Synthesis of 10-Amino-1,2,3,4-tetrahydrobenzo[*b*][1,6]-naphthyridines and Related Derivatives

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This paper describes the synthesis of some 10-amino-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridines and of the new 13-amino-6,6a,7,8,9,10-hexahydro-12*H*-benzo[*b*]pyrido[1,2-*g*][1,6]naphthyridines starting from isatins and 4-piperidones or quinolizidin-2-one.

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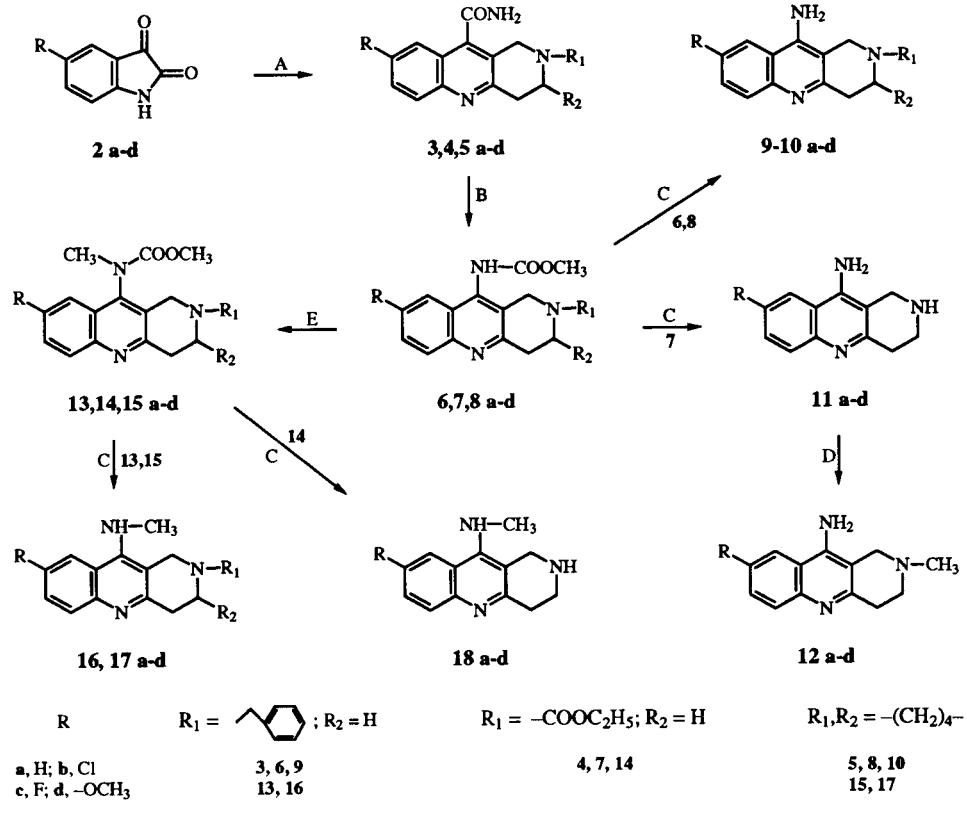
It has been reported in the patent literature [1,2] that 10-substituted-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridine derivatives exhibited a considerable activity as inhibitors of interleukine-1, which seems to be involved in the etiopathogenesis of Alzheimer's disease [3] and in the promotion of the related astrogliosis [4].

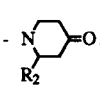
On the basis of these observations, and in connection with our present studies directed towards the search of new cholinesterasic agents, which may be useful as palliative therapy in Alzheimer's disease and other cognitive disorders [5], it seemed worthwhile to extend our investigations in preparing, by a new synthetic pathway, some 10-amino-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridines **1**, structurally related to Tacrine, the only approved drug for treating Alzheimer's disease in the United States.

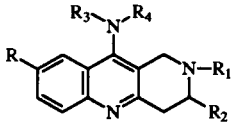
The syntheses are outlined in Scheme 1.

The 10-carboxamido-1,2,3,4-tetrahydrobenzo[*b*][1,6]-naphthyridines **3,4** and the 13-carboxamido-6,6a,7,8,9,10-hexahydro-12*H*-benzo[*b*]pyrido[1,2-*g*][1,6]naphthyridines **5**, prepared by bubbling anhydrous ammonia into a mix-

Scheme 1



Reagents; A: R_1 -  , NH_3, ethylene glycol, 150-160°; B: Br_2, CH_3ONa, CH_3OH; C; 20% KOH, reflux; D: 40% CH_2O, HCOOH; E: CH_3I, NaH, DMF.



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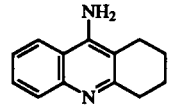

Tacrine

R = H, Cl, F, $-OCH_3$;

R_1 = H, $-CH_3$,  , $-COOC_2H_5$;

R_2 = H; R_1, R_2 = $-(CH_2)_4-$;

R_3 = H, $-CH_3$; R_4 = H, $-COOCH_3-$

ture of the isatins **2** and the appropriate 4-piperidones or quinolizidin-2-one in ethylene glycol at 150-160° for 1 hour, were the key intermediates of our syntheses.

Hofmann degradation of the amides to the corresponding amines, by the usual technique, in a solution of bromine and potassium hydroxide, gave very poor yields of the expected compounds. Thus, compounds **3-5** were smoothly converted to methyl carbamates **6-8** by treating with bromine in a methanolic solution of sodium methoxide. Hydrolysis of these uretanes in refluxing 20% potassium hydroxide gave the corresponding amine **9-11** in good to satisfactory yields. Compounds **11** were then reductively methylated with formaldehyde and formic acid to provide the corresponding 2-methyl derivatives **12**.

Finally, the 10-methoxycarbonylamines **6-8**, by reaction with methyl iodide/sodium hydride in anhydrous dimethylformamide, gave the *N*-methylcarbamates **13-15**, which were in turn hydrolyzed, following the same procedure previously reported for the preparation of amines **9-11**, to afford the 10-*N*-methyl derivatives **16-18**.

The synthetic route to 10-amino-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridines here described proved to be much more advantageous than that reported in the patents [1,2], since it starts from the readily available and quite cheap isatins, has only three steps and provides good yields of both intermediates and final compounds. Furthermore it is noteworthy that hitherto there are no data about the 6,6a,7,8,9,10-hexahydro-12*H*-benzo[*b*]pyrido-[1,2-*g*][1,6]naphthyridines in the chemical literature.

The amino derivatives **9-12** and **16-18** were evaluated for enzimatic inhibitory activity versus acetylcholinesterase from rat cerebral cortex, according to the procedure of Ellman [6]. All compounds tested possessed significantly reduced enzyme affinity as compared to Tacrine, with the only exception being compound **18a** which showed an IC_{50} = 0.86 μM, approximately 4 times less potent than Tacrine.

Further studies on the interleukine-1 inhibitory effect are in progress and will be reported elsewhere, if interesting.

In the experimental, spectral data of the most significant compounds have been reported.

EXPERIMENTAL

Melting points were taken on a Kofler hot stage apparatus and are uncorrected. The ^{1}H-nmr spectra were obtained in DMSO-d_6 on a Varian Gemini 200 MHz instrument; all values were reported in ppm (δ) and standard abbreviations were used (at = apparent triplet; b = broad; d = doublet; dd = doublet of doublets; m = multiplet; q = quadruplet; t = triplet; s = singlet); peak assignments were also based on ^{13}C-APT, ^{1}H-COSY and ^{13}C-^{1}H HETCOR nmr experiments; electron ionization mass spectra were recorded on a HP 59580 B spectrometer operating at 70 eV. Column chromatographic separations were accomplished on Merck silica gel (70-230 mesh) or Merck aluminium oxide 90. The purity of each compound was checked on silica gel C. Erba 60 F_{254} or Merck aluminium oxide 60 F_{254} (Type E) plates and spots were located by uv light. Sodium sulfate was used to dry organic solutions.

1-Benzyl-4-piperidone, 1-ethoxycarbonyl-4-piperidone and isatin **2a** were purchased from Aldrich Chemical Co. The syntheses of **2b** [7], **2c** [8] and **2d** [9] have been reported elsewhere.

Quinolizidin-2-one.

The synthesis of quinolizidin-2-one was carried out according to a modification of the method previously reported [10] in the last step. The yield was improved.

A suspension of sodium ethoxide (prepared from 2.6 g of sodium, 0.11 mole) in 1-(2-ethoxycarbonyl)ethyl-2-ethoxycarbonylmethylpiperidine (bp 137-143°/1 mm, 27.1 g, 0.1 mole) was gradually heated until the internal temperature was raised to 140°. The ethanol which formed was removed with a Dean-Stark apparatus. After 30 minutes at this temperature, the mixture was cooled, and the intermediate ketoester was hydrolyzed and decarboxylated by adding 20% hydrochloric acid (100 ml) and refluxing for 4 hours. The solution was concentrated under vacuum, made alkaline with 20% potassium hydroxide and extracted with chloroform. Removal of the solvent afforded an oil which was distilled to give 11 g (72%) of quinolizidin-2-one, bp 116-118°/14 mm (lit [10] bp 115-116°/15 mm).

General Procedure for the Preparation of 10-Carboxamido-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridines **3**, **4a-d** and 13-Carboxamido-6,6a,7,8,9,10-hexahydro-12*H*-benzo[*b*]pyrido-[1,2-*g*][1,6]naphthyridines **5a-d**.

A mixture of each compound **2** (0.1 mole) and 1-benzyl-4-piperidone (21 g, 0.11 mole, to obtain **3**), 1-ethoxycarbonyl-4-piperidone (20 g, 0.11 mole, to obtain **4**) or quinolizidin-2-one (17 g, 0.11 mole, to obtain **5**) in ethylene glycol (100 ml) was heated at 150-160° in an oil bath. Anhydrous ammonia was bubbled into the solution for about 1 hour. After cooling, water was added to the mixture and the resulting precipitate was collected by filtration, washed with water, dried at 60° at reduced pressure, then crystallized.

2-Benzyl-10-carboxamido-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridine **3a**.

This compound was obtained from **2a** in 73% yield, mp 242-244° (ethyl acetate); ^{1}H-nmr (DMSO-d_6): δ 8.15 and 7.96 (d, 2H, $CONH_2$), 7.92 (dd, 1H, H-6), 7.75 (dd, 1H, H-9), 7.70 (at, 1H, H-7), 7.54 (at, 1H, H-8), 7.30 (m, 5H, phenyl protons), 3.74 (s, 2H, benzyl CH_2), 3.73 (s, 2H, H-1), 3.12 (t, 2H, H-4), 2.86 (t, 2H, H-3).

Anal. Calcd. for $C_{20}H_{19}N_3O$: C, 75.69; H, 6.03; N, 13.24. Found: C, 75.42; H, 5.88; N, 13.51.

2-Benzyl-10-carboxamido-8-chloro-1,2,3,4-tetrahydrobenzo-[*b*][1,6]-naphthyridine **3b**.

This compound was obtained from **2b** in 70% yield, mp 272-274° (dimethylformamide).

Anal. Calcd. for $C_{20}H_{18}ClN_3O$: C, 68.28; H, 5.16; N, 11.94. Found: C, 68.17; H, 5.00; N, 11.77.

2-Benzyl-10-carboxamido-8-fluoro-1,2,3,4-tetrahydrobenzo-[*b*][1,6]-naphthyridine **3c**.

This compound was obtained from **2c** in 78% yield, mp 251-253° (ethanol).

Anal. Calcd. for $C_{20}H_{18}FN_3O$: C, 71.63; H, 5.41; N, 12.53. Found: C, 71.51; H, 5.66; N, 12.33.

2-Benzyl-10-carboxamido-8-methoxy-1,2,3,4-tetrahydrobenzo-[*b*][1,6]naphthyridine **3d**.

This compound was obtained from **2d** in 68% yield, mp 252-254° (dimethylformamide).

Anal. Calcd. for $C_{21}H_{21}N_3O_2$: C, 72.60; H, 6.09; N, 12.09. Found: C, 72.70; H, 6.01; N, 12.05.

10-Carboxamido-2-ethoxycarbonyl-1,2,3,4-tetrahydrobenzo-[*b*][1,6]naphthyridine **4a**.

This compound was obtained from **2a** in 74% yield, mp 236-238° (dimethylformamide); ^{1}H-nmr (DMSO-d_6): δ 8.25 and 8.12 (d, 2H, $CONH_2$), 7.96 (dd, 1H, H-6), 7.81 (dd, 1H, H-9), 7.75 (at, 1H, H-7), 7.59 (at, 1H, H-8), 4.73 (s, 2H, H-1), 4.10 (q, 2H, OCH_2), 3.77 (t, 2H, H-3), 3.14 (t, 2H, H-4), 1.21 (t, 3H, CH_3).

Anal. Calcd. for $C_{16}H_{17}N_3O_3$: C, 64.20; H, 5.72; N, 14.04. Found: C, 64.30; H, 5.94; N, 14.15.

10-Carboxamido-8-chloro-2-ethoxycarbonyl-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridine **4b**.

This compound was obtained from **2b** in 66% yield, mp 240-242° (ethyl acetate).

Anal. Calcd. for $C_{16}H_{16}ClN_3O_3 \cdot H_2O$: C, 54.63; H, 5.16; N, 11.94. Found: C, 54.92; H, 5.11; N, 11.90.

10-Carboxamido-2-ethoxycarbonyl-8-fluoro-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridine **4c**.

This compound was obtained from **2c** in 84% yield, mp 270-272° (dimethylformamide).

Anal. Calcd. for $C_{16}H_{16}FN_3O_3$: C, 60.56; H, 5.08; N, 13.24. Found: C, 60.41; H, 4.86; N, 13.04.

10-Carboxamido-2-ethoxycarbonyl-8-methoxy-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridine **4d**.

This compound was obtained from **2d** in 71% yield, mp 230-232° (dimethylformamide).

Anal. Calcd. for $C_{17}H_{19}N_3O_4$: C, 61.99; H, 5.82; N, 12.76. Found: C, 61.76; H, 5.83; N, 12.48.

13-Carboxamido-6,6a,7,8,9,10-hexahydro-12*H*-benzo-[*b*]pyrido[1,2-*g*][1,6]naphthyridine **5a**.

This compound was obtained from **2a** in 62% yield, mp 242-245° (methanol); ^{1}H-nmr (DMSO-d_6): δ 8.19 and 7.99 (d, 2H, $CONH_2$), 7.91 (d, 1H, H-4), 7.77 (d, 1H, H-1), 7.69 (at, 1H, H-3), 7.55 (at, 1H, H-2), 3.95 (d,1H, H-12eq, J_{gem} 16 Hz), 3.37 (d, 1H, H-12ax, J_{gem} 16 Hz), 3.11 (dd, 1H, H-6eq, J_{gem} 16 Hz, J_{6eq-6a} 4 Hz), 3.02 (bd, 1H, H-10eq, J_{gem} 16 Hz), 2.81 (dd, 1H, H-6ax, J_{gem} 16 Hz, J_{6ax-6a} 11 Hz), 2.32 (m, 1H, H-6a), 2.07 (t, 1H, H-10ax, J_{gem} 16 Hz, $J_{10ax-9ax}$ 11 Hz), 1.85 (d, 1H, H-7eq), 1.71-1.65 (m, 3H, H-8eq and H-9), 1.29 (m, 2H, H-7ax and H-8ax).

Anal. Calcd. for $C_{17}H_{19}N_3O \cdot 1.5H_2O$: C, 66.21; H, 7.19; N, 13.63. Found: C, 65.92; H, 7.30; N, 13.46.

13-Carboxamido-2-chloro-6,6a,7,8,9,10-hexahydro-12*H*-benzo[*b*]pyrido[1,2-*g*][1,6]naphthyridine **5b**.

This compound was obtained from **2b** in 62% yield, mp 264-267° dec (ethanol).

Anal. Calcd. for $C_{17}H_{18}ClN_3O$: C, 64.66; H, 5.75; N, 13.31. Found: C, 64.84; H, 5.95; N, 13.45.

13-Carboxamido-2-fluoro-6,6a,7,8,9,10-hexahydro-12*H*-benzo[*b*]pyrido[1,2-*g*][1,6]naphthyridine **5c**.

This compound was obtained from **2c** in 59% yield, mp 234-237° dec (methanol).

Anal. Calcd. for $C_{17}H_{18}FN_3O \cdot 0.25H_2O$: C, 67.20; H, 6.14; N, 13.83. Found: C, 67.01; H, 6.06; N, 13.63.

13-Carboxamido-2-methoxy-6,6a,7,8,9,10-hexahydro-12*H*-benzo[*b*]pyrido[1,2-*g*][1,6]naphthyridine **5d**.

This compound was obtained from **2d** in 54% yield, mp 244-247° dec (methanol).

Anal. Calcd. for $C_{18}H_{21}N_3O_2$: C, 69.43; H, 6.80; N, 13.49. Found: C, 69.62; H, 7.08; N, 13.52.

General Procedure for the Preparation of 10-Methoxycarbonylamino-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridines **6, 7a-d** and 13-Methoxycarbonylamino-6,6a,7,8,9,10-hexahydro-12*H*-benzo[*b*]pyrido[1,2-*g*][1,6]naphthyridines **8a-d**.

Compounds **3**, **4**, or **5** (10 mmoles) were mixed to a solution of sodium (0.5 g, 22 mmoles), in anhydrous methanol (200 ml). Bromine (1.6 g, 10 mmoles) in methanol (50 ml), was then added with stirring during 15 minutes, the temperature being kept below 25°. After the addition was completed, the mixture was refluxed for 20 minutes, after which it was separated from a small amount of insoluble material by filtration, then neutralized with acetic acid. The solvent was evaporated at reduced pressure, and the resulting solid, thoroughly washed with water to remove sodium bromide, was directly crystallized.

2-Benzyl-10-methoxycarbonylamino-1,2,3,4-tetrahydrobenzo-[*b*][1,6]naphthyridine **6a**.

This compound was obtained from **3a** in 82% yield, mp 183-185° (ethyl acetate); ^{1}H-nmr (DMSO-d_6): δ 9.56 (s, 1H, NH), 7.91 (d, 1H, H-6), 7.86 (d, 1H, H-9), 7.67 (at, 1H, H-7), 7.52 (at, 1H, H-8), 7.34 (m, 5H, phenyl protons), 3.71 (s, 3H, OCH_3), 3.67 (s, 2H, benzyl CH_2), 3.64 (s, 2H, H-1), 3.11 (t, 2H, H-4), 2.82 (t, 2H, H-3).

Anal. Calcd. for $C_{21}H_{21}N_3O_2 \cdot H_2O$: C, 69.02; H, 6.34; N, 11.50. Found: C, 69.36; H, 6.17; N, 11.40.

2-Benzyl-8-chloro-10-methoxycarbonylamino-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridine **6b**.

This compound was obtained from **3b** in 62% yield, mp 156-158° (ethyl acetate).

Anal. Calcd. for $C_{21}H_{20}ClN_3O_2$: C, 66.05; H, 5.28; N, 11.00. Found: C, 65.90; H, 5.35; N, 11.05.

2-Benzyl-8-fluoro-10-methoxycarbonylamino-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridine **6c**.

This compound was obtained from **3c** in 69% yield, mp 179-181° (methanol).

Anal. Calcd. for $C_{21}H_{20}FN_3O_2$: C, 69.03; H, 5.52; N, 11.50. Found: C, 69.09; H, 5.46; N, 11.43.

2-Benzyl-8-methoxy-10-methoxycarbonylamino-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridine **6d**.

This compound was obtained from **3d** in 74% yield, mp 195-197° (dimethylformamide/methanol).

Anal. Calcd. for $C_{22}H_{23}N_3O_3$: C, 70.01; H, 6.14; N, 11.13. Found: C, 69.85; H, 6.10; N, 11.02.

2-Ethoxycarbonyl-10-methoxycarbonylamino-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridine **7a**.

This compound was obtained from **4a** in 68% yield, mp 138-140° (methanol); ^{1}H-nmr (DMSO-d_6): δ 9.81 (s, 1H, NH), 7.94 (d, 2H, H-6 and H-9), 7.72 (at, 1H, H-7), 7.56 (at, 1H, H-8), 4.64 (s, 2H, H-1), 4.08 (q, 2H, OCH_2), 3.76 (t, 2H, H-3), 3.71 (s, 3H, OCH_3), 3.13 (t, 2H, H-4), 1.20 (t, 3H, CH_3).

Anal. Calcd. for $C_{17}H_{19}N_3O_4 \cdot H_2O$: C, 58.78; H, 6.09; N, 12.10. Found: C, 59.02; H, 5.81; N, 12.06.

8-Chloro-2-ethoxycarbonyl-10-methoxycarbonylamino-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridine **7b**.

This compound was obtained from **4b** in 76% yield, mp 173-175° (methanol).

Anal. Calcd. for $C_{17}H_{18}ClN_3O_4$: C, 56.13; H, 4.99; N, 11.55. Found: C, 55.94; H, 5.05; N, 11.59.

2-Ethoxycarbonyl-8-fluoro-10-methoxycarbonylamino-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridine **7c**.

This compound was obtained from **4c** in 70% yield, mp 157-159° (methanol).

Anal. Calcd. for $C_{17}H_{18}FN_3O_4 \cdot H_2O$: C, 55.89; H, 5.52; N, 11.50. Found: C, 55.67; H, 5.33; N, 11.36.

2-Ethoxycarbonyl-8-methoxy-10-methoxycarbonylamino-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridine **7d**.

This compound was obtained from **4d** in 63% yield, mp 174-176° (ethyl acetate).

Anal. Calcd. for $C_{18}H_{21}N_3O_5$: C, 60.16; H, 5.89; N, 11.69. Found: C, 59.87; H, 5.91; N, 11.53.

13-Methoxycarbonylamino-6,6a,7,8,9,10-hexahydro-12*H*-benzo[*b*]pyrido[1,2-*g*][1,6]naphthyridine **8a**.

This compound was obtained from **5a** in 68% yield, mp 179-181° (ethyl acetate); ^{1}H-nmr (DMSO-d_6): δ 9.57 (s, 1H, NH), 7.89 (d, 1H, H-4), 7.87 (d, 1H, H-1), 7.67 (t, 1H, H-3), 7.51 (t, 1H, H-2), 3.96 (d, 1H, H-12eq, J_{gem} 16 Hz), 3.67 (s, 3H, OCH_3), 3.23 (d, 1H, H-12ax, J_{gem} 16 Hz), 3.10 (dd, 1H, H-6eq, J_{gem} 16 Hz, $J_{6eq\text{-}6a}$ 4 Hz), 3.03 (bd, 1H, H-10eq, J_{gem} 15 Hz), 2.80 (dd, 1H, H-6ax, J_{gem} 15 Hz, $J_{6ax\text{-}6a}$ 10 Hz), 2.32 (m, 1H, H-6a), 2.06 (t, 1H, H-10ax, J_{gem} 15 Hz, $J_{10ax\text{-}9ax}$ 10 Hz), 1.84 (bd, 1H, H-7eq), 1.71-1.40 (m, 3H, H-9 and H-8eq), 1.28 (m. 2H, H-7ax and H-8ax).

Anal. Calcd. for $C_{18}H_{21}N_3O_2$: C, 69.43; H, 6.80; N, 13.49. Found: C, 69.24; H, 6.72; N, 13.18.

2-Chloro-13-methoxycarbonylamino-6,6a,7,8,9,10-hexahydro-12*H*-benzo[*b*]pyrido[1,2-*g*][1,6]naphthyridine **8b**.

This compound was obtained from **5b** in 70% yield, mp 211-213° (ethyl acetate).

Anal. Calcd. for $C_{18}H_{20}ClN_3O_2 \cdot 0.5H_2O$: C, 60.93; H, 5.97; N, 11.84. Found: C, 61.03; H, 5.74; N, 11.85.

2-Fluoro-13-methoxycarbonylamino-6,6a,7,8,9,10-hexahydro-12*H*-benzo[*b*]pyrido[1,2-*g*][1,6]naphthyridine **8c**.

This compound was obtained from **5c** in 73% yield, mp 198-200° (ethyl acetate).

Anal. Calcd. for $C_{18}H_{20}FN_3O_2 \cdot H_2O$: C, 62.23; H, 6.38; N, 12.10. Found: C, 62.05; H, 6.12; N, 12.28.

2-Methoxy-13-methoxycarbonylamino-6,6a,7,8,9,10-hexahydro-12*H*-benzo[*b*]pyrido[1,2-*g*][1,6]naphthyridine **8d**.

This compound was obtained from **5d** in 78% yield, mp 142-144° (ethyl acetate).

Anal. Calcd. for $C_{19}H_{23}N_3O_3 \cdot H_2O$: C, 63.49; H, 7.01; N, 11.69. Found: C, 63.45; H, 6.91; N, 11.40.

General Procedure for the Preparation of 10-Amino-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridines **9, 11a-d** and 13-Amino-6,6a,7,8,9,10-hexahydro-12*H*-benzo[*b*]pyrido[1,2-*g*][1,6]naphthyridines **10a-d**.

A suspension of the urethanes **6**, **7** or **8** (10 mmoles) in a 20% (1:1) hydroalcoholic solution of potassium hydroxide (60 ml) was refluxed for 4 hours. After cooling, ice water was added to the mixture and the resulting suspension was vigorously stirred for 10 minutes. The precipitate was collected by filtration, washed with water until neutral to litmus, dried at 60° at reduced pressure, then crystallized.

10-Amino-2-benzyl-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridine **9a**.

This compound was obtained from **6a** in 82% yield, mp 228-231° (ethanol); ^{1}H-nmr (DMSO-d_6): δ 8.14 (dd, 1H, H-9), 7.63 (dd, 1H, H-6), 7.49 (at, 1H, H-7), 7.36 (m, 5H, phenyl protons), 7.29 (at, 1H, H-8), 6.34 (bs, 2H, NH_2), 3.74 (s, 2H, benzyl CH_2), 3.55 (s, 2H, H-1), 2.88 (t, 2H, H-3), 2.72 (t, 2H, H-4); ms: (m/z) 289 (M^+), 272, 190.

Anal. Calcd. for $C_{19}H_{19}N_3$: C, 78.86; H, 6.62; N, 14.52. Found: C, 78.66; H, 6.91; N, 14.44.

10-Amino-2-benzyl-8-chloro-1,2,3,4-tetrahydrobenzo-[*b*][1,6]naphthyridine **9b**.

This compound was obtained from **6b** in 72% yield, mp 156-158° (ethanol/water).

Anal. Calcd. for $C_{19}H_{18}ClN_3$: C, 70.47, H, 5.60; N, 12.98. Found: C, 70.76; H, 5.77; N, 13.13.

10-Amino-2-benzyl-8-fluoro-1,2,3,4-tetrahydrobenzo-[*b*][1,6]naphthyridine **9c**.

This compound was obtained from **6c** in 68% yield, mp 221-223° (ethanol).

Anal. Calcd. for $C_{19}H_{18}FN_3$: C, 74.25; H, 5.90; N, 13.67. Found: C, 73.99; H, 5.68; N, 13.59.

10-Amino-2-benzyl-8-methoxy-1,2,3,4-tetrahydrobenzo-[*b*][1,6]naphthyridine **9d**.

This compound was obtained from **6d** in 79% yield, mp 245-247° (methanol).

Anal. Calcd. for $C_{20}H_{21}N_3O$: C, 75.21; H, 6.63; N, 13.16. Found: C, 75.17; H, 6.44; N, 13.12.

13-Amino-6,6a,7,8,9,10-hexahydro-12*H*-benzo[*b*]pyrido[1,2-*g*]-[1,6]naphthyridine **10a**.

This compound was obtained from **8a** in 71% yield, mp 208-210° (ethanol); ^{1}H-nmr (DMSO-d_6): δ 8.20 (d, 1H, H-1), 7.66 (d, 1H, H-4), 7.55 (at, 1H, H-3), 7.32 (at, 1H, H-2), 6.76 (s, 2H, NH_2), 3.90 (d, 1H, H-12eq, J_{gem} 15 Hz), 3.02 (d, 1H, H-12ax, J_{gem} 15 Hz), 3.05 (d, 1H, H-10eq, J_{gem} 15 Hz), 2.85 (dd, 1H, H-6eq, J_{gem} 15 Hz, $J_{6eq\text{-}6a}$ 4 Hz), 2.68 (dd, 1H, H-6ax, J_{gem} 15

Hz, J_{6ax-6a} 10 Hz), 2.25 (m, 1H, H-6a), 2.13 (t, 1H, H-10ax, J_{gem} 15 Hz, $J_{10ax-9ax}$ 10 Hz), 1.81 (d, 1H, H-7eq), 1.70-1.50 (m, 3H, H-8eq and H-9), 1.26 (m, 2H, H-7ax and H-8ax); ms: (m/z) 253 (M^+), 236, 170.

Anal. Calcd. for $C_{16}H_{19}N_3 \cdot 2H_2O$: C, 66.41; H, 8.01; N, 14.52. Found: C, 66.22; H, 8.20; N, 14.67.

13-Amino-2-chloro-6,6a,7,8,9,10-hexahydro-12*H*-benzo-[*b*]pyrido[1,2-*g*][1,6]naphthyridine **10b**.

This compound was obtained from **8b** in 67% yield, mp 242-245° (methanol).

Anal. Calcd. for $C_{16}H_{18}ClN_3$: C, 66.78; H, 6.30; N, 14.60. Found: C, 66.78; H, 6.56; N, 14.59.

13-Amino-2-fluoro-6,6a,7,8,9,10-hexahydro-12*H*-benzo-[*b*]pyrido[1,2-*g*][1,6]naphthyridine **10c**.

This compound was obtained from **8c** in 70% yield, mp 254-256° dec (methanol).

Anal. Calcd. for $C_{16}H_{18}FN_3$: C, 70.83; H, 6.69; N, 15.49. Found: C, 70.56; H, 6.74; N, 15.37.

13-Amino-2-methoxy-6,6a,7,8,9,10-hexahydro-12*H*-benzo-[*b*]pyrido[1,2-*g*][1,6]naphthyridine **10d**.

This compound was obtained from **8d** in 77% yield, mp 253-256° (ethanol).

Anal. Calcd. for $C_{17}H_{21}N_3O \cdot 0.25H_2O$: C, 70.93; H, 7.53; N, 14.60. Found: C, 70.87; H, 7.63; N, 14.62.

10-Amino-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridine **11a**.

This compound was obtained from **7a** in 66% yield, mp 181-183° (ethanol/ water); ^{1}H-nmr (DMSO-d_6): δ 8.14 (dd, 1H, H-9), 7.64 (dd, 1H, H-6), 7.48 (at, 1H, H-7), 7.27 (at, 1H, H-8), 6.30 (bs, 2H, NH_2), 3.76 (d, 2H, H-1), 2.98 (m, 2H, H-3), 2.78 (t, 2H, H-4), 2.46 (m, 1H, NH); ms: (m/z) 199 (M^+), 198, 182, 170.

Anal. Calcd. for $C_{12}H_{13}N_3 \cdot H_2O$: C, 66.34; H, 6.96; N, 19.34. Found: C, 66.68; H, 6.96; N, 19.22.

10-Amino-8-chlorotetrahydrobenzo[*b*][1,6]naphthyridine **11b**.

This compound was obtained from **7b** in 76% yield, mp 236-238° (ethanol).

Anal. Calcd. for $C_{12}H_{12}ClN_3$: C, 61.67; H, 5.18; N, 17.98. Found: C, 61.66; H, 5.38; N, 17.81.

10-Amino-8-fluorotetrahydrobenzo[*b*][1,6]naphthyridine **11c**.

This compound was obtained from **7c** in 70% yield, mp 236-238° (methanol).

Anal. Calcd. for $C_{12}H_{12}FN_3 \cdot H_2O$: C, 61.26; H, 6.00; N, 17.86. Found: C, 61.20; H, 5.74; N, 18.18.

10-Amino-8-methoxytetrahydrobenzo[*b*][1,6]naphthyridine **11d**.

This compound was obtained from **7d** in 62% yield, mp 244-246° (ethanol).

Anal. Calcd. for $C_{13}H_{15}N_3O \cdot H_2O$: C, 63.14; H, 6.93; N, 16.99. Found: C, 62.97; H, 7.18; N, 16.74.

General Procedure for the Preparation of 10-Amino-2-methyltetrahydrobenzo[*b*][1,6]naphthyridines **12a-d**.

Each compound **11** (10 mmoles) was added to a stirred solution of 40% formaldehyde (1.1 ml, 15 mmoles) and 99% formic acid (1.2 ml, 30 mmoles) at room temperature. The mixture was heated at 80° for 4 hours. After cooling, water was added and the resulting solution, made alkaline with 10% sodium carbonate, was extracted with ethyl acetate. The solvent was removed and the residue purified by chromathography on aluminium oxide by eluting with 2% methanol (v/v) in ethyl acetate.

10-Amino-2-methyltetrahydrobenzo[*b*][1,6]naphthyridine **12a**.

This compound was obtained from **11a** in 55% yield, mp 177-179°(diethyl ether/*n*-hexane); ^{1}H-nmr (DMSO-d_6): δ 8.15 (d, 1H, H-9), 7.63 (d, 1H, H-6), 7.49 (at, 1H, H-7), 7.27 (at, 1H, H-8), 6.37 (bs, 2H, NH_2), 3.42 (s, 2H, H-1), 2.90 (t, 2H, H-3), 2.67 (t, 2H, H-4), 2.42 (s, 3H, CH_3); ms: (m/z) 213 (M^+), 212, 196, 170.

Anal. Calcd. for $C_{13}H_{15}N_3 \cdot 2H_2O$: C, 62.63; H, 7.68, N, 16.85. Found: C, 62.78; H, 7.96; N, 17.02.

10-Amino-8-chloro-2-methyltetrahydrobenzo[*b*][1,6]naphthyridine **12b**.

This compound was obtained from **11b** in 60% yield, mp 225-227° (ethyl acetate/n-hexane).

Anal. Calcd. for $C_{13}H_{14}ClN_3$: C, 63.03; H, 5.70; N, 16.96. C, Found: C, 62.72; H, 5.96; N, 16.74.

10-Amino-8-fluoro-2-methyltetrahydrobenzo[*b*][1,6]naphthyridine **12c**.

This compound was obtained from **11c** in 68% yield, mp 218-220° (ethyl acetate).

Anal. Calcd. for $C_{13}H_{14}FN_3 \cdot H_2O$: C, 62.64; H, 6.47; N, 16.86. Found: C, 62.72; H, 6.27; N, 16.61.

10-Amino-8-methoxy-2-methyltetrahydrobenzo[*b*][1,6]naphthyridine **12d**.

This compound was obtained from **11d** in 66% yield, mp 100-102° (ethyl acetate/*n*-hexane).

Anal. Calcd. for $C_{14}H_{17}N_3O \cdot 2H_2O$: C, 60.20; H, 7.58; N, 15.04. Found: C, 60.32; H, 7.37; N, 15.31.

General Procedure for the Preparation of 10-*N*-Methoxycarbonyl-*N*-methylamino-1,2,3,4-tetrahydrobenzo[*b*][1,6]-naphthyridines **13, 14a-d** and 13-*N*-Methoxycarbonyl-*N*-methylamino-6,6a,7,8,9,10-hexahydro-12*H*-benzo[*b*]pyrido[1,2-*g*]-[1,6]naphthyridines **15a-d**.

To a stirred suspension of sodium hydride (0.75 g of 50% oil dispersion, 15 mmoles) was added in several portions each compound **13, 14** or **15** (10 mmoles). After 30 minutes stirring at room temperature, methyl iodide (1.0 ml, 16 mmoles) was added and the reaction mixture was stirred at room temperature for 2 hours. The inorganic salts were then filtered, the filtrate evaporated to dryness, and the residue purified by column chromatography, by eluting with ethyl acetate.

2-Benzyl-10-*N*-methoxycarbonyl-*N*-methylamino-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridine **13a**.

This compound was obtained from **6a** in 77% yield, mp 108-110° (diethyl ether); ^{1}H-nmr (DMSO-d_6): δ 7.96 (dd, 1H, H-6), 7.74 (dd, 1H, H-9), 7.68 (at, 1H, H-7), 7.57 (at, 1H, H-8), 7.34 (m, 5H, phenyl protons), 3.75 (dd, 2H, H-1, J_{gem} 13 Hz), 3.67 (dd, 2H, benzyl CH_2), 3.70 and 3.40 (2s, 3H, OCH_3, 30 and 70%), 3.12 (t, 2H, H-4), 3.10 (s, 3H, NCH_3), 2.87 (t, 2H, H-3).

Anal. Calcd. for $C_{22}H_{23}N_3O_2$: C, 73.11; H, 6.41; N, 11.63. Found: C, 73.40; H, 6.21; N, 11.70.

2-Benzyl-8-chloro-10-*N*-methoxycarbonyl-*N*-methylamino-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridine **13b**.

This compound was obtained from **6b** in 81% yield, mp 137-139° (ethyl acetate).

Anal. Calcd. for $C_{22}H_{22}ClN_3O_2$: C, 66.75; H, 5.60; N, 10.61. Found: C, 67.01; H, 5.68; N, 10.66.

2-Benzyl-8-fluoro-10-*N*-methoxycarbonyl-*N*-methylamino-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridine **13c**.

This compound was obtained from **6c** in 72% yield, mp 158-160° (ethyl acetate).

Anal. Calcd. for $C_{22}H_{22}FN_3O_2$: C, 69.64; H, 5.84; N, 11.07. Found: C, 69.67; H, 5.77; N, 11.04.

2-Benzyl-8-methoxy-10-*N*-methoxycarbonyl-*N*-methylamino-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridine **13d**.

This compound was obtained from **6d** in 76% yield, mp 173-175° (methanol).

Anal. Calcd. for $C_{23}H_{25}N_3O_3$: C, 70.57; H, 6.44; N, 10.73. Found: C, 70.84; H, 6.45; N, 10.67.

2-Ethoxycarbonyl-10-*N*-methoxycarbonyl-*N*-methylamino-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridine **14a**.

This compound was obtained from **7a** in 48% yield, mp 146-148° (ethyl acetate); ^{1}H-nmr (DMSO-d_6): δ 8.00 (d, 1H, H-6), 7.76 (at, 1H, H-7), 7.73 (d, 1H, H-9), 7.61 (at, 1H, H-8), 4.61 (s, 2H, H-1), 4.09 (q, 2H, OCH_2), 3.80 (m, 2H, H-3), 3.78 and 3.50 (2s, 3H, OCH_3, 34 and 66%), 3.21 (s, 3H, NCH_3), 3.13 (t, 2H, H-4), 1.20 (t, 3H, CH_3).

Anal. Calcd. for $C_{18}H_{21}N_3O_4$: C, 62.96; H, 6.16; N, 12.24. Found: C, 63.20; H, 6.26; N, 12.29.

8-Chloro-2-ethoxycarbonyl-10-*N*-methoxycarbonyl-*N*-methylamino-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridine **14b**.

This compound was obtained from **7b** in 59% yield, mp 177-179° (ethyl acetate).

Anal. Calcd. for $C_{18}H_{20}ClN_3O_4$: C, 57.22; H, 5.34; N, 11.12. Found: C, 57.55; H, 5.50; N,11.08.

8-Chloro-2-ethoxycarbonyl-10-methoxycarbonylamino-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridine **14c**.

This compound was obtained from **7c** in 78% yield, mp 200-202° (methanol).

Anal. Calcd. for $C_{18}H_{20}FN_3O_4$: C, 59.83; H, 5.58; N, 11.63. Found: C, 59.92; H, 5.59; N, 11.62.

2-Ethoxycarbonyl-8-methoxy-10-*N*-methoxycarbonyl-*N*-methylamino-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridine **14d**.

This compound was obtained from **7d** in 71% yield, mp 135-137° (ethyl acetate).

Anal. Calcd. for $C_{19}H_{23}N_3O_5$: C, 61.11; H, 6.21; N, 11.25. Found: C, 61.13; H, 6.34; N, 11.34.

13-*N*-Methoxycarbonyl-*N*-methylamino-6,6a,7,8,9,10-hexahydro-12*H*-benzo[*b*]pyrido[1,2-*g*][1,6]naphthyridine **15a**.

This compound was obtained from **8a** in 66% yield, mp 139-141° (methanol); ^{1}H-nmr (DMSO-d_6): δ 7.95 (d, 1H, H-4), 7.71 (t, 1H, H-3), 7.69 (d, 1H, H-1), 7.57 (t, 1H, H-2), 3.92 and 3.88 (2d, 1H, H-12eq, J_{gem} 16 Hz), 3.75, 3.49, 3.47 (3s, 3H, OCH_3), 3.30 and 3.26 (2d, 1H, H-12ax, J_{gem} 16 Hz), 3.24-3.00 (m, 2H, H-6eq and H-10eq), 3.15 (s, 3H, NCH_3), 2.85 (dd, 1H, H-6ax), 2.35 (m, 1H, H-6a), 2.07 (bt, 1H, H-10ax), 1.87 (bd, 1H, H-7eq), 1.65 (m, 3H, H-8eq and H9), 1.28 (bt, 2H, H-7ax and H-8ax).

Anal. Calcd. for $C_{19}H_{23}N_3O_2$: C, 70.13; H, 7.12; N, 12.91. Found: C, 69.90; H, 7.00; N, 13.12.

2-Chloro-13-*N*-methoxycarbonyl-*N*-methylamino-6,6a,7,8,9,10-hexahydro-12*H*-benzo[*b*]pyrido[1,2-*g*][1,6]naphthyridine **15b**.

This compound was obtained from **8b** in 82% yield, mp 194-196° (ethyl acetate).

Anal. Calcd. for $C_{19}H_{22}ClN_3O_2$: C, 63.42; H, 6.16; N, 11.68. Found: C, 63.46; H, 6.19; N, 11.70.

2-Fluoro-13-*N*-methoxycarbonyl-*N*-methylamino-6,6a,7,8,9,10-hexahydro-12*H*-benzo[*b*]pyrido[1,2-*g*][1,6]naphthyridine **15c**.

This compound was obtained from **8c** in 58% yield, mp 169-171° (ethyl acetate).

Anal. Calcd. for $C_{19}H_{22}FN_3O_2$: C, 66.46; H, 6.46; N, 12.24. Found: C, 66.52; H, 6.66; N, 12.30.

2-Methoxy-13-*N*-methoxycarbonyl-*N*-methylamino-6,6a,7,8,9,10-hexahydro-12*H*-benzo[*b*]pyrido[1,2-*g*][1,6]naphthyridine **15d**.

This compound was obtained from **8d** in 72% yield, mp 151-153° (methanol).

Anal. Calcd. for $C_{20}H_{25}N_3O_3$: C, 67.58; H, 7.09; N, 11.82. Found: C, 67.66; H, 7.18; N, 11.67.

General Procedure for the Preparation of 10-Methylamino-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridines **16, 18a-d** and 13-Methylamino-6,6a,7,8,9,10-hexahydro-12*H*-benzo[*b*]pyrido[1,2-*g*][1,6]naphthyridines **17a-d**.

These compounds were obtained by hydrolysis with 20% potassium hydroxide of the *N*-methylcarbamates **13, 14** and **15**, following the same procedure previously described for compounds **9, 10** and **11**.

2-Benzyl-10-methylamino-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridine **16a**.

This compound was obtained from **13a** in 85% yield, mp 123-125° (ethanol); ^{1}H-nmr (DMSO-d_6): δ 8.16 (dd, 1H, H-9), 7.68 (dd, 1H, H-6), 7.51 (at, 1H, H-7), 7.34 (m, 6H, H-8 and phenyl protons), 5.91 (q, 1H, NH), 3.72 (s, 2H, benzyl CH_2), 3.65 (s, 2H, H-1), 3.03 (d, 3H, CH_3), 2.95 (t, 2H, H-3), 2.75 (t, 2H, H-4).

Anal. Calcd. for $C_{20}H_{21}N_3 \cdot H_2O$: C, 74.74; H, 7.21; N, 13.07. Found: C, 75.02; H, 7.24; N, 13.16.

2-Benzyl-8-chloro-10-methylamino-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridine **16b**.

This compound was obtained from **13b** in 71% yield, mp 133-135° (ethanol).

Anal. Calcd. for $C_{20}H_{20}ClN_3$: C, 71.10; H, 5.97; N, 12.44. Found: C, 71.29; H, 6.23; N, 12.68.

2-Benzyl-8-fluoro-10-methylamino-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridine **16c**.

This compound was obtained from **13c** in 67% yield, mp 128-130° (ethyl acetate).

Anal. Calcd. for $C_{20}H_{20}FN_3 \cdot 0.25H_2O$: C, 73.71; H, 6.34; N, 12.89. Found: C, 73.56; H, 6.42; N, 12.80.

2-Benzyl-8-methoxy-10-methylamino-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridine **16d**.

This compound was obtained from **13d** in 76% yield, mp 84-86° (methanol/diethyl ether).

Anal. Calcd. for $C_{21}H_{23}N_3O \cdot 1.5H_2O$: C, 69.98; H, 7.27; N, 11.66. Found: C, 69.94; H, 7.08; N, 11.70.

13-Methylamino-6,6a,7,8,9,10-hexahydro-12*H*-benzo[*b*]pyrido[1,2-*g*][1,6]naphthyridine **17a**.

This compound was obtained from **15a** in 66% yield, mp 100-102° (methanol/water); ^{1}H-nmr (DMSO-d_6): δ 8.17 (d, 1H, H-1), 7.68 (d, 1H, H-4), 7.50 (at, 1H, H-3), 7.29 (at, 1H, H-2), 5.88 (bq, 1H, NH), 3.94 (d, 1H, H-12eq, J_{gem} 15 Hz), 3.18 (d, 1H, H-12ax, J_{gem} 15 Hz), 3.10 (d, 3H, CH_3), 3.03 (bd, 1H, H-10eq, J_{gem} 15 Hz), 2.90 (dd, 1H, H-6eq, J_{gem} 15 Hz, J_{6eq-6a} 4 Hz) 2.64 (dd, 1H, H-6ax, J_{gem} 15 Hz, J_{6ax-6a} 11 Hz), 2.20 (m, 1H, H-6a), 2.05 (t, 1H, H-10ax, J_{gem} 15 Hz, $J_{10ax-9ax}$ 11 Hz), 1.78-1.47 (m, 4H, H-7eq, H-9 and H-8eq), 1.22 (m, 2H, H-7ax and H-8ax).

Anal. Calcd. for $C_{17}H_{21}N_3 \cdot 2H_2O$: C, 67.30; H, 8.31; N, 13.85. Found: C, 67.15; H, 8.02; N, 13.60.

2-Chloro-13-methylamino-6,6a,7,8,9,10-hexahydro-12*H*-benzo[*b*]pyrido[1,2-*g*][1,6]naphthyridine **17b**.

This compound was obtained from **15b** in 64% yield, mp 106-108° (methanol).

Anal. Calcd. for $C_{17}H_{20}ClN_3 \cdot 1.5H_2O$: C, 62.09; H, 7.05; N, 12.78. Found: C, 62.18; H, 6.78; N, 12.66.

2-Fluoro-13-methylamino-6,6a,7,8,9,10-hexahydro-12*H*-benzo[*b*]pyrido[1,2-*g*][1,6]naphthyridine **17c**.

This compound was obtained from **15c** in 59% yield, mp 200-203° dec (methanol).

Anal. Calcd. for $C_{17}H_{20}FN_3$: C, 71.55; H, 7.06; N, 14.73. Found: C, 71.28; H, 6.88; N, 14.66.

2-Methoxy-13-methylamino-6,6a,7,8,9,10-hexahydro-12*H*-benzo[*b*]pyrido[1,2-*g*][1,6]naphthyridine **17d**.

This compound was obtained from **15c** in 59% yield, mp 200-203° dec (methanol).

Anal. Calcd. for $C_{18}H_{23}N_3O$: C, 72.70; H, 7.80; N, 14.13. Found: C, 72.43; H, 7.99; N, 14.12.

10-Methylamino-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridine **18a**.

This compound was obtained from **14a** in 50% yield, hydrochloride mp 290-293° dec (ethanol); ^{1}H-nmr (base, DMSO-d_6): δ 8.20 (d, 1H, H-9), 7.69 (d, 1H, H-6), 7.48 (at, 1H, H-7), 7.28 (at, 1H, H-8), 5.99 (q, 1H, 10-NH), 3.90 (d, 2H, H-1), 3.05 (d, 3H, CH_3), 2.99 (m, 2H, H-3), 2.82 (t, 2H, H-4), 2.40 (m, 1H, 2-NH); ms: (m/z) 213 (M^+), 212, 198, 183.

Anal. Calcd. for $C_{13}H_{15}N_3 \cdot H_2O \cdot 2HCl$: C, 51.33; H, 6.30; N, 13.81: Found: C, 51.32; H, 6.29; N, 13.71.

8-Chloro-10-methylamino-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridine **18b**.

This compound was obtained from **14b** in 58% yield, mp 97-99° (methanol/diethyl ether).

Anal. Calcd. for $C_{13}H_{14}ClN_3 \cdot 1.5H_2O$: C, 56.83; H, 6.24; N, 15.29. Found: C, 56.98; H, 6.12; N, 15.03.

8-Fluoro-10-methylamino-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridine **18c**.

This compound was obtained from **14c** in 62% yield, mp 165-167° (ethyl acetate/*n*-hexane).

Anal. Calcd. for $C_{13}H_{14}FN_3 \cdot 2H_2O$: C, 58.41; H, 6.79; N, 15.72. Found: C, 58.18; H, 6.78; N, 15.66.

8-Methoxy-10-methylamino-1,2,3,4-tetrahydrobenzo-[*b*][1,6]naphthyridine **18d**.

This compound was obtained from **14d** in 65% yield, hydrochloride mp 209-212° dec (ethanol).

Anal. Calcd. for $C_{14}H_{17}N_3O \cdot H_2O \cdot 2HCl$: C, 50.31; H, 6.33; N, 12.57. Found: C, 50.60; H, 6.22; N, 12.29.

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