g, 11 mmoles, 80% in white oil) and *N,N*-dimethylformamide (30 ml) were stirred at room temperature for 3 hours. The reaction mixture was poured into water (30 ml) and extracted with chloroform (2 x 30 ml). The organic layer was dried with sodium sulfate and evaporated in vacuum. The residue was purified by column chromatography on silica gel (eluent:chloroform-acetone, 9:1), yield 1.4 g (79%), mp 144-146°; <sup>1</sup>H-nmr: δ 5.18 (m, 2H), 5.92 (m, 1H), 6.51 (m, 1H), 7.32 (m, 1H), 7.54 (m, 1H), 7.57 (s, 1H), 7.62 (m, 1H), 7.78 (m, 1H); ms: m/z 183 (M<sup>+</sup>, 88), 182 (100), 154 (53).

Anal. Calcd. for C<sub>12</sub>H<sub>9</sub>NO: C, 78.67; H, 4.95; N, 7.65. Found: C, 78.80; H, 4.82; N, 7.77.

### 8-Chloro-2H-pyrano[2,3-*b*]quinoline (10b).

This compound was produced from **6b** (3.0 g, 10 mmoles) just as **10a** was produced from **6a**, yield 0.8 g (38%), mp 143-145°; <sup>1</sup>H-nmr: δ 5.22 (m, 2H), 5.96 (m, 1H), 6.51 (m, 1H), 7.28 (dd, J<sub>1</sub> = 8.5 Hz, J<sub>2</sub> = 2 Hz, 1H), 7.52 (s, 1H), 7.56 (d, J = 8.5 Hz, 1H), 7.75 (d, J = 2 Hz, 1H); ms: m/z 217 (M<sup>+</sup>, 96), 216 (100), 182 (47).

Anal. Calcd. for C<sub>12</sub>H<sub>8</sub>ClNO: C, 66.22; H, 3.71; N, 6.44. Found: C, 66.13; H, 3.85; N, 6.43.

### 8-Methyl-2H-pyrano[2,3-*b*]quinoline (10c).

Compound **6c** (2.8 g, 10 mmoles), treated in the same way described above for the preparation of **10a**, afforded **10c**, yield 1.1 g (57%), mp 128-130°; <sup>1</sup>H-nmr: δ 2.47 (s, 3H), 5.18 (m, 2H), 5.89 (m, 1H), 6.50 (m, 1H), 7.15 (dd, J<sub>1</sub> = 8 Hz, J<sub>2</sub> = 1.5 Hz, 1H), 7.50 (m, 3H); ms: m/z 197 (M<sup>+</sup>, 100), 196 (97), 182 (23).

Anal. Calcd. for C<sub>13</sub>H<sub>11</sub>NO: C, 79.17; H, 5.62; N, 7.10. Found: C, 79.19; H, 5.55; N, 7.28.

### trans-3-Bromo-3,4-dihydro-4-hydroxy-2H-pyrano[2,3-*b*]quinoline (11a).

To the mixture of pyranoquinoline **10a** (1.8 g, 10 mmoles), water (0.05 ml) and DMSO (20 ml), NBS (1.8 g, 10 mmoles) was added in portions. The solution was stirred at room temperature for 2 hours. The reaction mixture was poured into ice-water (30 ml). The precipitated solid material was collected by filtration

and purified by silica gel column chromatography with benzene-methanol, 4:1 eluent, yield 2.2 g (79%), mp 188-190°; <sup>1</sup>H-nmr (DMSO-*d*<sub>6</sub>): δ 4.56 (m, 2H), 4.78 (m, 1H), 4.92 (m, 1H), 6.46-6.53 (broad, 1H), 7.43 (m, 1H), 7.70 (m, 2H), 7.92 (m, 1H), 8.38 (s, 1H); ms: *m/z* 279 (M<sup>+</sup>, 44), 200 (100), 182 (24).

*Anal.* Calcd. for C<sub>12</sub>H<sub>10</sub>BrNO<sub>2</sub>: C, 51.45; H, 3.60; N, 5.00. Found: C, 51.44; H, 3.71; N, 5.19.

*trans*-3-Bromo-8-chloro-3,4-dihydro-4-hydroxy-2*H*-pyrano[2,3-*b*]quinoline (**11b**).

Compound **10b** (2.2 g, 10 mmoles) was treated in a manner similar to that described above for the preparation of **11a**, yield: 2.5 g (79%), mp 189-191°; <sup>1</sup>H-nmr (DMSO-*d*<sub>6</sub>): δ 4.57 (m, 2H), 4.80 (m, 1H), 4.91 (m, 1H), 6.50-6.58 (broad, 1H), 7.49 (dd, J<sub>1</sub> = 8.5 Hz, J<sub>2</sub> = 2 Hz, 1H), 7.79 (d, J = 2 Hz, 1H), 7.99 (d, J = 8.5 Hz, 1H), 8.43 (s, 1H); ms: *m/z* 315 (M<sup>+</sup> + 2, 44), 234 (100), 206 (37).

*Anal.* Calcd. for C<sub>12</sub>H<sub>9</sub>ClBrNO<sub>2</sub>: C, 45.82; H, 2.88; N, 4.45. Found: C, 45.70; H, 3.02; N, 4.40.

*trans*-3-Bromo-3,4-dihydro-4-hydroxy-8-methyl-2*H*-pyrano[2,3-*b*]quinoline (**11c**).

This compound was prepared from **10c** (2.0 g, 10 mmoles) just as **11a** was prepared from **10a**, yield 2.4 g (83%), mp 183-185°; <sup>1</sup>H-nmr (DMSO-*d*<sub>6</sub>): δ 2.48 (s, 3H), 4.54 (m, 2H), 4.77 (m, 1H), 4.90 (m, 1H), 6.35-6.52 (broad, 1H), 7.28 (dd, J<sub>1</sub> = 8 Hz, J<sub>2</sub> = 1.5 Hz, 1H), 7.51 (d, J = 1.5 Hz, 1H), 7.81 (d, J = 8 Hz, 1H), 8.31 (s, 1H); ms: *m/z* 293 (M<sup>+</sup>, 42), 214 (100), 199 (73).

*Anal.* Calcd. for C<sub>13</sub>H<sub>12</sub>BrNO<sub>2</sub>: C, 53.08; H, 4.11; N, 4.76. Found: C, 53.11; H, 4.19; N, 4.66.

*trans*-3,4-Dihydro-3-hydroxy-4-(2-oxo-1-pyrrolidinyl)-2*H*-pyrano[2,3-*b*]quinoline (**13a**).

To a solution of bromohydrine **11a** (1.4 g, 5 mmoles) in 2-pyrrolidinone (15 ml), potassium *tert*-butoxide (1.2 g, 11 mmoles) was added in portions in the course of 1 hour. The reaction mixture was stirred at room temperature for 2 hours, then chloroform (50 ml) was added to it. The solution was extracted 3 times with water (25 ml), the organic layer was dried with sodium sulfate and evaporated in vacuum. The residue was purified by silica gel column chromatography with chloroform-methanol 15:1 mixture as eluent, yield 1.3 g (90%), mp 247-249°; <sup>1</sup>H-nmr: δ 1.62-1.85 (broad, 1H), 2.11 (m, 2H), 2.60 (m, 2H), 3.16 (m, 1H), 3.39 (m, 1H), 4.24 (m, 2H), 4.58 (m, 1H), 5.54 (m, 1H), 7.40 (m, 1H), 7.65 (m, 1H), 7.70 (m, 1H), 7.80 (s, 1H), 7.85 (m, 1H); ms: *m/z* 284 (M<sup>+</sup>, 6), 266 (100), 237 (59).

*Anal.* Calcd. for C<sub>16</sub>H<sub>16</sub>N<sub>2</sub>O<sub>3</sub>: C, 67.59; H, 5.67; N, 9.85. Found: C, 67.59; H, 5.63; N, 9.92.

*trans*-8-Chloro-3,4-dihydro-3-hydroxy-4-(2-oxo-1-pyrrolidinyl)-2*H*-pyrano[2,3-*b*]quinoline (**13b**).

Using the same treatment described in the foregoing preparation of **13a**, **11b** (1.6 g, 5 mmoles) gave **13b**, yield 1.3 g (80%), mp 293-295°; <sup>1</sup>H-nmr: δ 2.02 (m, 2H), 2.42 (m, 2H), 3.04 (m, 1H), 3.53 (m, 1H), 4.03-4.19 (broad, 1H), 4.23 (m, 1H), 4.39 (m, 1H), 5.19 (m, 1H), 5.70 (m, 1H), 7.44 (dd, J<sub>1</sub> = 8.5 Hz, J<sub>2</sub> = 2 Hz, 1H), 7.75 (d, J = 2 Hz, 1H), 7.96 (d, J = 8.5 Hz, 1H), 8.03 (s, 1H); ms: *m/z* 318 (M<sup>+</sup>, 2), 300 (42), 85 (100).

*Anal.* Calcd. for C<sub>16</sub>H<sub>15</sub>ClN<sub>2</sub>O<sub>3</sub>: C, 60.29; H, 4.74; N, 8.79. Found: C, 60.09; H, 4.70; N, 8.85.

*trans*-3,4-dihydro-3-hydroxy-8-methyl-4-(2-oxo-1-pyrrolidinyl)-2*H*-pyrano[2,3-*b*]quinoline (**13c**).

Compound **11c** (1.5 g, 5 mmoles) was subjected to the same procedure as described above for the preparation of **13a**, yield 0.86 g (58%), mp 291-293°; <sup>1</sup>H-nmr: δ 1.58-1.74 (broad, 1H), 2.12 (m, 1H), 2.51 (s, 3H), 2.60 (m, 2H), 3.14 (m, 1H), 3.33 (m, 2H), 4.23 (m, 2H), 4.57 (m, 1H), 5.53 (m, 1H), 7.23 (dd, J<sub>1</sub> = 8 Hz, J<sub>2</sub> = 1.5 Hz, 1H), 7.59 (d, J = 8 Hz, 1H), 7.62 (d, J = 1.5 Hz, 1H), 7.76 (s, 1H); ms: *m/z* 298 (M<sup>+</sup>, 3), 280 (100), 251 (46).

*Anal.* Calcd. for C<sub>17</sub>H<sub>18</sub>N<sub>2</sub>O<sub>3</sub>: C, 68.44; H, 6.08; N, 9.39. Found: C, 68.59; H, 6.00; N, 9.51.

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