Methylamination of Some 3-Nitro-1,5-Naphthyridines with Liquid Methylamine / Potassium Permanganate

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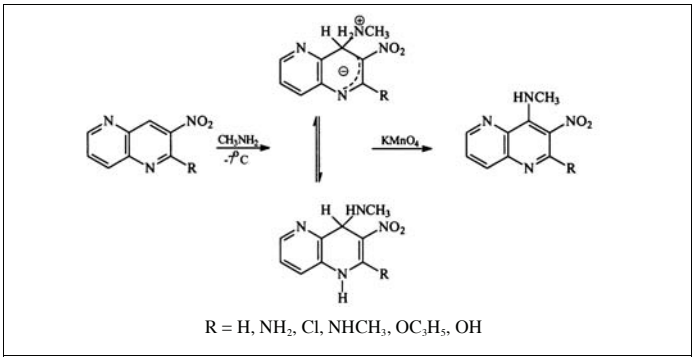

3-Nitro-1,5-naphthyridine and its 2-substituted derivatives (**1a**-**f**) are dehydro-methylaminated with a solution of potassium permanganate in liquid methylamine (LMA-PP) to the corresponding 4-methylamino-3-nitro-1,5-naphthyridines (**3a**-**e**). The intermediary 4-methylamino σ adducts of 2-R-3-nitro-1,5-naphthyridines (R = H, NH_2, Cl, $NHCH_3$, OC_2H_5, OH) (**2a**-**f**) are detected by ^{1}H nmr spectroscopy. The observed highly regioselective course of study reactions was confirmed by PM3 quantum chemical calculations of the reaction pathway. The calculations show satisfactory agreement between calculated and observed results. A convenient synthesis of 2-hydroxy- and 4-methylamino-3-nitro-1,5-naphthyridine are reported.

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Introduction.

Our interest in the reactivity of nitronaphthyridines towards nucleophilic agents induced us to study the reaction of methylamination of 3-nitro-1,5-naphthyridine and some of its 2-substituted derivatives. In a previous paper it has been reported that 3-nitro-1,5-naphthyridines, undergo amination using liquid ammonium and potassium permanganate as reagents in moderate yield [1]. The oxidative amination of 3-nitro-1,5-naphthyridines proceeds selectively in position 4. Similarly, the reaction of 3-nitro-1,6- and -1,8-naphthyridines [2,3] introduces the amino group into the *ortho* position relative to the nitro group in all cases. The mentioned reactions proceed *via* intermediate amino σ adducts, detected by ^{1}H nmr spectroscopy, which were then subsequently oxidized with $KMnO_4$ to the amino products [1-3]. Similarly, the high regioselectivity and excellent yields we observed in the reaction of 3-nitro-1,8-naphthyridines [4], using stronger nucleophile *i.e.* the liquid methylamine in presence potassium permanganate (LMA/PP). It can be expected that new methylamino derivatives of nitronaphthyridines synthesized in this manner will also show interesting biological and useful properties similar to methylamino-nitroquinolines, which are known as antiflammatory agents [5], cardiotonics [5] and hair-coloring compounds [6]. Therefore we are interested in study these reactions.

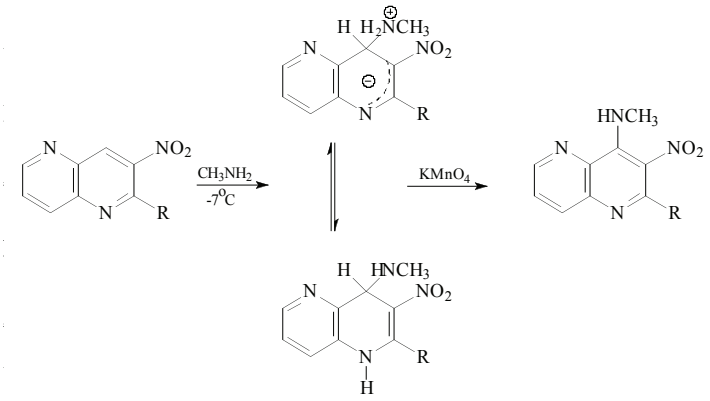
Results and Discussion.

The methylamination of 2-R-3-nitro-1,5-naphthyridines (R = H (**1a**), NH_2 (**1b**), Cl (**1c**), $NHCH_3$ (**1d**), OEt (**1e**), OH (**1f**)) was carried out at the boiling point (*ca.* -7 °C) of liquid methylamine in the presence of $KMnO_4$. The results obtained are compiled in Scheme 1. Nitronaphthyridines, applied as substrates, were obtained according to literature procedures, except of 2-hydroxy-3-nitro-1,5-naphthyridine (**1f**). The compound **1f** was prepared by the modification of the method described by Hart [7]. At the first step we carried out the acetylation of 2-amino-1,5-naphthyridine to 2-acetamido-1,5-naphthyridine and then nitration by mixture of fuming nitric acid and oleum (detail, see Experimental section) obtaining 2-hydroxy-3-nitro-1,5-naphthyridine (**1f**) with much better yield. Additionally the reference compound, 4-methylamino-3-nitro-1,5-naphthyridine (**3a**) was obtained from 4-chloro-3-nitro-1,5-naphthyridine [8].

Methylamination of unsubstituted 3-nitro-1,5-naphthyridine (**1a**) with LMA/PP affords 4-methylamino-3-nitro-1,5-naphthyridine (**3a**) with good yield (75%). The structure of this compound was determined by comparison properties (mp., R_f and ir) with the reference sample **3a** which was prepared independently.

2-Amino-3-nitro-1,5-naphthyridine (**1b**) undergoes with LMA/PP dehydro-methylamination in position 4 to give

Scheme 1



1 σ adduct **2** **3**

1a R = H
1b R = NH_2
1c R = Cl
1d R = $NHCH_3$
1e R = OC_2H_5
1f R = OH

3a R = H (75%)
3b R = NH_2 (70%)
3c R = $NHCH_3$ (76%) + **1d** (10%)
3c R = $NHCH_3$ (81%)
3d R = OC_2H_5 (40%)
3e R = OH (52%)

4-methylamino-3-nitro-1,5-naphthyridine (**3b**) with good yield (70%).

The reaction of 2-chloro-3-nitro-1,5-naphthyridine (**1c**) with LMA/PP gives, as the main product 2,4-bis(methylamino)-3-nitro-1,5-naphthyridine (**3c**) with fair yield and some 2-methylamino-3-nitro-1,5-naphthyridine (**1d**). Besides the dehydro-methylamination in the position 4, the dechloro-methylamination in position 2 takes place also. In this reaction we could not detect any traces of 2-chloro-4-methylamino-3-nitro-1,5-naphthyridine.

The results above reaction are explained below, discussing the ^{1}H nmr spectra of methylamino σ adduct **2c** and are confirmed by quantum-chemical calculations.

Amination of 2-methylamino-3-nitro-1,5-naphthyridine (**1d**) with LMA/PP affords 2,4-bis(methylamino)-3-nitro-1,5-naphthyridine (**3c**) with excellent yields (81%).

Treatment of 2-ethoxy-(**1e**) and 2-hydroxy-3-nitro-1,5-naphthyridine (**1f**) with LMA/PP affords 2-ethoxy-4-methylamino- (**3d**) and 2-hydroxy-4-methylamino-3-nitro-1,5-naphthyridine (**3e**) in moderate yield, respectively. In both cases the small amount of starting material were recovered.

To confirm the mechanism of oxidative dehydro-methylamination (Scheme 1) we detected intermediary covalent σ adducts, like **2**, by ^{1}H nmr spectroscopy and determined their structures.

We measured the ^{1}H nmr spectra of methylamino σ adducts of 3-nitro-1,5-naphthyridines (**2a**-**f**) in liquid methylamine at -15 °C and the results are given in Table 1.

Comparison of σ adducts **2a**-**f** spectra with that of the corresponding compounds **1a**-**f** in neutral solvents (DMSO-d_6) shows that all the protons signals are shifted upfield. In all cases especially the upfield shift of 4-H is considerable (Δδ = 3.16 - 3.87) due to the C-4 rehybrydization from sp^2 in the nitronaphthyridines to sp^3 on adduct formation into their 4-methylamino-covalent σ adducts (see Table 1). The values of shift (Δδ) are in agreement with those reported earlier in related systems and are usually in the range of 2.55 - 4.61 ppm [9].

In the ^{1}H nmr spectrum of the solution of 3-nitro-1,5-naphthyridine (**1a**) in liquid methylamine was observed a signal in high-field region at δ = 5.32 that indicates formation of the intermediate σ adduct by addition of methylamine to the C-2 or C-4 position. Additionally to assign unequivocally, we measured the ^{1}H nmr spectra of 2-deuterio-3-nitro-1,5-naphthyridine (**1a'**) in the same conditions. In both spectra of **2a** and **2a'** we observed the signals in high-field at δ = 5.32. The signal at δ = 8.68 was only observed in the case of **2a**. These observations confirmed the structure of 4-methylamino σ adduct (**2a**) of 3-nitro-1,5-naphthyridine (**1a**).

The ^{1}H nmr spectra of methylamino σ adduct (**2c**) of 2-chloro-3-nitro-1,5-naphthyridine (**1c**) shows that addition of the methylamino group occurs at the C-4 position giving a signal from 4-H in high-field region at δ = 5.38 ppm (Δδ =

Table 1
^{1}H NMR data of some 3-nitro-1,5-naphthyridines (**1a-f**) and their 4-methylamino σ adducts (**2a-f**). [a]

Compound	Solvent	Chemical shifts δ (ppm)				
		2-H	4-H	6-H	7-H	8-H
3-nitro-1,5-naphthyridine (**1a**)	DMSO-d_6	9.66	9.17	9.21	8.01	8.60
4-methylamino σ adduct of **1a** (**2a**)	CH_3NH_2	8.68	5.32	8.24	7.21	7.57
	Δδ	0.98	3.85	0.97	0.80	1.03
2-amino-3-nitro-1,5-naphthyridine (**1b**)	DMSO-d_6	-	8.88	8.71	7.66	7.93
4-methylamino σ adduct of **1b** (**2b**)	CH_3NH_2	-	5.25	8.01	7.12	7.30
	Δδ	-	3.63	0.70	0.54	0.63
2-chloro-3-nitro-1,5-naphthyridine (**1c**)	DMSO-d_6	-	9.25	9.19	8.02	8.52
4-methylamino σ adduct of **1c** (**2c**)	CH_3NH_2	-	5.38	8.26	7.25	7.50
	Δδ	-	3.87	0.93	0.77	1.02
2-methylamino-3-nitro-1,5-naphthyridine (**1d**)	DMSO-d_6	-	8.87	8.70	7.68	8.08
4-methylamino σ adduct of **1d** (**2d**)	CH_3NH_2	-	5.23	7.97	7.07	7.28
	Δδ	-	3.64	0.73	0.61	0.80
2-ethoxy-3-nitro-1,5-naphthyridine (**1e**)	DMSO-d_6	-	8.46	8.79	7.68	8.16
4-methylamino σ adduct of **1e** (**2e**)	CH_3NH_2	-	5.30	8.08	7.16	7.38
	Δδ	-	3.16	0.71	0.52	0.78
2-hydroxy-3-nitro-1,5-naphthyridine (**1f**)	DMSO-d_6	-	8.75	8.63	7.68	7.76
4-methylamino σ adduct of **1f** (**2f**)	CH_3NH_2	-	5.37	8.12	7.14	7.21
	Δδ	-	3.38	0.51	0.54	0.55

[a] The spectra were measured in liquid CH_3NH_2 at -15°C.

3.87) (Table 1). Despite the rapid formation of the 4-methylamino σ adduct from **1c**, the corresponding 2-chloro-4-methylamino product could not be obtained. Apparently the nucleophilic displacement of the highly labile chloro atom at C-2 by $NHCH_3$ takes place more rapidly than the oxidative amination at C-4.

In order to explain the highly regioselective course of the studied reactions, we carried out quantum-chemical calculations for the S_NH methylamination reactions of 3-nitro-1,5-naphthyridines (**1a-f**) using the PM3 method. We calculated heats of formation (ΔH) of the ground state of the reaction system (**1**+CH_3NH_2) and of the intermediate σ adducts **2a-f** and transition state (TS) for the position C-4 (**1a-f**) and C-2 (**1a**, **1c**). Additionally we calculated the energy of activation $\Delta H^{\#}$ for the reactions studied (see Table 2) [10].

Table 2

Results of PM3 calculations : geometry [a] and heats of formation of the ground-state of the reaction system (**1**+ CH_3NH_2), transition state (TS), intermediary structures (σ adducts) of **2a-f** [b] and energy of activation $\Delta H^{\#}$.

Structure	**1**+CH_3NH_2		Transition State (TS)			σ Adduct (**2**)		Energy of Activation
	ΔH [kcal/mol]	r_1 [Å]	ΔH [kcal/mol]	r_2 [Å]		ΔH [kcal/mol]	r_3 [Å]	$\Delta H^{\#}$ [kcal/mol]
1a	39.59	4.19	-	-	C-2	55.02	1.75	-
	39.63	3.75	49.69	2.06	C-4	45.58	1.62	10.10
1b	36.71	4.91	45.98	2.09	C-4	41.07	1.62	9.27
1c	36.24	4.89	49.59	1.94	C-2	45.75	1.58	13.35
	36.63	4.55	45.91	2.09	C-4	40.86	1.61	9.24
1d	36.72	4.26	45.96	2.09	C-4	41.21	1.61	9.24
1e	-4.74	3.55	5.83	2.07	C-4	1.61	1.61	10.57
1f	-7.15	3.53	3.20	2.09	C-4	-2.14	1.61	10.35

[a] r_1, r_2, r_3 - The distance between the unsubstituted carbon atom C-2 and C-4 in **1**, TS and **2** respectively and N atom in CH_3NH_2.
[b] The result of calculations were corrected for temperature 266

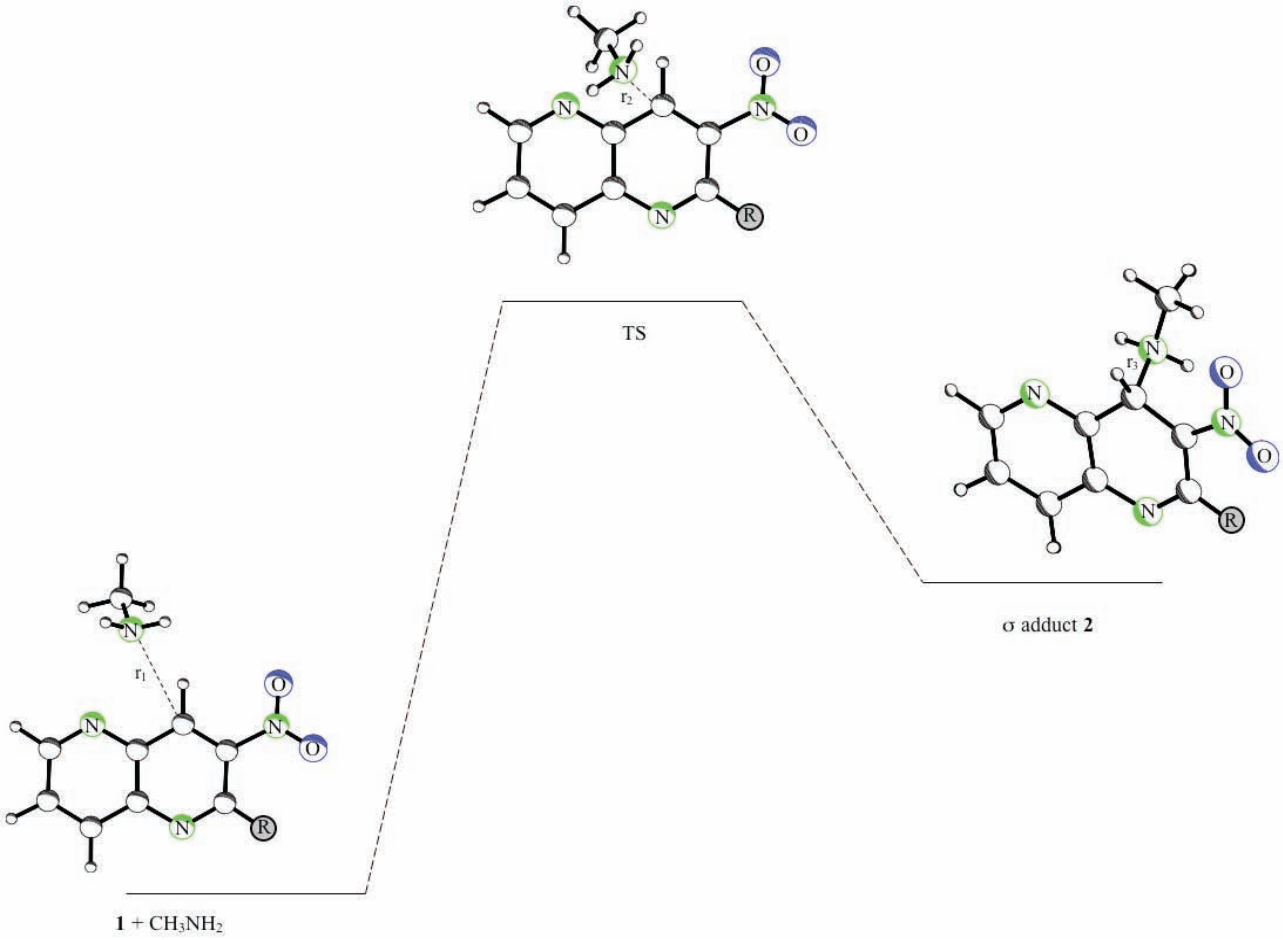


Figure 1. PM3 results for pathway from **1** to **2**; R = H, NH_2 , Cl, $NHCH_3$, OC_2H_5, OH; details are given in Table 2.

Figure 1 presents the reaction pathway from **1** to **2** obtained by calculations with PM3 method.

For comparison, we have tried to calculate the transition state and heats of formation of σ adducts for the other unsubstituted positions C-6, C-7 and C-8 in **1a**-**f**. However, we were unable to find and optimized these values using the same method as for the pathways of 3-nitro-1,8-naphthyridines with methylamine, published by us earlier [4]. In case of 3-nitro-1,5-naphthyridine (**1a**) one would expect the susceptibility for attack by nucleophiles to be equal at the C-4 and C-2 positions, *ortho* position to NO_2 group. However, quantum-chemical calculations show substantially lower heats of formation for σ adducts at C-4 position such that it excludes the possibility of nucleophilic substitution at C-2 position. Likewise in the case of compound **1c**, with labile substituent chloro atom at the C-2 position, it was observed that the heats of formation of the σ adducts and the energy of activation ($\Delta H^{\#}$) are 4.9 and 4.11 kcal/mol respectively lower at C-4 than at the C-2 position (see Table 2). These results, as well as those of the ^{1}H nmr spectra and quantum chemical calculations indicate that dehydro-methylamination takes place before dechloro-methylamination but not the reverse.

These results explain the mode of formation of 2,4-bis(methylamino)-3-nitro-1,5-naphthyridine (**3c**) as the main product of the methylamination reaction of **1c**.

The PM3 calculations confirm the regioselectivity of methylamination of 3-nitro-1,5-naphthyridines (**1a**-**e**) and correlate well with experimental results.

In conclusion, all the results of the experimental data, the ^{1}H NMR study of the intermediate methylamino σ adducts and quantum chemical calculations indicate, that the C-4 position of the 3-nitro-1,5-naphthyridines is strongly favoured for nucleophilic attack of the methylamine. These results confirm the regioselectivity of the oxidative methylamination reaction.

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EXPERIMENTAL

Melting points (uncorrected) were determined on a Boetius apparatus. The ^{1}H nmr spectra were recorded on Tesla BS-587A (80 MHz) and on a Varian Mercury 300 (300 MHz) spectrometers using TMS as an internal standard; the chemical shifts are given in ppm (δ); and coupling constants are taken from the expanded spectra. The infrared spectra were recorded on Bio-Rad FTS-175C spectrophotometer (in potassium bromide pellets). The mass spectra (EI) were recorded on LKB GC/MS 9000 spectrometer at 70 eV. The reaction products were monitored by TLC on Merck Silica gel 60 PF 254. Silica gel (Merck, 230-400 mesh) was used for column chromatography; preparative thin-layer chromatography (PTLC) was carried out on standard plate (20 x 40). Quantum-chemical calculations were carried out with PM3 method using MOPAC program (version 6.00).

Synthesis of Starting and Reference Compounds.

3-Nitro- (**1a**) [8], 2-deuterio-3-nitro- (**1a′**) [1], 2-amino-3-nitro- (**1b**) [1], 2-chloro-3-nitro- (**1c**) [1], 2-methylamino-3-nitro- (**1d**) [11], 2-ethoxy-3-nitro-1,5-naphthyridine (**1e**) [12] were prepared according literature procedures.

Synthesis of 2-Hydroxy-3-nitro-1,5- naphthyridine (**1f**).

A solution of 2-amino-1,5-naphthyridine (2.0 g, 13.8 mmol) in 20 mL acetic anhydride and 20 mL glacial acetic acid was refluxed for 2 h. A resulting brown solution was cooled and slowly poured onto *ca*. 50 g of ice with a small volume of water. The precipitate was collected by filtration and dried to give 2.37 g (80%) as a light-brown solid. Recrystallization from methanol afforded 2.12 g (72%) of 2-acetamido-1,5-naphthyridine, cream-colored crystals mp 210 °C; - ms: *m/z* (%): 187 (M^+, 100), 172 (M^+-CH_3), 145 (M^+-$COCH_3$); ^{1}H nmr (DMSO-d_6): δ 10.97 (s, NH), 8.88 (dd, 6H), 8.60 - 8.17 (m, 3H, 4H, 8H), 7.74 (q, 7H), 2.19 (s, CH_3). $J_{6,8}$ = 1.46 Hz, $J_{6,7}$ = 4.15 Hz, $J_{7,8}$ = 8.54 Hz; ir: 3243 (NH), 3100-3500 (br., H_2O), 1675 (C=O) cm^{-1}.

Anal. Calcd. for $C_{10}H_9N_3O•1.5H_2O$ (214.21): C, 56.07, H, 5.65, N, 19.62. Found: C, 56.16, H, 5.66, N, 19.56.

A solution of 2.0 g, (9.3 mmol) of 2-acetamido-1,5-naphthyridine in 18 mL of fuming nitric acid (d 1.51) and 18 mL of 35% oleum (sulfuric acid) was heated on a water bath for 4 h. Pouring the cooled solution onto *ca*. 120 g of ice gave yellow-orange crystals. The precipitate was collected by filtration, washed with cold water and dried. Crystallization from aqueous methanol (1:1) gave 1.64 g (92%) of 2-hydroxy-3-nitro-1,5-naphthyridine (**1f**), yellow needles, mp 273 -275 °C (lit. 272-274 °C [7]). The compound proved to be identical (mp, ir, ^{1}H nmr) as prepared according to literature procedures [7].

Synthesis of 4-Methylamino-3-nitro-1,5-naphthyridine (**3a**).

4-Chloro-3-nitro-1,5-naphthyridine (**1g**) [8] (0.1 g, 0.48 mmol) was dissolved in 20 mL of methanol saturated at 0 °C, with gaseous methylamine. The solution was kept at room temp. for 24 h. After cooling, the yellow crystalline precipitate was collected by filtration, washed with cold methanol, dried to give 76 mg (78%) of **3a** as orange needles with mp 208-210 °C; ms; *m/z* (%): 204 (M^+, 15), 187 (M^+-OH, 40); ^{1}H nmr (DMSO-d_6): δ 9,08 (s, 2H), 8,89 (dd, 6H), 8.28 (dd, 8H), 7.84 (q, 7H), 3.42 (d, CH_3, NH), $J_{6,7}$ = 3.78 Hz, $J_{6,8}$ = 1,46 Hz, $J_{7,8}$ = 8.18 Hz, $J_{CH3,NH}$ = 5.0 Hz; ir: 3208 (NH), 1497 (NO_2, as), 1329 (NO_2, s) cm^{-1}.

Anal. Calcd. for $C_9H_8N_4O_2$ (204.19): C, 52.94, H, 3,95, N, 27.44. Found: C, 52.66, H, 3.84, N, 27.15.

Amination of 3-Nitro-1,5-naphthyridines (**1a-f**) with Methylamine/ Potassium Permanganate.

General Procedure.

To 25 - 30 mL of liquid methylamine 0.1 g (0.46-0.57 mmol) of 3-nitro-1,5-naphthyridines (**1a**-**f**) and 0.2 g of potassium permanganate were added and the resulting mixture was stirred at -7 °C for 0.5 -1 h. After evaporation of methylamine *ca*. 30 mL of water was added to the residue and the mixture was extracted continuously with chloroform for 20 h. The residue obtained after evaporation of the solvent from the extract was worked up in the manner described below.

Methylamination of 3-Nitro-1,5-naphthyridine (**1a**).

Compound **1a** (0.1 g, 0.57 mmol) was treated according to the general procedure. The residue was crystallized from methanol to give 0.087 g (75%) of 4-(methylamino)-3-nitro-1,5-naphthyridine (**3a**) as orange needles with mp 207-208 °C. The compound showed the identical properties (mp, ir and ^{1}H nmr) to those of reference sample.

Methylamination of 2-Amino- 3-nitro-1,5-naphthyridine (**1b**).

Compound **1b** (0.1 g, 0.53 mmol) was treated according to the general procedure. The residue was crystallized from methanol to give 0.081 g (70%) of 2-amino-4-methylamino-3-nitro-1,5-naphthyridine (**3b**) as orange needles with mp 222-223 °C; ms: *m/z* (%): 219 (M^+, 38), 202 (M^+-OH, 100); ^{1}H nmr ($CDCl_3$): δ 8.44 (dd, 6H), 7.73 (dd, 8H), 7.45 (q, 7H), 6.41 (br.s, NH_2), 3.49 (s, CH_3, NH), $J_{6,7}$ = 3.91 Hz, $J_{6,8}$ = 1,46 Hz, $J_{7,8}$ = 8.54 Hz; ir: 3433, 3126 (NH_2), 3271 (NH), 1527 (NO_2,as), 1326 (NO_2, s) cm^{-1}.

Anal. Calcd. for $C_9H_9N_5O_2$ (219.19): C, 49.32, H, 4.14, N, 31.95. Found: C, 48.95, H, 3.97, N, 31.57.

Methylamination of 2-Chloro-3-nitro-1,5-naphthyridine (**1c**).

Compound **1c** (0.1 g, 0.48 mmol) was treated according to the general procedure. The residue was separated by PTLC using chlorofom as the eluent. The band obtained was extracted with chloroform in a Soxhlett apparatus for 4 h. From the first band (the highest R_f), 0.084 g (76%) of 2,4-bis(methylamino)-3-nitro-1,5-naphthyridine (**3c**) was obtained, after the crystallization from octane as orange needles with mp 182-183 °C; ms: m/z (%): 233 (M^+, 46), 216 (M^+-OH, 100); ^{1}H nmr (DMSO): δ 8.86 (br.s, NH), 8.43 (dd, 6H), 7.78 (dd, 8H), 7.57 (q, 7H), 7.45 (br.s, NH), 2.94 (d, CH_3, NH), 2.88 (d, CH_3, NH), $J_{6,7}$ = 4.10 Hz, $J_{6,8}$ = 1,54 Hz, $J_{7,8}$ = 8.46 Hz, $J_{CH3,NH}$ = 5.64 Hz, $J_{CH3,NH}$ = 4.36 Hz; ir: 3392, 3203 (NH), 1528 (NO_2, as), 1335 (NO_2, s) cm^{-1}.

Anal. Calcd. for $C_{10}H_{11}N_5O_2$ (233.2): C, 51.49, H, 4.75, N, 30.03. Found: C, 51.22, H, 4.65, N, 29.93.

The residue from the extracts of the second band (the lowest R_f) was washed with diethyl ether to give 0.010 g (10%) of 2-methylamino-3-nitro-1,5-naphthyridine (**1d**) [11].

Methylamination of 2-Methylamino-3-nitro-1,5-naphthyridine (**1d**).

Compound **1d** (0.1 g, 0.5 mmol) was treated according to the general procedure. The residue was crystallized from octane to

give 0.092 g (81%) of 2,4-bis(methylamino)-3-nitro-1,5-naphthyridine (**3c**) as orange needles with mp 182-183 °C. The compound showed identical properties (mp, ir, ^{1}H nmr) to **3c** obtained from **1c**.

Methylamination of 2-Ethoxy-3-nitro-1,5-naphthyridine (**1e**).

Compound **1e** (0.1 g, 0.46 mmol) was treated according to the general procedure. The residue was separated by column chromatography using chloroform as eluent. The first fraction was washed with hexane to yield 0.045 g (40%) of 2-ethoxy-4-methylamino-3-nitro-1,5-naphthyridine (**3d**) as yellow crystals with mp 103-105 °C; ms: m/z (%): 248 (M^+, 72), 231 (M^+-OH, 100); ^{1}H nmr ($CDCl_3$): δ 8.55 (dd, 6H), 7.98 (dd, 8H), 7.53 (q, 7H), 7.47 (br.,s, NH), 4.54 (q, CH_2), 3.04 (d, CH_3, NH), 1.41 (t, CH_3), $J_{6,7}$ = 4.15 Hz, $J_{6,8}$ = 1,59 Hz, $J_{7,8}$ = 8.42 Hz, J_{C2H5} = 7.08 Hz, J_{CH3NH} = 5.86 Hz; ir: 3340 (NH), 1505 (NO_2, as), 1338 (NO_2, s) cm^{-1}.

Anal. Calcd. for $C_{11}H_{12}N_4O_3$ (248.23): C, 53.22, H, 4.87, N, 22.57. Found: C, 52.93, H, 4.79, N, 22.33.

The second fraction gave 0.030 g of recovered starting material.

Methylamination of 2-Hydroxy-3-nitro-1,5-naphthyridine (**1f**).

Compound **1f** (0.1 g, 0.52 mmol) was treated according to the general procedure. The residue was separated by column chromatography using chloroform/methanol (9:1) as eluent. From the first fraction 0.060 g (52%) of 2-hydroxy-4-methylamino-3-nitro-1,5-naphthyridine (**3e**) was obtained as yellow needles with mp 275-277 °C; ms: m/z (%): 220 (M^+, 73), 203 (M^+-OH, 30); ^{1}H nmr ($CDCl_3$): δ 11.50 (br., s, OH) 8.50 (dd, 6H and br.,s, NH), 7.67 (d, 7H and 8H) (deceptive simplicity), 2.84 (d, CH_3, NH), J_{CH3NH} = 5.36 Hz; ir: 3299 (NH), 1527 (NO_2, as), 1326 (NO_2, s) cm^{-1}.

Anal. Calcd. for $C_9H_8N_4O_3$ (220.17): C, 49.50, H, 3.66, N, 25.48. Found: C, 49.15, H, 3.75, N, 25.17.

REFERENCES AND NOTES

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[10] The PM3 method was used for the semiempirical MO calculations using the MOPAC (version 6) molecular orbital package. The starting geometry's and intermediary structures were obtained from the corresponding molecular models, fully optimized using keyword PRECISE. The transition states TS were calculated using SADDLE subroutine. An NLLSQ procedure was used for gradient optimization (<0.1 kcal/mol/Å), Calculations were performed until at least one negative Hessian was obtained. The THERMO procedure was used to correct the results of calculations for temperature 266 K.

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