

**SYNTHESES OF 1, 2, AND 9-METHYL DERIVATIVES  
OF 4,9-DIHYDRO-3-METHYL-4-OXO-1H(2H)-  
-PYRAZOLO[3,4-*b*]QUINOLINE AND THEIR ANTIVIRAL ACTIVITY**

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The paper describes syntheses of 4,9-dihydro-3-methyl-4-oxo-1H(2H)-pyrazolo[3,4-*b*]quinoline (*Ia*), its 1-methyl derivative (*Ib*), 2-methyl derivative (*Ia*), 9-methyl derivative (*Ic*), 1,9-dimethyl derivative (*Id*) and 2,9-dimethyl derivative (*Iib*). Sodium salts of compounds *Ia*, *Ib*, *Ic* and *Ia* were methylated with methyl iodide in dimethylformamide at room temperature, compounds *Id* and *Iib* were demethylated with pyridine hydrochloride. The compounds prepared were tested for antiviral activity *in vivo* in mice against influenza virus A2-Hongkong and the Encephalomyocarditis virus.

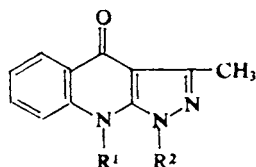
In our search for compounds with antiviral activity we also prepared 4,9-dihydro-3-methyl-4-oxo-1H(2H)-pyrazolo[3,4-*b*]quinoline (*Ia*) and its derivatives *Ib*, *Ic*, *Id* *Iia* and *Iib*.

Compound *Ia* was obtained from 3-anilino-5-methyl-4-pyrazolocarboxylic acid by ring closure effected with polyphosphoric acid. It is known from the literature<sup>1</sup> that cyclization of N-(5-methyl-3-pyrazolyl)anthranilic acid with polyphosphoric acid gives compound *IIia* as a sole product. Reaction of 3-acetyl-4-hydroxyquinoline-2(1H)-one with hydrazine hydrate also failed to yield *Ia*, the only product being 4,5-dihydro-3-methyl-4-oxo-1H-pyrazolo[4,3-*c*]quinoline<sup>2</sup>.

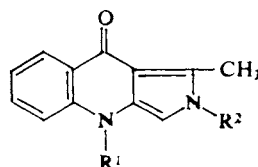
The literature describes synthesis of *Ib* by cyclization of N-(1,3-dimethyl-5-pyrazolyl)anthranilic acid with polyphosphoric acid<sup>3</sup> and by cyclization of 5-amino-4-(2-fluorobenzoyl)-1,3-dimethylpyrazole indimethyl sulphoxide<sup>4</sup>. The similar 4,9-dihydro-6-chloro-1-methyl-4-oxo-1H-pyrazolo[3,4-*b*]quinoline is the main product of pyrolysis of 5-chloro-3-(1-methyl-5-pyrazolyl)-2,1-benzisoxazole<sup>5</sup>. In our work we found it advantageous to prepare *Ib* from the known 4-chloro-1,3-dimethyl-1H-pyrazolo[3,4-*b*]quinoline<sup>1,3</sup> by hydrolysis in boiling dilute hydrochloric acid.

Methylation of sodium ethyl-3-anilino-5-methyl-4-pyrazolocarboxylate with methyl iodide in dimethylformamide at room temperature gave exclusively ethyl-3-anilino-1,5-dimethyl-4-pyrazolocarboxylate; the acid obtained from it by hydrolysis was cyclized by means of polyphosphoric acid into *Iia*. The compound *Iia* cannot be obtained by cyclization of N-(1,5-dimethyl-3-pyrazolyl)anthranilic acids, since this reaction produces compound *IIIb* (ref.<sup>1</sup>).

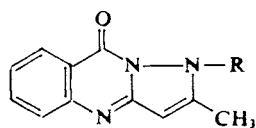
In studying the syntheses of *Id* and *Iib* we also investigated methylation of sodium salts of *Ia*, *Ib*, *Ic* and *Iia* with methyl iodide in dimethylformamide at room temperature. Methylation of the sodium salt of *Ib* gave *Id*. Similarly, methylation of the sodium salt of *Iia* afforded *Iib*. The latter was also formed as a sole product by methylation of the sodium salt of *Ic*. Further we studied methylation of *Ia* in the use of two-fold molar amounts of sodium hydride and methyl iodide in dimethylformamide at room temperature. TLC (Silufol 254, benzene-ethanol-dioxan-concentrated aqueous ammonia) of the reaction mixture revealed *Id*, *Iib* and a small amount of 4-methoxy-1,3-dimethyl-1*H*-pyrazolo[3,4-*b*]quinoline. 4-Methoxy-2,3-dimethyl-2*H*-pyrazolo[3,4-*b*]quinoline was not detected. The two 4-methoxy derivatives were prepared for comparison by reactions of the corresponding 4-chloro derivatives with sodium methoxide in methanol. 4-Chloro-2,3-dimethyl-2*H*-pyrazolo[3,4-*b*]quinoline was obtained by cyclization of 3-anilino-1,5-dimethyl-4-pyrazolcarboxylic acid with phosphorus oxychloride. After methylation of *Ia*, crystallization of the mixture from ethanol afforded a mixture of *Id* and *Iib*. This was resolved by column chromatography (silica gel Merck 7754, 0.063–0.2 mm, benzene); yields 21.6% of *Id* and 40.5% of *Iib*.



*Ia*; R<sup>1</sup> = H, R<sup>2</sup> = H  
*Ib*; R<sup>1</sup> = H, R<sup>2</sup> = CH<sub>3</sub>  
*Ic*; R<sup>1</sup> = CH<sub>3</sub>, R<sup>2</sup> = H  
*Id*; R<sup>1</sup> = CH<sub>3</sub>, R<sup>2</sup> = CH<sub>3</sub>



*Iia*; R<sup>1</sup> = H, R<sup>2</sup> = CH<sub>3</sub>  
*Iib*; R<sup>1</sup> = CH<sub>3</sub>, R<sup>2</sup> = CH<sub>3</sub>



*Iii*<sub>a</sub>; R = H  
*Iii*<sub>b</sub>; R = CH<sub>3</sub>

Another well-known compound of this group is *Ic*, formed by heating 4-(2-fluorophenyl)-6,8-dihydro-1,3,8-trimethylpyrazolo[3,4-*e*]-1,4-diazepin-7(1*H*)-one with pyridine hydrochloride<sup>4</sup>. In our work *Ic* was obtained by partial selective demethylation of *Id*, *Iid*, or their mixture, by heating with pyridine hydrochloride. The literature describes the use of pyridine hydrochloride for demethylation of a series of pyrazoles<sup>6</sup>

and some condensed heterocycles containing the pyrazole ring, such as 1,3-dimethyl-1*H*-indazole<sup>6</sup> and 4-(2-fluorophenyl)-4,5,6,8-tetrahydro-1,3,8-trimethylpyrazolo[3,4-*e*]-1,4-diazepin-7(1*H*)-one<sup>4</sup>. This, however, is not a general N-dealkylation method. It is applicable to dealkylation of N-alkylphenothiazines<sup>7</sup>, but not N-alkylcarbazoles.

The compounds *Ia*, *Ib*, *Ic*, *Id*, *Iia* and *Iib* were tested *in vivo* in mice for their activity against the influenza virus A2-Hongkong and encephalomyocarditis virus (EMC) after peroral or subcutaneous application. The experimental animals were females of white mice SPF, weighing 10 to 11 g. The A2-Hongkong virus was administered intranasally under a light ethereal narcosis. The EMC virus was administered subcutaneously in a dose of 0.2 ml to the skin folding on the back. The LD<sub>50</sub> of the viruses were determined according to Reed and Muench<sup>8</sup>. The tested substances were suspended in Tween 80. In the infection with the A2-Hongkong virus the mice were cured by two daily doses of 150 mg/kg administered perorally or subcutaneously for 5 days (1 day before and 4 days following the infection). In the EMC virus infection, the mice were treated with one peroral dose of 400 mg/kg 24 h prior to the infection, and 4 subcutaneous doses of 100 mg/kg, applied 28, 22 and 2 h before the infection and 2 h after it. The efficacy against the two viruses was assessed by extension of the average time of survival compared with controls. Compound *Ia* administered *s.c.* to mice infected with 50 LD<sub>50</sub> of A2-Hongkong virus extended the survival by 37%; in the infection with 5 LD<sub>50</sub> of the EMC virus the extension was 96%. Compound *Ib* administered *s.c.* to mice infected with 5 LD<sub>50</sub> of the A2-Hongkong virus extended the survival by 37%, in the *p.o.* administration by 48%. With 5 LD<sub>50</sub> of the EMC virus, *s.c.* administration of *Ib* extended the survival by 36%. Compound *Ic* and *Id* administered *s.c.* to mice infected with 50 LD<sub>50</sub> of the A2-Hongkong virus extended the survival by 55% and 48%, respectively. With the EMC virus, *Id* extended the survival by 70%.

## EXPERIMENTAL

The melting points were determined in an apparatus Mettler FP5, those higher than 300°C were determined in the capillary on a copper block and are not corrected. The IR spectra were measured in an apparatus Perkin-Elmer 577. The UV spectra were measured in an apparatus Perkin-Elmer 550S. The <sup>1</sup>H NMR spectra were measured in an apparatus BS-487 C (Tesla Brno) at 80 MHz. The standard was tetramethylsilane (TMS) or pentadeuterated 3-trimethylsilylpropionic acid (TMS PA-d<sub>5</sub>). The substances were dissolved in hexadeuterodimethyl sulphoxide or deuterated trifluoro acetic acid. The mass spectra were measured in apparatuses MCH 1320 and MAT 44S.

### 4,9-Dihydro-3-methyl-4-oxo-1*H*-pyrazolo[3,4-*b*]quinoline (*Ia*)

A mixture of 3-anilino-5-methyl-4-pyrazolcarboxylic acid (10.9 g, 0.05 mol) and polyphosphoric acid (75 g, 85% P<sub>2</sub>O<sub>5</sub>) was stirred 4 h at 90°C. After an addition of water (350 ml) the mixture

was cooled down to 5°C and stirred 1 h at this temperature. The separated solid was collected on a filter, washed with water and crystallized from ethanol; yield 8.8 g (88%), m.p. 333–336°C. For  $C_{11}H_9N_3O$  (199.2) calculated: 66.32% C, 4.55% H, 21.09% N; found: 65.43% C, 4.77% H, 20.83% N. IR spectrum (KBr): 3 420, 3 180 (NH), 1 550 (C=C quinoline, C=N), 1 580 (C=O), 752  $cm^{-1}$  (*ortho*-subst. arom.). UV spectrum (ethanol):  $\lambda_{max}$  235 nm ( $\log \epsilon$  4.66), 349 nm (3.71),  $\lambda_{infl.}$  267 nm, 278 nm. Mass spectrum:  $m/z = 199$  ( $M^+$ ).  $^1H$  NMR spectrum ( $(C^2H_3)_2SO$ , TMSPA-d5): 12.40 (flat band, 1 H, NH of pyrazole), 11.60 (bs, 1 H, NH of quinoline), 8.18 (bd, 1 H, 5-H), 7.00–7.70 (m, 3 H, 6,7,8-H), 2.62 (s, 3 H,  $CH_3$ ).

#### 4,9-Dihydro-1,3-dimethyl-4-oxo-1*H*-pyrazolo[3,4-*b*]quinoline (*Ib*)

A mixture of 4-chloro-1,3-dimethyl-1*H*-pyrazolo[3,4-*b*]quinoline (2.32 g, 0.01 mol) and 1*M*-HCl (23 ml) was refluxed for 2 h, cooled down and alkalized with water ammonia. The insoluble portion was collected on a filter, washed with water and crystallized from acetone; yield 1.73 g (81%), m.p. 335–337°C. For  $C_{12}H_{11}N_3O$  (213.2) calculated: 67.59% C, 5.20% H, 19.71% N; found: 67.63% C, 5.25% H, 19.87% N. IR spectrum (KBr): 3 200–3 400 (NH), 1 620, 1 550; (C=C of quinoline, C=N), 1 585 (C=O), 740  $cm^{-1}$  (*ortho*-subst. arom.). UV spectrum (ethanol):  $\lambda_{max}$  237 nm ( $\log \epsilon$  4.625), 268 nm (3.75), 334 nm (3.80),  $\lambda_{infl.}$  342 nm. Mass spectrum ( $(CH_3)_2SO$ , 100°C, TMSPA-d5): 11.70 (bs, 1 H, NH), 8.20 (bd, 1 H, 5-H), 7.00–7.70 (m, 3 H, 6,7,8-H), 3.85 (s, 3 H,  $NCH_3$ ), 2.48 (s, 3 H,  $CH_3$ ). Mass spectrum:  $m/z = 213$  ( $M^+$ ).

#### Ethyl-3-anilino-1,5-dimethyl-4-pyrazolecarboxylate

To a solution of ethyl-3-anilino-5-methyl-4-pyrazolecarboxylate (18.5 g, 0.075 mol) in dimethylformamide (100 ml) under nitrogen was added 80% sodium hydride (2.50 g) and the mixture was stirred 1 h at room temperature. After an addition of methyl iodide (11.80 g, 0.083 mol) the stirring was continued for 2 more h. The insoluble portion was filtered off and the filtrate was taken to dryness. The residue was crystallized from ethanol; yield 16.7 g (86%), m.p. 90.6 to 91.0°C. For  $C_{14}H_{17}N_3O_2$  (259.3) calculated: 64.85% C, 6.61% H, 16.20% N; found: 64.93% C, 6.43% H, 16.08% N.  $^1H$  NMR spectrum ( $(C^2H_3)_2SO$ , TMSPA-d5): 11.90 (bs, 1 H, NH), 7.58 (bd, 2 H, 2,6-H phenyl), 4.26 (q,  $J = 7$  Hz, 2 H,  $CH_2$ ), 3.68 (s, 3 H,  $NCH_3$ ), 2.41 (s, 3 H,  $CH_3$ ), 1.30 (t,  $J = 7.0$  Hz, 3 H,  $CH_2CH_3$ ).

#### 3-Anilino-1,5-dimethylpyrazole-4-carboxylic Acid

To a solution of ethyl-3-anilino-1,5-dimethyl-4-pyrazolecarboxylate (13 g, 0.05 mol) in ethanol (200 ml) was added a solution of sodium hydroxide (20 g) in water (250 ml). The mixture was refluxed for 2 h, cooled down and acidified to pH 4 with concd. hydrochloric acid. The insoluble portion was collected on a filter and washed with water till the filtrate was neutral; yield 10.2 g (88%), m.p. 184.5–185.7°C. The analytical sample was obtained by recrystallization from 50% aqueous ethanol, m.p. 185.8–186.3°C. For  $C_{12}H_{13}N_3O_2$  (231.3) calculated: 62.33% C, 5.67% H, 18.18% N; found: 62.13% C, 5.65% H, 18.12% N.

#### 4,9-Dihydro-2,3-dimethyl-4-oxo-2*H*-pyrazolo[3,4-*b*]quinoline (*IIa*)

A mixture of 3-anilino-1,5-dimethyl-4-pyrazolecarboxylic acid (6.9 g, 0.03 mol) and polyphosphoric acid (45 g, 83%  $P_2O_5$ ) was stirred 4 h at 90°C. After an addition of water (750 ml) it was cooled down to 5°C. The separated substance was collected on a filter and washed with water. Crystallization from ethanol gave a yield of 5.55 g (87%), m.p. 324–328°C. For  $C_{12}H_{11}N_3O$  (213.2) calculated: 67.59% C, 5.20% H, 19.71% N; found: 67.39% C, 5.18% H, 20.02% N. UV spec-

trum (ethanol):  $\lambda_{\max}$  215 nm ( $\log \epsilon$  4.17), 238 nm (4.67), 283 nm (3.93), 365 nm (4.84).  $^1\text{H}$  NMR spectrum ( $\text{CF}_3\text{COO}^2\text{H}$ , TMSPA-d5): 8.40 (bd, 1 H, 5-H), 7.30–8.00 (m, 3 H, 6,7,8-H), 4.11 (s, 3 H,  $\text{NCH}_3$ ), 2.93 (s, 3 H,  $\text{CH}_3$ ).

#### 4,9-Dihydro-1,3,9-trimethyl-4-oxo-1*H*-pyrazolo[3,4-*b*]quinoline (*Id*)

To a solution of *Ib* (2.13 g, 0.01 mol) in dimethylformamide (25 ml) was added 80% sodium hydride (0.36 g, 0.012 mol) and the mixture was stirred under nitrogen for 1 h at room temperature. After cooling to 5°C, methyl iodide (1.69 g, 0.012 mol) was added and the stirring at room temperature was continued for another 5 h; then methyl iodide (1.13 g, 0.008 mol) was added again and the mixture was stirred for 2 more h. After an addition of water (50 ml) and cooling to 5°C the separated crystals were collected on a filter and washed with water. Recrystallization from methanol gave 1.77 g of the product (78%), m.p. 223.7–224.8°C. For  $\text{C}_{13}\text{H}_{13}\text{N}_3\text{O}$  (227.3) calculated: 68.70% C, 5.77% H, 18.49% N; found: 68.86% C, 5.91% H, 18.33% N. UV spectrum (ethanol):  $\lambda_{\max}$  242 nm ( $\log \epsilon$  4.65), 273 nm (3.75), 340 nm (3.84),  $\lambda_{\text{infl}}$  204 nm, 214 nm.  $^1\text{H}$  NMR spectrum ( $\text{CF}_3\text{COO}^2\text{H}$ , TMSPA-d5): 8.51 (bd, 1 H, 5-H), 7.98 (m, 1 H, 7-H), 7.90 (bd, 1 H, 8-H), 7.62 (m, 1 H, 6-H), 4.40, 4.28 (s, 3 H,  $\text{NCH}_3$ ), 2.90 (s, 3 H,  $\text{CH}_3$ ).

#### 4,9-Dihydro-2,3,9-trimethyl-4-oxo-2*H*-pyrazolo[3,4-*b*]quinoline (*Iib*)

A) To a stirred suspension of *Iia* (1.07 g) (0.005 mol) in dimethylformamide (25 ml) was added 80% sodium hydride (0.18 g, 0.006 mol) and the mixture was stirred 1 h at room temperature under nitrogen. Methyl iodide (0.85 g, 0.006 mol) was added dropwise and the mixture was stirred at room temperature for 2 h. After an addition of water (25 ml) the mixture was cooled to 5°C, the separated solid product was collected on a filter, washed with water and recrystallized from ethanol; yield 0.87 g (77%), m.p. 198.4–198.8°C. For  $\text{C}_{13}\text{H}_{13}\text{N}_3\text{O}$  (227.3) calculated: 68.70% C, 5.77% H, 18.49% N; found: 68.96% C, 5.85% H, 18.59% N. UV spectrum (ethanol):  $\lambda_{\max}$  240 nm ( $\log \epsilon$  4.67), 285 nm (3.87), 370 nm (3.86),  $\lambda_{\text{infl}}$  212 nm.

B) Analogous methylation of *Ic* afforded *Iib* in a yield of 80%.

C) To a suspension of *Ia* (1.99 g, 0.01 mol) in dimethylformamide (50 ml) was added 80% sodium hydride (0.72 g, 0.024 mol) and the mixture was stirred at room temperature under nitrogen for 2 h. After cooling to 5°C methyl iodide (2.13 g, 0.015 mol) was added dropwise and the mixture was stirred 4 h at room temperature. Another 2.13 g of methyl iodide was added and the stirring continued for 2 h. The mixture was left standing overnight and taken to dryness. The residue was taken into 50 ml of water and extracted into ether. The solvent was removed and the remaining mixture (1.6 g) was analysed by TLC (Silufol UV 254, benzene–ethanol–dioxan–conc. aqueous ammonia 5 : 2 : 4 : 1); it was found to be composed of *Id* ( $R_F$  0.6), *Iib* ( $R_F$  0.8) and a trace of 4-methoxy-1,3-dimethyl-1*H*-pyrazolo [3,4-*b*] quinoline ( $R_F$  0.95). Recrystallization from ethanol gave 1.48 g of a mixture of *Id* and *Iib*. This was resolved by column chromatography on silica gel (Merck 7754, 0.063–0.2 mm, benzene); yield 0.92 g (41%) of *Iib* and 0.49 g (22%) of *Id*.

#### 4-Methoxy-1,3-dimethyl-1*H*-pyrazolo[3,4-*b*]quinoline

To 5 ml of methanol containing 0.05 g (2.1 mmol) of dissolved sodium was added 0.23 g (1 mmol) of 4-chloro-1,3-dimethyl-1*H*-pyrazolo[3,4-*b*]quinoline and the stirred mixture was refluxed for 2 h. After cooling, the insoluble portion was filtered off and the filtrate was taken to dryness. Recrystallization of the residue from hexane afforded 0.2 g (88%) of the product, m.p. 58.5 to 59.6°C. For  $\text{C}_{13}\text{H}_{13}\text{N}_3\text{O}$  (227.3) calculated: 68.70% C, 5.77% H, 18.49% N; found: 68.56% C,

5.83% H, 17.97% N. UV spectrum (ethanol):  $\lambda_{\max}$  244 nm ( $\log \epsilon$  4.92), 305 nm (3.69), 318 nm (3.73), 373 nm (3.81), 391 nm (3.74),  $\lambda_{\text{infl}}$  294 nm, 358 nm.  $^1\text{H}$  NMR spectrum ( $(\text{C}^2\text{H}_3)_2\text{SO}$ , TMS): 8.20 (bd, 1 H, 5-H), 7.96 (bd, 1 H, 8-H), 7.40–7.72 (m, 2 H, 6,7-H), 4.25, 4.05 (s, 3 H,  $\text{NCH}_3$ ,  $\text{OCH}_3$ ), 2.78 (s, 3 H,  $\text{CH}_3$ ).

#### 4-Methoxy-2,3-dimethyl-2*H*-pyrazolo[3,4-*b*]quinoline

Using the procedure for the synthesis of 4-methoxy-1,3-dimethyl-1*H*-pyrazolo [3,4-*b*] quinoline, the same amount of 4-chloro-2,3-dimethyl-2*H*-pyrazolo [3,4-*b*] quinoline and crystallization from cyclohexane gave 0.21 g (92%) of the product, m.p. 131.8 to 133.6°C. For  $\text{C}_{13}\text{H}_{13}\text{N}_3\text{O}$  (227.3) calculated: 68.70% C, 5.77% H, 18.49% N; found: 68.91% C, 5.95% H, 18.42% N. UV spectrum (ethanol):  $\lambda_{\max}$  244 nm ( $\log \epsilon$  4.81), 334 nm (3.94), 319 (3.83),  $\lambda_{\text{infl}}$  309.  $^1\text{H}$  NMR spectrum ( $(\text{C}^2\text{H}_3)_2\text{SO}$ , TMSPA-d5): 8.14 (bd, 1 H, 5-H), 7.90 (bd, 1 H, 8-H), 7.62 (m, 1 H, 7-H), 7.39 (m, 1 H, 6-H), 4.20 (s, 6 H,  $\text{NCH}_3$ ,  $\text{OCH}_3$ ), 2.88 (s, 3 H,  $\text{CH}_3$ ).

#### 4-Chloro-2,3-dimethyl-2*H*-pyrazolo[3,4-*b*]quinoline

A mixture of 3-anilino-1,5-dimethyl-4-pyrazolecarboxylic acid (4.6 g, 0.02 mol) and phosphorus oxychloride (46 ml) was refluxed for 1 h. The bulk of phosphorus oxychloride was distilled off, ice was added to the residue and the mixture was neutralized with 20% sodium hydroxide under cooling in an ice bath. The insoluble portion was collected on a filter, washed with water and recrystallized from ethyl acetate; yield 4.1 g (89%) of yellow crystals melting at 188.7–192.1°C. For  $\text{C}_{12}\text{H}_{10}\text{ClN}_3$  (231.7) calculated: 62.21% C, 4.35% H, 18.14% N, 15.30% Cl; found: 62.49% C, 4.27% H, 18.08% N, 15.20% Cl. UV spectrum (ethanol):  $\lambda_{\max}$  244 nm ( $\log \epsilon$  4.80), 322 nm (3.86), 337 nm (4.02), 4.15 nm (3.82),  $\lambda_{\text{infl}}$  309 nm.  $^1\text{H}$  NMR spectrum ( $(\text{C}^2\text{H}_3)_2\text{SO}$ , 100°C, TMSPA-d5): 8.12 (dd,  $J = 8.5$  Hz, 1.5 Hz, 1 H, 5-H), 6.90–7.60 (m, 3 H, 6,7,8-H), 3.80 (s, 3 H,  $\text{NCH}_3$ ), 2.70 (s, 3 H,  $\text{CH}_3$ ).

#### 4,9-Dihydro-3,9-dimethyl-4-oxo-1*H*-pyrazolo[3,4-*b*]quinoline (*Ic*)

A) A stirred mixture of pyridine (30 g) and concd. hydrochloric acid (44 ml) was gradually heated up to 160°C, to remove water. At this temperature *Id* (3.2 g, 0.014 mol) was added and the mixture was stirred 2 h at 220°C. After reducing the temperature to 160°C it was poured into water (240 ml), boiled and filtered. The filtrate was cooled and the separated crystals were collected on a filter, washed with water, recrystallized from ethanol and dried to constant weight at 110°C and 3 kPa; yield 2.35 g (79%), m.p. 248.7–249.5°C. For  $\text{C}_{12}\text{H}_{11}\text{N}_3\text{O}$  (213.2) calculated: 67.59% C, 5.20% H, 19.71% N; found: 68.12% C, 5.27% H, 20.00% N. UV spectrum (ethanol):  $\lambda_{\max}$  212 nm ( $\log \epsilon$  4.08), 246 nm (4.69), 370 nm (3.82),  $\lambda_{\text{infl}}$  275 nm.  $^1\text{H}$  NMR spectrum ( $(\text{C}^2\text{H}_3)_2\text{SO}$ , TMS): 13.26 (bs, 1 H, NH), 8.20 (dd,  $J = 8.0$  Hz, 2.0 Hz, 1 H, 5-H), 7.68 (m, 1 H, 7-H), 7.45 (bd, 1 H, 8-H), 7.15 (m, 1 H, 6-H), 3.75 (s, 3 H,  $\text{NCH}_3$ ), 2.68 (s, 3 H,  $\text{CH}_3$ ). Mass spectrum:  $m/z = 213$  ( $\text{M}^+$ ).

B) Analogous demethylation of *Iib*. The yield of *Ic* was 78%.

C) To a suspension of *Ia* (9.86 g, 0.05 mol) in dimethylformamide (200 ml), stirred under nitrogen, was added 80% sodium hydride (3.6 g, 0.12 mol) and the stirring was continued for 2 h at room temperature. Then methyl iodide (21.3 g, 0.15 mol) was added dropwise, the mixture was stirred for 8 h and taken to dryness. The residue was recrystallized from ethanol; yield 7.2 g of *Id* + *Iib*. From a mixture of pyridine (70 ml) and concentrated hydrochloric acid (105 ml) water was removed by elevating the temperature to 160°C. To this melt was added the mixture

of *Id* to *Ib* and stirred for 2 h at 220°C. For further procedure see *A*); yield 5.1 g (48%) of *Ic*, m.p. 248.1–249.3°C.

*The elemental analyses were carried out by Mrs J. Komancová and Mrs V. Šmidová (head: Dr J. Körtl). The <sup>1</sup>H NMR spectra were interpreted by Dr J. Holubek, the IR and UV spectra by Dr B. Kakač. The mass spectra were measured and interpreted by Drs M. Ryska and I. Koruna.*

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