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# On the reactivity of 4-cyano-1,3-dichloro-7-methyl-5,6,7,8-tetrahydro-2,7-naphthyridine with several amines in different experimental conditions: monosubstitution, disubstitution, and a new unexpected rearrangement

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This article is dedicated to the memory of Professor Alan R. Katritzky (1928–2014; firstly Full Professor at the East Anglia University and then Kenan Professor of Organic Chemistry at the Florida University). ARK has been for more than 50 years the big 'Magister' in the field of Heterocyclic Chemistry: his lectures, everywhere in the world, have been able to open new horizons to the audiences

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5,6,7,8-Tetrahydro-2,7-naphthyridines
Mono- and di-amino 2,7-naphthyridines
1-Oxo-3,4-dihydro-2,7-naphthyridines
Nucleophilic substitution
Ring-into-ring rearrangement

ABSTRACT

The reactivity of 4-cyano-1,3-dichloro-7-methyl-5,6,7,8-tetrahydro-2,7-naphthyridine **1** with nucleophiles has been investigated. The different reactivity of the two chlorine atoms in **1** enabled us to obtain, by using different experimental conditions, the mono- and the di-amino-substituted derivatives of 5,6,7,8-tetrahydro-2,7-naphthyridines **2** and **3**, respectively. Thus, by carrying out the reaction in a low-boiling solvent and in the presence of a quasi-stoichiometric amount of amine, the mono-substituted derivatives **2** were obtained, which under harsher conditions was transformed into the diamino derivatives **3** when using an excess of amine. During the synthesis of some diamino derivatives **3** a new rearrangement was observed with formation of 1-oxo derivatives of 3,4-dihydro-2,7-naphthyridines **4**. The structure of the unexpected compounds **4** was confirmed by X-ray crystallography. A mechanism for the rearrangement is tentatively suggested.



## 1. Introduction

The study of the derivatives of five- and six-membered heterocycles containing nitrogen represents a 'key' field in the study of organic and biological chemistry.[1] Their involvements in life processes, their pharmacological activities, their large use as intermediates in organic syntheses, and their variegated reactivity make the study of properties of these compounds an attractive

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research field. In this research area we have been involved in the study of the reactivity of several five- and six-membered nitrogen-containing derivatives.[2,3]

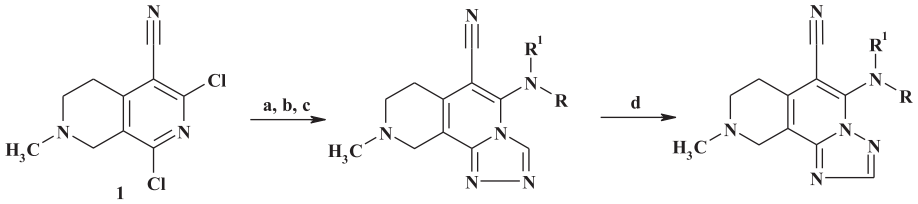
Recently some of us have examined the reactivity of 1,3-dichloro-4-cyano-7-methyl-5,6,7,8-tetrahydro-2,7-naphthyridine with some nucleophiles.[4–8] As a matter of fact this compound is a very interesting substrate: it is decorated by several functional groups (two chlorine atoms with different reactivity towards nucleophiles, a cyano group, a pyridinic nitrogen, and a benzylic nitrogen), which in turn, reacting, for example, with nucleophiles could furnish new functional groups able to open the way to new heterocyclic systems. As a continuation of our previous studies we have reported the synthesis of several 5-amino-6-cyano-9-methyl-7,8,9,10-tetrahydro[1,2,4]triazolo[3,4-*a*]-2,7-naphthyridines and some 5-amino-6-cyano-9-methyl-7,8,9,10-tetrahydro[1,2,4]triazolo[5,1-*a*]-2,7-naphthyridines (Scheme 1) with excellent yields (average yield, ca. 83%).[4]

By lengthening the reaction times (5 h) we have extended the scope of the nucleophilic substitution on compounds **2a**, **b**, **g**. Several other amines were used, which gave the relevant 1,3-diamino-4-cyano-7-methyl-5,6,7,8-tetrahydro-2,7-naphthyridines (**3h**–**t**) again in very high yields (again, average yield, ca. 76%).

Thus, by exploiting the different reactivity with nucleophiles of chlorine atoms at C-1 and C-3 of the dichloro derivative **1** both the mono- and the di-amino derivatives (**2** and **3**, respectively) of 2,7-naphthyridines were obtained in either 'very high' or 'excellent' yields.

This easily controlled step by step substitution provided us the opportunity, by varying the substituent at C-1 of the naphthyridine ring, to synthesize a large number of derivatives of 2,7-naphthyridines (Scheme 2), which appear very promising from a biological point of view.

In spite of the apparent simplicity of the reactions, the compounds of series **3** were synthesized and isolated with some difficulty not only because the final products are easily soluble in a large number of solvents, but also because, in this kind of nucleophilic substitution, sometimes an unexpected process is observed, which does not lead to the expected products.




(a) $N_2H_4.H_2O$, MeOH; (b) $HC(OEt)_3$, reflux, 10 h; (c) NHRR¹, reflux, 2 h; (d) NHRR¹, reflux, 5 h

**Scheme 1.** From 1,3-dichloro-4-cyano-7-methyl-5,6,7,8-tetrahydro-2,7-naphthyridine **1** to some triazolonaphthyridines.

In the field of condensed heterocyclic compounds the 2,7-naphthyridine derivatives occupy an important place because of their very large spectrum of biological activity, as evidenced by the literature data[9–13] and by the results of some our investigations.[14–17]

## 2. Results and discussion

### 2.1. Synthesis of 1-amino and 1,3-diamino 4-cyano-7-methyl-5,6,7,8-tetrahydro-2,7-naphthyridines

Taking into account the above considerations we have now enlarged our interest to the study of the behavior of 1,3-dichloro-4-cyano-7-methyl-5,6,7,8-tetrahydro-2,7-naphthyridine **1** with nitrogen-nucleophiles [a series of amines (primary and secondary, cyclic and acyclic)] in different experimental conditions.[18]

Firstly we have tested the nucleophilic reactivity of **1** with some secondary cyclic amines and with a primary amine in quite smooth experimental conditions: i.e., by refluxing (5 h) in a low-boiling solvent (methanol) and using a quasi-stoichiometric substrate:-amine ratio (1:2.2; only a 10% excess has been used). In such a way we were able to realize the monosubstitution of chlorine at C-1, thus obtaining the relevant 1-amino-3-chloro-4-cyano-7-methyl-5,6,7,8-tetrahydro-2,7-naphthyridines (**2a**–**g**) with excellent yields (average yield, ca. 85%).

The next step was the examination of the nucleophilic reactivity of some monosubstituted products (**2a**–**c**) with some amines under harsher experimental conditions: i.e., by refluxing (30 min) in the absence of any solvent and using an excess of amine (substrate:amine ratio=1:5). Under these experimental conditions the substitution of the chlorine at C-3 was also achieved. As a result the relevant 1,3-diamino-4-cyano-7-methyl-5,6,7,8-tetrahydro-2,7-naphthyridines (**3a**–**g**) were obtained with very high yields (average yield ca. 76%).

For example, if at C-1 the chlorine atom was substituted by the cyclic amine pyrrolidine, as in **2a**, the subsequent substitution of the second chlorine atom by some primary amines (e.g., ethanolamine, in excess) in harsh experimental conditions (by 5 h refluxing) did not produce the target products **3a**, but the unexpected compound **4a** (Scheme 3).

For this reason we have deeply investigated this aspect of the reaction examining the behavior of some compounds **2** with different amines under variable experimental conditions to ascertain, which factors determine the occurrence of this new reaction.

A well chosen series of targeted experiments has allowed to understand that this new reaction is observed 'only' when: 1) the C-1 of the 2,7-naphthyridine ring is substituted by a cyclic amine, 2) the second amine substituting at the C-3 of the ring is a primary amine, 3) the boiling temperature of this primary amine is not lower than 145 °C.

In all the remaining cases (cyclic amine at C-1 and C-3; acyclic amine at C-1 and C-3, and acyclic amine at C-1 and cyclic amine at C-3; or reaction carried out at temperature lower than 145 °C) the substitution reaction to provide product **3** proceeds as usual and no unexpected rearrangement reaction was observed.

### 2.2. On the structure of compounds 4

To gain information about the structure of these unexpected products (e.g., **4b**) the $^1H$ NMR spectra of **4b** was examined. The presence of a one proton singlet at 5.34 ppm was observed, while the signal of the $CH_2$ group at C-8 seen in **3b** at 3.34 ppm was absent. Moreover the triplet of the NH group of **3b** in the region of 5.80 ppm was shifted to 9.12 ppm in **4b**.

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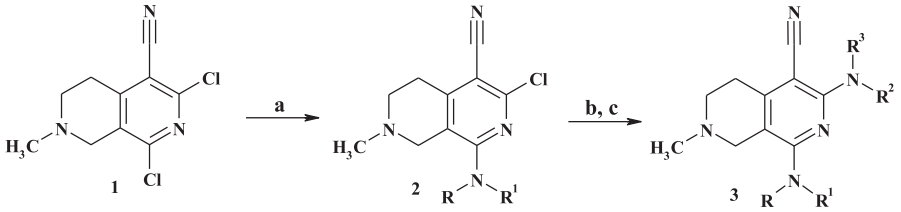

a: NHRR[1], MeOH, substrate:amine ratio 1:2.2, reflux 5 h; b: NHR[2]R[3], substrate:amine ratio 1:5, reflux 30 min; c: NHR[2]R[3], substrate:amine ratio 1:5, reflux 5 h

| Compound | R | $R^1$ | –N(R+$R^1$) | $R^2$ | $R^3$ | –N($R^2$+$R^3$) | Yield[a] (%) |
|---|---|---|---|---|---|---|---|
| **2a** | – | – |  | – | – | – | 85 |
| **2b** | – | – |  | – | – | – | 80 |
| **2c** | – | – |  | – | – | – | 83 |
| **2d** | – | – |  | – | – | – | 87 |
| **2e** | – | – |  | – | – | – | 84 |
| **2f** | – | – |  | – | – | – | 85 |
| **2g** | H | –$CH_2CH(OH)Me$ | – | – | – | – | 88 |
| **3a** | – | – |  | H | –$CH_2CH_2OH$ | – | 74 |
| **3b** | – | – |  | H | –$CH_2CH(OH)Me$ | – | 77 |
| **3c** | – | – |  | H | –$CH_2CH_2N(Et)_2$ | – | 72 |
| **3d** | – | – |  | H |  | – | 78 |
| **3e** | – | – |  | H | –$CH_2CH(OH)Me$ | – | 80 |
| **3f** | – | – |  | H | –$CH_2CH_2OH$ | – | 73 |
| **3g** | – | – |  | H | –$CH(Et)CH_2OH$ | – | 76 |
| **3h** | – | – |  | – | – |  | 74 |
| **3i** | – | – |  | – | – |  | 78 |
| **3j** | – | – |  | – | – |  | 75 |
| **3k** | – | – |  | – | – |  | 73 |
| **3l** | – | – |  | – | – |  | 81 |
| **3m** | – | – |  | H | –$CH_2CH_2CH(Me)_2$ | – | 77 |
| **3n** | – | – |  | H | –$CH_2CH_2NH_2$ | – | 72 |
| **3o** | – | – |  | H | –$CH_2CH_2N(Me)_2$ | – | 75 |
| **3p** | – | – |  | H | –$(CH_2)_3OMe$ | – | 81 |
| **3q** | – | – |  | H | –$(CH_2)_3N(Me)_2$ | – | 76 |
| **3r** | H | –$CH_2CH(OH)Me$ | – | H | –$CH_2CH(OH)Me$ | – | 79 |
| **3s** | H | –$CH_2CH(OH)Me$ | – | – | – |  | 75 |
| **3t** | H | –$CH_2CH(OH)Me$ | – | – | – |  | 77 |

[a] Isolated yields after recrystallization.

**Scheme 2.** Syntheses of 1-amino **2** and of 1,3-diamino **3** derivatives of 4-cyano-7-methyl-5,6,7,8-tetrahydro-2,7-naphthyridines.

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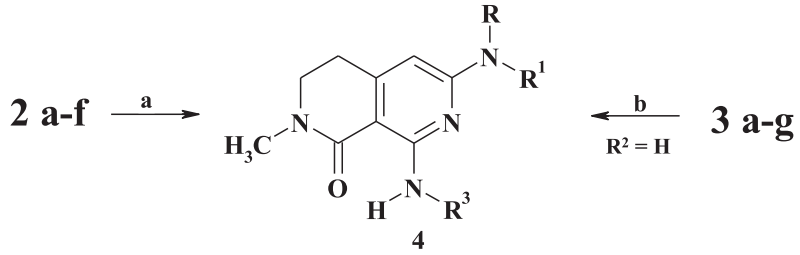
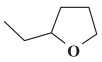
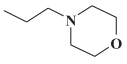
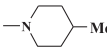
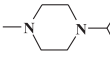



a: $NH_2R^3$, substrate:amine ratio 1:5, reflux 5 h; b: $NHR^2R^3$, substrate:amine ratio 1:5, reflux 4.5 h

| Compound | –N(R+R¹) | R³ | Yield[a] (%) | |
|---|---|---|---|---|
| | | | A method | B method |
| 4a |  | –$CH_2CH_2OH$ | 70 | 72 |
| 4b |  | –$CH_2CH(OH)Me$ | 73 | 76 |
| 4c |  | –$CH_2CH_2N(Et)_2$ | 72 | 75 |
| 4d |  |  | 70 | 72 |
| 4e |  | –$CH_2CH(OH)Me$ | 73 | 77 |
| 4f |  | –$CH_2CH_2OH$ | 71 | 75 |
| 4g |  | –$CH(Et)CH_2OH$ | 72 | 74 |
| 4h |  | –$CH(Et)CH_2OH$ | 70 | – |
| 4i |  | –$CH_2CH(OH)Me$ | 75 | – |
| 4j |  |  | 73 | – |
| 4k |  | –$CH_2CH(OH)Me$ | 71 | – |
| 4l |  | –$CH(Et)CH_2OH$ | 76 | – |
| 4m |  | –$CH_2CH_2OH$ | 74 | – |

[a] Isolated yields after recrystallization.

**Scheme 3.** Synthesis of 6,8-diamino-2-methyl-3,4-dihydro-2,7-naphthyridines **4**.

Looking at the IR spectrum, it was observed that the band of the nitrile group at 2220 $cm^{-1}$ was absent (this fact was confirmed also by the absence of the signal of nitrile group in the $^{13}C$ NMR spectrum: for example, compare the $^{13}C$ NMR spectra of **3b** and **4b**) while an absorption band at 1600 $cm^{-1}$ (suggesting the presence of a carbonyl group of amidic cyclic type) was present.

The data gave us some nice information on the structure of the obtained compound, indicating the presence of a cyclic system condensed with the pyridine ring and at the same time the 'disappearance' of the nitrile group and the 'appearance' of an amide group.

Moreover to gain further information about the structure of compounds **4** we have registered the mass spectra of some of them, in every case observing molecular weights 11 units lower than those of the expected compounds **3**.

For example, the MS calculated for 3-[(2-hydroxypropyl) amino]-7-methyl-1-pyrrolidin-1-yl-5,6,7,8-tetrahydro-2,7-naphthyridine-4-carbonitrile **3b** obtained from the relevant 3-chloro-7-methyl-1-pyrrolidin-1-yl-5,6,7,8-tetrahydro-2,7-naphthyridine-4-carbonitrile **2a** by short treatment (30 min) with 1-amino-2-propanol (see Section 4.4) furnished the expected value for the chemical formula $C_{17}H_{25}N_5O$ (MW 315).

In contrast, the product obtained from the same 3-chloro-7-methyl-1-pyrrolidin-1-yl-5,6,7,8-tetrahydro-2,7-naphthyridine-4-carbonitrile **2a** by treatment with 1-amino-2-propanol by long refluxing (5 h, see Section 4.6, method A) furnished an MS value in line with the chemical formula $C_{16}H_{24}N_4O_2$ (MW 304). This was consistent with structure **4b**.

With the aim of determining with certainty the structure of the compounds obtained X-ray crystallography was used. In two cases

suitable crystals were obtained and their structures analyzed. The obtained results (Fig. 1) clearly indicated that a rearrangement had occurred via a ring-opening at the level of the C-8/$C_{pyr}$ bond followed by a recyclization process occurring by addition onto the nitrile group.

According to the results reported in Section 2.1 compounds **3** are considering as starting point. Benzylic-like protons at C-8, linked to the pyridine ring and to N-7, show some acidic character, thus in the experimental conditions (an excess of primary amine is present) a proton abstraction from the methylene group could occur

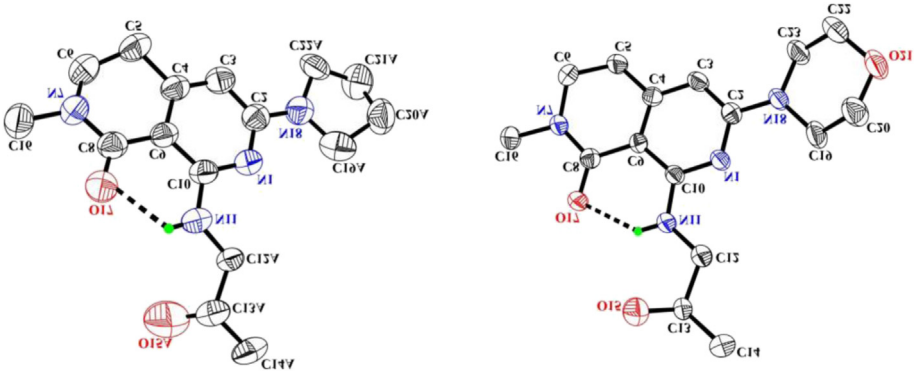


**Fig. 1.** Single crystals X-ray structures of compounds **4b** and **4e**, respectively.

The structure determined by X-ray analysis for **4b** (8-[(2-hydroxypropyl)amino]-2-methyl-6-pyrrolidin-1-yl-3,4-dihydro-2,7-naphthyridin-1(2*H*)-one) is in agreement with the above cited data collected by using MS, $^{1}$H, and $^{13}$C NMR, and IR data.

Interestingly, the large shift of the signal of the NH group observed in the $^{1}$H NMR spectra of **4b** could be related to the hydrogen bond arising from the interaction between the proton of the N–H group and the oxygen of the carbonyl.

The chemical structure of compounds **4** and their syntheses are reported in Scheme 3.

The structure of **4e** determined by X-ray analysis confirmed the previous observations.

### 2.3. NMR study on the formation of compounds 4

For a better understanding of the reaction course, the reaction mixture of compound **2b** and 1-amino-2-propanol was examined every 30 min starting from the beginning of the reaction till the end of it (5 h). The analysis showed that after 25–30 min only the product of substitution at C-3, that is, 3-[(2-hydroxypropyl)amino]-7-methyl-1-pyrrolidin-1-yl-5,6,7,8-tetrahydro-2,7-naphthyridine-4-carbonitrile **3b**, was present in the reaction mixture.

The rearrangement occurred only when the reaction mixture was heated further and the new compound **4b** appeared in gradually increasing quantity, while that of **3b** obviously decreased. After 5 h the rearrangement process was complete and only **4b** was present. The course of the reaction was followed by thin-layer chromatography while the quantitative analysis was performed by means of $^{1}$H NMR spectroscopy (Fig. 2).

Details of the $^{1}$H NMR analysis are shown in Figs. 3–5. The spectra reported in Figs. 3 and 4, recorded 30 min and 5 h after the start of the reaction are in agreement with the spectra of the compounds **3b** and **4b**, respectively. A spectrum collected 2 h after the beginning of the reaction (Fig. 5) showed the presence of both **3b** and **4b** (ca. 40 and 60%, respectively).

### 2.4. A hypothesis on the rearrangement mechanism

An attempt to describe and comment on the different steps of the rearrangement, following the hypothesis that the reaction occurred according to the tentative pathway in Scheme 4, is now reported.

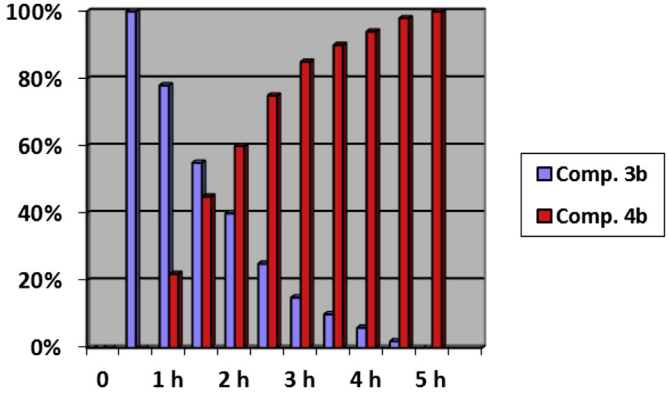



**Fig. 2.** Diagram of the change in the contents of the compounds **3b** and **4b** in the reaction mixture determined by $^{1}$H NMR spectroscopy.

followed by the breaking of the C-8/$C_{pyr}$ bond and then by a proton addition (a protonated primary amine or in the instance of the aminoalcohols their hydroxyls can act as acids) on the aromatic carbon of the pyridine ring (*path a*) with formation of the zwitterionic intermediate **A**.

This zwitterion could assume a proton from one of the acids present (see above) thus giving the indicated imminium cation **B** (*path b*). In the presence of the large excess of the primary amine, **B** could give (*path c*), by transamination (or by hydrolysis) and by rotation around the indicated C–C bond, the amine **C**, having the right geometry for a nucleophilic attack at the carbon of the nitrile group.

The attack (*path d*) was thermodynamically guided by the formation of a six-membered ring[1b] and furnished the cyclic ketimine **D**, which in turn, by hydrolysis gave the relevant cyclic amide **4** (*path e*).[19,20]

## 3. Conclusions

It has been found that the nucleophilic substitution with amines in the series of 1-amino-3-chloro-5,6,7,8-tetrahydro-2,7-naphthyridines **2** could proceed in different ways, depending on

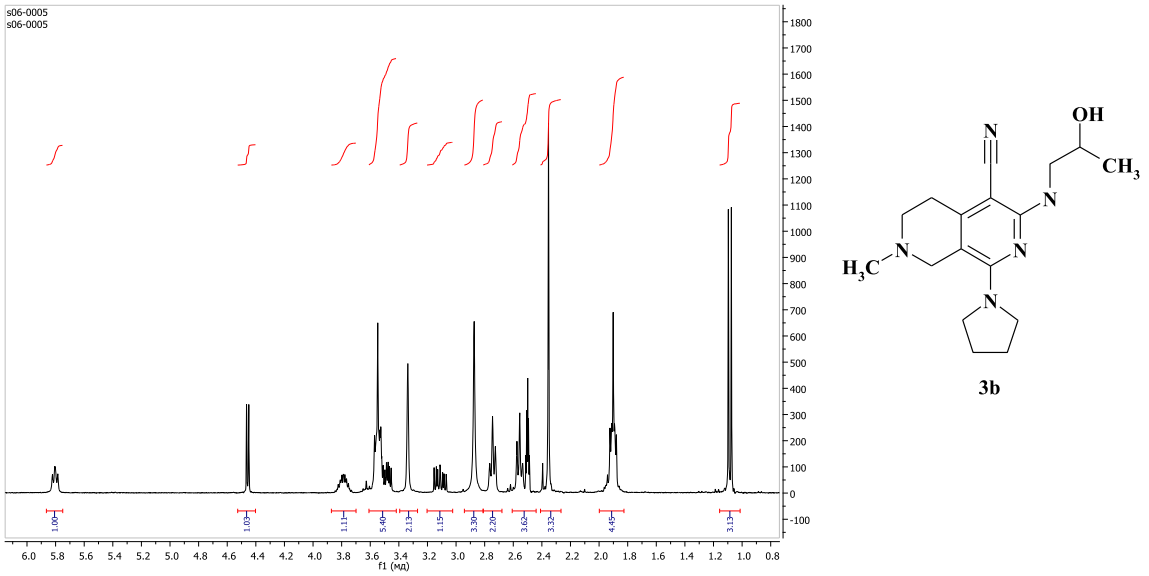



**Fig. 3.** $^{1}$H NMR spectrum of the compound **3b** 30 min after the beginning of the reaction.

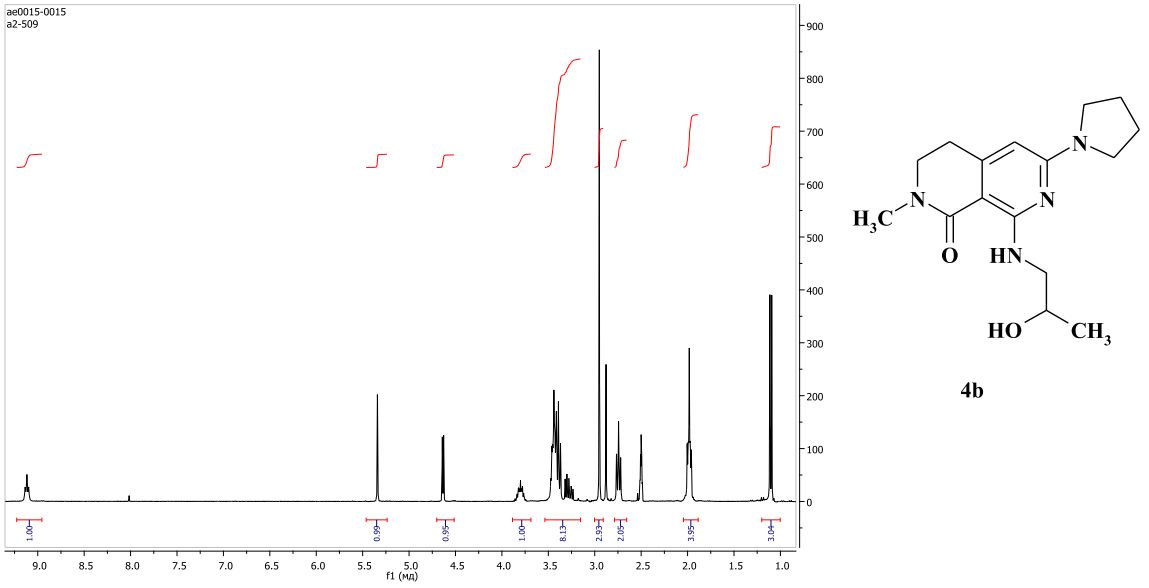



**Fig. 4.** $^{1}$H NMR spectrum of the compound **4b** 5 h after the beginning of the reaction.

the structure of **2** and on the nature of the used amines (see Schemes 2 and 3).

In some cases, a new and unexpected rearrangement was observed (see Scheme 3) with formation of derivatives of 2-methyl-3,4-dihydro-2,7-naphthyridin-1(2*H*)one **4**, which could be interesting from the biological point of view.

In fact, literature data showed that 1-oxo-2,7-naphthyridine could provide high biological activity[21,22] and this fact gives to this rearrangement a practical significance. The same compounds could be obtained in similar experimental conditions also from the relevant **3**.

A deep investigation of the course of the nucleophilic reaction on **2** and **3** revealed that the rearrangement could occur only when the three following conditions were satisfied: 1) the C-1 of the 2,7-naphthyridine ring must be substituted by a cyclic amine; 2) the amine at C-3 in **3** (or acting as nucleophile on **2**) must be a primary one; 3) the boiling points of the primary amine shall be above 145 °C. This last requirement suggests that the rearrangement process is characterized by a high activation energy barrier.

The structure of the unexpected compounds **4** obtained in the rearrangement has been confirmed by X-ray structural analysis and supported by MS, $^{1}$H, and $^{13}$C NMR, IR and elemental analysis.

It should be remarked that the average yield in all the processes (both nucleophilic substitutions and rearrangements) was from very good to excellent, ranging from 76 to 85%, while no process occurred with yield lower than 70%.

## 4. Experimental section

### 4.1. General

$^{1}$H and $^{13}$C NMR spectra were recorded in DMSO-$d_6$ solution (300 MHz for $^{1}$H and 75 MHz for $^{13}$C, respectively) on a Varian Mercury 300VX spectrometer. Chemical shifts are reported as

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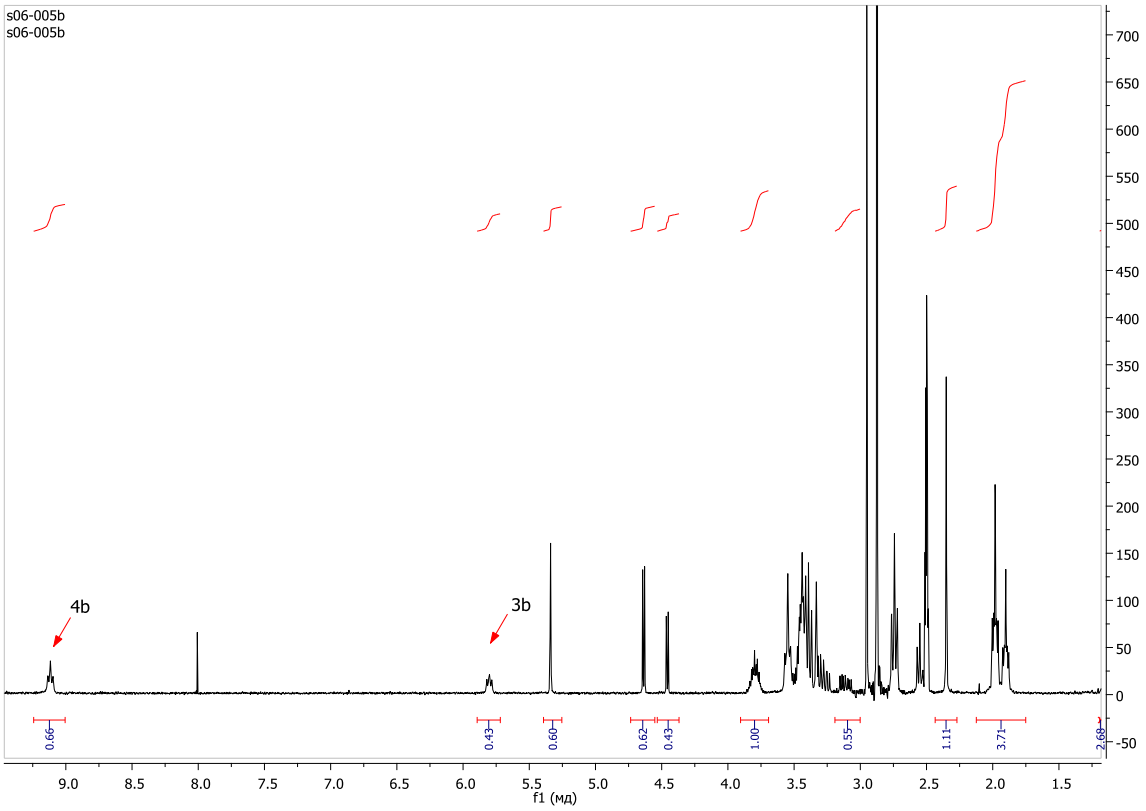
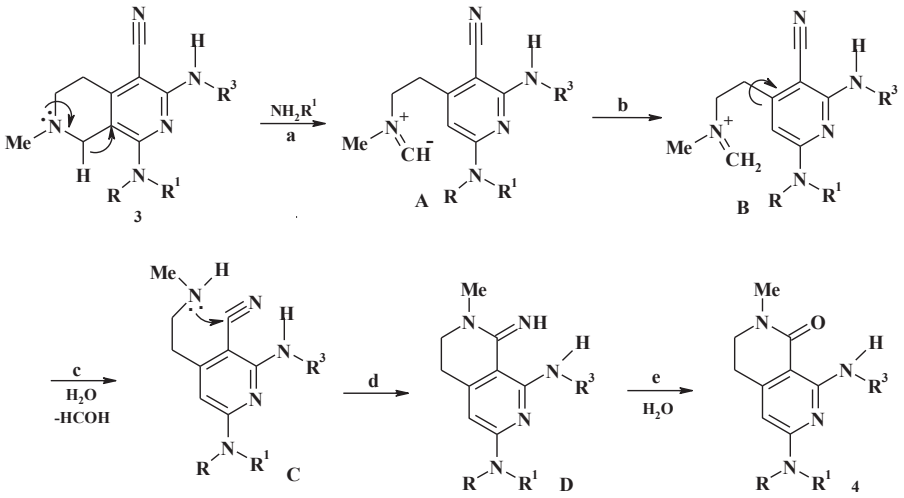



**Fig. 5.** $^1$H NMR spectrum of the mixture of the compounds **3b**+**4b** 2 h after the beginning of the reaction.



**Scheme 4.** Mechanism proposed for the synthesis of **4** from **3**.

$\delta$ (parts per million) relative to TMS as internal standard. IR spectra were recorded on Nicolet Avatar 330-FT-IR spectrophotometer and the reported wave numbers are given in cm$^{-1}$. Mass spectra (MS) were recorded on a spectrometer 'MX-1321A' with direct entry of matter into the ion source at ionization energy 60ev, $m/z$ ($I_{\text{отн, \%}}$). All melting points were determined in an open capillary and are uncorrected. Elemental analyses were performed on a Carlo Erba 1108 machine. Quoted values are in the range ±0.4% of the theoretical ones.

Crystallographic data for the structure of compounds **4b** and **4e** have been deposited with the Cambridge Crystallographic Data Center as supplementary publication for compound **4b** CCDC 885576 and for **4e** CCDC 884790. Copies of the dates can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax. +44-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

### 4.2. Procedure for the synthesis of compound 1

A mixture of 1,3-dihydroxy-7-methyl-5,6,7,8-tetrahydro-2,7-naphthyridine-4-carbonitrile[23] (20.5 g, 100 mmol) and phosphorus oxychloride (60 ml) was heated in a glass ampoule (180 ml) at

180 °C for 3 h. After cooling the mixture was poured onto ice and, with stirring, neutralized with a solution of potassium hydroxide (10%). The resulting crystals were filtered off, washed with water, dried, and recrystallized from ethanol.

*4.2.1. 1,3-Dichloro-7-methyl-5,6,7,8-tetrahydro-2,7-naphthyridine-4-carbonitrile (**1**).* A light-yellow solid; yield 71%; mp 132–134 °C; IR $\nu$/cm$^{-1}$: 2218 (CN). $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 2.48 (s, 3H, $CH_3$), 2.71 (t, $J$=5.7 Hz, 2H, NC$H_2$CH$_2$), 3.05 (tt, $J$=5.7, 1.3 Hz, 2H, NCH$_2$C$H_2$), 3.50 (t, $J$=1.3 Hz, 2H, NC$H_2$). Anal. Calcd for $C_{10}H_9Cl_2N_3$: C 49.61, H 3.75, N 17.36. Found: C 49.50, H 3.67, N 17.22%.

### 4.3. General procedure for the synthesis of compounds 2a–g

A mixture of dichloride **1** (1.21 g, 5 mmol) and the corresponding amine (11 mmol) in absolute methanol (30 ml) was refluxed for 5 h. The solvent was removed under vacuum and water (50 ml) was added. The separated crystals were filtered off, washed with water, dried, and recrystallized from ethanol.

*4.3.1. 3-Chloro-7-methyl-1-pyrrolidin-1-yl-5,6,7,8-tetrahydro-2,7-naphthyridine-4-carbonitrile (**2a**).* Reaction of compound **1** with pyrrolidine gave a yellow solid; mp 179–181 °C; IR $\nu$/cm$^{-1}$: 2213 (CN). $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 1.88–2.00 (m, 4H, (CH$_2$)$_2$), 2.40 (s, 3H, NCH$_3$), 2.62 (t, $J$=6.0 Hz, 2H, NC$H_2$CH$_2$), 2.86 (tt, $J$=6.0, 1.4 Hz, 2H, NCH$_2$C$H_2$), 3.48 (t, $J$=1.4 Hz, 2H, NCH$_2$), 3.57–3.69 (m, 4H, N(CH$_2$)$_2$). Anal. Calcd for $C_{14}H_{17}ClN_4$: C 60.76; H 6.19; N 20.24. Found: C 60.87; H 6.31; N 20.16%.

*4.3.2. 3-Chloro-7-methyl-1-morpholin-4-yl-5,6,7,8-tetrahydro-2,7-naphthyridine-4-carbonitrile (**2b**).* Reaction of compound **1** with morpholine gave a yellow solid; mp 173–175 °C; IR $\nu$/cm$^{-1}$: 2214 (CN). $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 2.42 (s, 3H, NCH$_3$), 2.68 (t, $J$=6.1 Hz, 2H, NC$H_2$CH$_2$), 2.95 (t, $J$=6.1 Hz, 2H, NCH$_2$C$H_2$), 3.28 (s, 2H, NCH$_2$), 3.29–3.37 (m, 4H, N(CH$_2$)$_2$), 3.68–3.78 (m, 4H, O(CH$_2$)$_2$). Anal. Calcd for $C_{14}H_{17}ClN_4O$: C 57.44; H 5.85; N 19.14. Found: C 57.52; H 5.92; N 19.32%.

*4.3.3. 3-Chloro-7-methyl-1-piperidin-1-yl-5,6,7,8-tetrahydro-2,7-naphthyridine-4-carbonitrile (**2c**).* Reaction of compound **1** with piperidine gave a pale yellow solid; mp 148–150 °C; IR $\nu$/cm$^{-1}$: 2215 (CN). $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 1.65–1.71 (m, 6H, (CH$_2$)$_3$), 2.41 (s, 3H, NCH$_3$), 2.67 (t, $J$=6.1 Hz, 2H, NC$H_2$CH$_2$), 2.93 (tt, $J$=6.1, 1.2 Hz, 2H, NCH$_2$C$H_2$), 3.25 (t, $J$=1.2 Hz, 2H, NCH$_2$), 3.25–3.33 (m, 4H, N(CH$_2$)$_2$). Anal. Calcd for $C_{15}H_{19}ClN_4$: C 61.96; H 6.59; N 19.27. Found: C 61.89; H 6.65; N 19.33%.

*4.3.4. 3-Chloro-7-methyl-1-(4-methylpiperidin-1-yl)-5,6,7,8-tetrahydro-2,7-naphthyridine-4-carbonitrile (**2d**).* Reaction of compound **1** with 4-methylpiperidine gave a light-yellow solid; mp 157–159 °C; IR $\nu$/cm$^{-1}$: 2215 (CN). $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 1.00 (d, $J$=6.4 Hz, 3H, CH$_3$), 1.21–1.37 and 1.69–1.79 (m, 4H, CH(C$H_2$)$_2$), 1.56–1.70 (m, 1H, CH), 2.41 (s, 3H, NCH$_3$), 2.68 (t, $J$=6.0 Hz, 2H, NC$H_2$CH$_2$), 2.86–2.92 (m, 2H, NCH$_2$, C$_6$H$_{12}$N), 2.94 (br t, $J$=6.0 Hz, 2H, NCH$_2$C$H_2$), 3.25 (s, 2H, NCH$_2$), 3.66–3.76 (m, 2H, NCH$_2$, C$_6$H$_{12}$N). Anal. Calcd for $C_{16}H_{21}ClN_4$: C 63.04; H 6.94; N 18.38. Found: C 63.11; H 6.87; N 18.46%.

*4.3.5. 1-(4-Benzylpiperidin-1-yl)-3-chloro-7-methyl-5,6,7,8-tetrahydro-2,7-naphthyridine-4-car-bonitrile (**2e**).* Reaction of compound **1** with 4-benzylpiperidine gave a white solid; mp 128–130 °C; IR $\nu$/cm$^{-1}$: 2220 (CN). $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 1.26–1.42 (m, 2H), and 1.70–1.85 (m, 3H, CH$_2$CHCH$_2$), 2.41 (s, 3H, NCH$_3$), 2.57 (d, $J$=6.9 Hz, 2H, C$H_2$Ph), 2.67 (t, $J$=6.1 Hz, 2H, NC$H_2$CH$_2$), 2.79–2.91 (m, 2H), and 3.65–3.76 (m, 2H, N(CH$_2$)$_2$), 2.93 (t, $J$=6.1 Hz, 2H, NCH$_2$C$H_2$), 3.24 (br s, 2H, NCH$_2$), 7.09–7.17 and 7.19–7.27 (both m, 3H and 2H, Ph). Anal. Calcd for $C_{22}H_{25}ClN_4$: C 69.37; H 6.62; N 14.71. Found: C 69.44; H 6.75; N 14.66%.

*4.3.6. 3-Chloro-1-[4-(diphenylmethyl)piperazin-1-yl]-7-methyl-5,6,7,8-tetrahydro-2,7-naphthy-ridine-4-carbonitrile (**2f**).* Reaction of compound **1** with 1-(diphenylmethyl)piperazine gave a yellow solid; mp 186–188 °C; IR $\nu$/cm$^{-1}$: 2218 (CN). $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 2.37 (s, 3H, NCH$_3$), 2.45–2.55 (m, 4H, CHN(C$H_2$)$_2$), 2.65 (t, $J$=6.0 Hz, 2H, NC$H_2$CH$_2$), 2.93 (t, $J$=6.0 Hz, 2H, NCH$_2$C$H_2$), 3.21 (br s, 2H, NCH$_2$), 3.32–3.43 (m, 4H, N(CH$_2$)$_2$), 4.28 (s, 1H, CH), 7.15 (tt, $J$=7.3, 1.5 Hz, 2H, 4′-CH, Ph), 7.21–7.29 (m, 4H, 3′,5′-CH, Ph), 7.38–7.44 (m, 4H, 2′,6′-CH, Ph). Anal. Calcd for $C_{27}H_{28}ClN_5$: C 70.81; H 6.16; N 15.29. Found: C 70.73; H 6.22; N 15.31%.

*4.3.7. 3-Chloro-1-[(2-hydroxypropyl)amino]-7-methyl-5,6,7,8-tetrahydro-2,7-naphthyridine-4-carbonitrile (**2g**).* Reaction of compound **1** with 1-amino-2-propanol gave a pale yellow solid; mp 234–236 °C; IR $\nu$/cm$^{-1}$: 2221 (CN). $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 1.11 (d, $J$=6.3 Hz, 3H, CHC$H_3$), 2.44 (s, 3H, NCH$_3$), 2.55–2.67 (m, 2H, NC$H_2$CH$_2$), 2.79 (tt, $J$=5.7, 1.5 Hz, 2H, NCH$_2$C$H_2$), 3.12–3.26 (m, 2H, NCH$_2$), 3.19 (ddd, $J$=13.3, 7.7, 5.0 Hz, 1H, NHC$H_2$), 3.48 (ddd, $J$=13.3, 6.0, 4.0 Hz, 1H, NHC$H_2$), 3.76–3.90 (m, 1H, C$H$CH$_3$), 4.45 (d, $J$=4.6 Hz, 1H, OH), 6.61 (dd, $J$=6.0, 5.0 Hz, 1H, NH). $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$: 20.6, 27.9, 45.2, 48.6, 50.0, 51.4, 64.5, 94.7, 113.0, 114.9, 145.9, 149.2, 155.5. Anal. Calcd for $C_{13}H_{17}ClN_4O$: C 55.61; H 6.10; N 19.96. Found: C 55.49; H 5.97; N 19.84%.

### 4.4. General procedure for the synthesis of compounds 3a–g

A mixture of compounds **2a**, **b**, or **c** (5 mmol) and the corresponding amine (25 mmol) was refluxed for 30 min. The reaction mixture was cooled, water (50 ml) was added, and the separated crystals were filtered off, washed with water, dried, and recrystallized from ethanol.

*4.4.1. 3-[(2-Hydroxyethyl)amino]-7-methyl-1-pyrrolidin-1-yl-5,6,7,8-tetrahydro-2,7-naphthyridine-4-carbonitrile (**3a**).* Reaction of compound **2a** with 2-aminoethanol a yellow solid; mp 168–170 °C; IR $\nu$/cm$^{-1}$: 3380, 3320 (NH), 2215 (CN). $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 1.85–1.95 (m, 4H, (CH$_2$)$_2$), 2.34 (s, 3H, NCH$_3$), 2.58 (t, $J$=5.8 Hz, 2H, NC$H_2$CH$_2$), 2.76 (t, $J$=5.8 Hz, 2H, NCH$_2$C$H_2$), 3.34 (br s, 2H, NCH$_2$), 3.42–3.52 (m, 2H, NHC$H_2$), 3.52–3.58 (m, 4H, N(CH$_2$)$_2$), 3.56–3.65 (m, 2H, C$H_2$OH), 4.38 (t, $J$=5.4 Hz, 1H, OH), 5.96 (t, $J$=5.3 Hz, 1H, NH). Anal. Calcd for $C_{16}H_{23}N_5O$: C 63.76; H 7.69; N 23.24. Found: C 63.85; H 7.75; N 23.32%.

*4.4.2. 3-[(2-Hydroxypropyl)amino]-7-methyl-1-pyrrolidin-1-yl-5,6,7,8-tetrahydro-2,7-naphthyridine-4-carbonitrile (**3b**).* Reaction of compound **2a** with 1-amino-2-propanol gave an orange solid; mp 144–146 °C; IR $\nu$/cm$^{-1}$: 3460, 3330 (NH), 2220 (CN). $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 1.09 (d, $J$=6.3 Hz, 3H, CHC$H_3$), 1.86–1.96 (m, 4H, (CH$_2$)$_2$), 2.36 (s, 3H, NCH$_3$), 2.56 (t, $J$=5.8 Hz, 2H, NC$H_2$CH$_2$), 2.75 (t, $J$=5.8 Hz, 2H, NCH$_2$C$H_2$), 3.11 (ddd, $J$=13.3, 7.6, 4.7 Hz, 1H, NHC$H_2$), 3.34 (br s, 2H, NCH$_2$), 3.49 (ddd, $J$=13.3, 6.6, 3.6 Hz, 1H, NHC$H_2$), 3.51–3.59 (m, 4H, N(CH$_2$)$_2$), 3.71–3.87 (m, 1H, CH), 4.46 (d, $J$=4.4 Hz, 1H, OH), 5.80 (dd, $J$=6.6, 4.7 Hz, 1H, NH). $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$: 20.9, 24.9, 28.3, 45.5, 48.0, 49.1, 50.7, 55.1, 65.4, 77.9, 104.9, 117.3, 147.1, 155.5, 157.3. MS: $m/z$ ($I_{\text{отн}}$, %), [M$^+$] 315. 315 (10), 297 (1), 240 (73), 244 (61). Anal. Calcd for $C_{17}H_{25}N_5O$: C 64.74; H 7.99; N 22.20. Found: C 64.81; H 7.88; N 22.31%.

*4.4.3. 3-{[2-(Diethylamino)ethyl]amino}-7-methyl-1-pyrrolidin-1-yl-5,6,7,8-tetrahydro-2,7-naphthyridine-4-carbonitrile (**3c**).* Reaction of compound **2a** with 2-diethylaminoethylamine gave a pale yellow solid; mp 95–97 °C; IR $\nu$/cm$^{-1}$: 3390, 3332

(NH), 2220 (CN). $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 1.02 (t, $J$=7.1 Hz, 6H, N(CH$_2$*CH*$_3$)$_2$), 1.85–1.93 (m, 4H, (CH$_2$)$_2$), 2.34 (s, 3H, NCH$_3$), 2.52 (q, $J$=7.1 Hz, 4H, N(*CH*$_2$CH$_3$)$_2$), 2.54 (t, $J$=6.0 Hz, 2H, N*CH*$_2$CH$_2$), 2.57 (t, $J$=6.5 Hz, 2H, NHCH$_2$*CH*$_2$), 2.73 (t, $J$=6.0 Hz, 2H, NCH$_2$*CH*$_2$), 3.32 (s, 2H, NCH$_2$), 3.37 (td, $J$=6.5, 5.4 Hz, 2H, NH*CH*$_2$), 3.50–3.60 (m, 4H, N(CH$_2$)$_2$), 5.73 (t, $J$=5.4 Hz, 1H, NH). Anal. Calcd for $C_{20}H_{32}N_6$: C 67.38; H 9.05; N 23.57. Found: C 67.42; H 9.11; N 23.51%.

*4.4.4. 7-Methyl-1-pyrrolidin-1-yl-3-[(tetrahydrofuran-2-ylmethyl) amino]-5,6,7,8-tetrahydro-2,7-naphthyridine-4-carbonitrile (**3d**).* Reaction of compound **2a** with 2-tetrahydrofurfurylamine gave a brown solid; mp 105–107 °C; IR $\nu$/cm$^{-1}$: 3395, 3318 (NH), 2210 (CN). $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 1.58–1.70 and 1.81–1.96 (both m, 1H and 7H, CH*CH*$_2$*CH*$_2$ and N(CH$_2$)$_2$), 2.35 (s, 3H, NCH$_3$), 2.55 (t, $J$=6.0 Hz, 2H, N*CH*$_2$CH$_2$), 2.74 (tt, $J$=6.0, 1.3 Hz, 2H, NCH$_2$*CH*$_2$), 3.34 (t, $J$=1.3 Hz, 2H, NCH$_2$), 3.35–3.50 (m, 2H, NH*CH*$_2$), 3.52–3.60 (m, 4H, N(CH$_2$)$_2$), 3.62–3.72 and 3.78–3.88 (both m, 1H and 1H, OCH$_2$), 3.97–4.07 (m, 1H, OCH), 5.65 (t, $J$=5.7 Hz, 1H, NH). Anal. Calcd for $C_{19}H_{27}N_5O$: C 66.83; H 7.97; N 20.51. Found: C 66.73; H 7.88; N 20.59%.

*4.4.5. 3-[(2-Hydroxypropyl)amino]-7-methyl-1-morpholin-4-yl-5,6,7,8-tetrahydro-2,7-naphthyridine-4-carbonitrile (**3e**).* Reaction of compound **2b** with 1-amino-2-propanol gave a yellow solid; mp 129–131 °C; IR $\nu$/cm$^{-1}$: 3500, 3290 (NH), 2211 (CN). $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 1.10 (d, $J$=6.3 Hz, 3H, CH$_3$), 2.37 (s, 3H, NCH$_3$), 2.59 (t, $J$=6.1 Hz, 2H, N*CH*$_2$CH$_2$), 2.81 (t, $J$=6.1 Hz, 2H, NCH$_2$*CH*$_2$), 3.14 (ddd, $J$=13.3, 7.5, 4.7 Hz, 1H, NH*CH*$_2$), 3.16 (s, 2H, NCH$_2$), 3.13–3.23 (m, 4H, N(CH$_2$)$_2$), 3.49 (ddd, $J$=13.3, 6.5, 3.8 Hz, 1H, NH*CH*$_2$), 3.65–3.77 (m, 4H, O(CH$_2$)$_2$), 3.74–3.86 (m, 1H, CH), 4.47 (d, $J$=4.5 Hz, 1H, OH), 6.04 (dd, $J$=6.5, 4.7 Hz, 1H, NH). $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$: 20.8, 28.1, 45.5, 48.1, 48.9, 51.3, 54.3, 65.1, 65.9, 82.2, 108.8, 116.3, 148.6, 156.6, 159.7. Anal. Calcd for $C_{17}H_{25}N_5O_2$: C 61.61; H 7.60; N 21.13. Found: C 61.72; H 7.68; N 21.22%.

*4.4.6. 3-[(2-Hydroxyethyl)amino]-7-methyl-1-piperidin-1-yl-5,6,7,8-tetrahydro-2,7-naphthyridine-4-carbonitrile (**3f**).* Reaction of compound **2c** with 2-aminoethanol gave a yellow solid; mp 156–158 °C; IR $\nu$/cm$^{-1}$: 3378, 3170 (NH), 2192 (CN). $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 1.60–1.70 (m, 6H, (CH$_2$)$_3$), 2.36 (s, 3H, NCH$_3$), 2.59 (t, $J$=6.0 Hz, 2H, N*CH*$_2$CH$_2$), 2.79 (t, $J$=6.0 Hz, 2H, NCH$_2$*CH*$_2$), 3.14 (s, 2H, NCH$_2$), 3.12–3.20 (m, 4H, N(CH$_2$)$_2$), 3.42–3.50 (m, 2H, NH*CH*$_2$), 3.52–3.60 (m, 2H, *CH*$_2$OH), 4.38 (t, $J$=5.4 Hz, 1H, OH), 5.98 (t, $J$=5.3 Hz, 1H, NH). Anal. Calcd for $C_{17}H_{25}N_5O$: C 64.73; H 7.99; N 22.20. Found: C 64.68; H 7.87; N 22.26%.

*4.4.7. 3-{[1-(Hydroxymethyl)propyl]amino}-7-methyl-1-piperidin-1-yl-5,6,7,8-tetrahydro-2,7-naphthyridine-4-carbonitrile (**3g**).* Reaction of compound **2c** with 2-amino-1-butanol gave an orange solid; mp 111–113 °C; IR $\nu$/cm$^{-1}$: 3378, 3312 (NH), 2218 (CN). $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 0.93 (t, $J$=7.5 Hz, 3H, CH$_3$), 1.52–1.76 (both m, 2H and 6H, *CH*$_2$CH$_3$ and (CH$_2$)$_3$), 2.36 (s, 3H, NCH$_3$), 2.58 (t, $J$=6.2 Hz, 2H, N*CH*$_2$CH$_2$), 2.78 (t, $J$=6.2 Hz, 2H, NCH$_2$*CH*$_2$), 3.09–3.25 (m, 6H, N(CH$_2$)$_2$ and NCH$_2$), 3.45–358 (m, 2H, *CH*$_2$OH), 3.91–4.03 (m, 1H, CH), 4.40 (dd, $J$=5.6, 4.6 Hz, 1H, OH), 5.53 (d, $J$=7.6 Hz, 1H, NH). Anal. Calcd for $C_{19}H_{29}N_5O$: C 66.44; H 8.51; N 20.39. Found: C 66.31; H 8.65; N 20.28%.

### 4.5. General procedure for the synthesis of compounds 3h–t

A mixture of compounds **2a**, **b**, or **g** (5 mmol) and the corresponding amine (25 mmol) was refluxed for 5 h. The reaction mixture was cooled, water (50 ml) was added, and the separated crystals were filtered off, washed with water, dried, and recrystallized from ethanol.

*4.5.1. 7-Methyl-1,3-dipyrrolidin-1-yl-5,6,7,8-tetrahydro-2,7-naphthyridine-4-carbonitrile (**3h**).* Reaction of compound **2a** with pyrrolidine gave a gray solid; mp 154–156 °C; IR $\nu$/cm$^{-1}$: 2222 (CN). $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 1.85–1.98 (m, 8H, 2(CH$_2$)$_2$), 2.36 (s, 3H, NCH$_3$), 2.57 (t, $J$=6.0 Hz, 2H, N*CH*$_2$CH$_2$), 2.76 (t, $J$=6.0 Hz, 2H, NCH$_2$*CH*$_2$), 3.33 (s, 2H, NCH$_2$), 3.48–3.58 (m, 4H, N(CH$_2$)$_2$), 3.62–3.72 (m, 4H, N(CH$_2$)$_2$). Anal. Calcd for $C_{18}H_{25}N_5$: C 69.42; H 8.09; N 22.49. Found: C 69.51; H 8.18; N 22.60%.

*4.5.2. 7-Methyl-3-morpholin-4-yl-1-pyrrolidin-1-yl-5,6,7,8-tetrahydro-2,7-naphthyridine-4-carbonitrile (**3i**).* Reaction of compound **2a** with morpholine gave a yellow solid; mp 138–140 °C; IR $\nu$/cm$^{-1}$: 2220 (CN). $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 1.85–1.98 (m, 4H, (CH$_2$)$_2$), 2.36 (s, 3H, NCH$_3$), 2.55 (t, $J$=6.0 Hz, 2H, N*CH*$_2$CH$_2$), 2.78 (t, $J$=6.0 Hz, 2H, NCH$_2$*CH*$_2$), 3.38 (s, 2H, NCH$_2$), 3.45–3.62 (m, 8H, N(CH$_2$)$_2$ and N(CH$_2$)$_2$ of morpholine), 3.68–3.75 (m, 4H, O(CH$_2$)$_2$). Anal. Calcd for $C_{18}H_{25}N_5O$: C 66.03; H 7.70; N 21.39. Found: C 66.14; H 7.81; N 21.52%.

*4.5.3. 7-Methyl-3-piperidin-1-yl-1-pyrrolidin-1-yl-5,6,7,8-tetrahydro-2,7-naphthyridine-4-carbonitrile (**3j**).* Reaction of compound **2a** with piperidine gave a white solid; mp 145–147 °C; IR $\nu$/cm$^{-1}$: 2221 (CN). $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 1.55–1.68 (m, 6H, (CH$_2$)$_3$), 1.85–1.95 (m, 4H, (CH$_2$)$_2$), 2.38 (s, 3H, NCH$_3$), 2.58 (t, $J$=6.0 Hz, 2H, N*CH*$_2$CH$_2$), 2.76 (t, $J$=6.0 Hz, 2H, NCH$_2$*CH*$_2$), 3.36 (s, 2H, NCH$_2$), 3.45–3.62 (m, 8H, N(CH$_2$)$_2$ and N(CH$_2$)$_2$ of piperidine). Anal. Calcd for $C_{19}H_{27}N_5$: C 70.12; H 8.36; N 21.52. Found: C 70.01; H 8.47; N 21.39%.

*4.5.4. 7-Methyl-1-morpholin-4-yl-3-pyrrolidin-1-yl-5,6,7,8-tetrahydro-2,7-naphthyridine-4-carbonitrile (**3k**).* Reaction of compound **2b** with pyrrolidine gave a pale yellow solid; mp 139–141 °C; IR $\nu$/cm$^{-1}$: 2219 (CN). $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 1.89–1.95 (m, 4H, (CH$_2$)$_2$), 2.35 (s, 3H, NCH$_3$), 2.59 (t, $J$=6.1 Hz, 2H, N*CH*$_2$CH$_2$), 2.82 (t, $J$=6.1 Hz, 2H, NCH$_2$*CH*$_2$), 3.19–3.32 (m, 6H, NCH$_2$ and N(CH$_2$)$_2$ of morpholine), 3.60–3.75 (m, 8H, N(CH$_2$)$_2$ of pyrrolidine and O(CH$_2$)$_2$ of morpholine). Anal. Calcd for $C_{18}H_{25}N_5O$: C 66.03; H 7.70; N 21.39. Found: C 66.16; H 7.84; N 21.25%.

*4.5.5. 7-Methyl-1,3-dimorpholin-4-yl-5,6,7,8-tetrahydro-2,7-naphthyridine-4-carbonitrile (**3l**).* Reaction of compound **2b** with morpholine gave a white solid; mp 160–162 °C; IR $\nu$/cm$^{-1}$: 2221 (CN). $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 2.38 (s, 3H, NCH$_3$), 2.61 (t, $J$=6.1 Hz, 2H, N*CH*$_2$CH$_2$), 2.82 (t, $J$=6.1 Hz, 2H, NCH$_2$*CH*$_2$), 3.15–3.35 (m, 8H, 2N(CH$_2$)$_2$), 3.45–3.68 (m, 4H, O(CH$_2$)$_2$), 3.65–3.75 (m, 6H, NCH$_2$ and O(CH$_2$)$_2$ of morpholine). Anal. Calcd for $C_{18}H_{25}N_5O_2$: C 62.95; H 7.34; N 20.39. Found: C 63.10; H 7.21; N 20.28%.

*4.5.6. 7-Methyl-3-[(3-methylbutyl)amino]-1-pyrrolidin-1-yl-5,6,7,8-tetrahydro-2,7-naphthyridine-4-carbonitrile (**3m**).* Reaction of compound **2a** with isopentylamine gave a brown solid; mp 114–116 °C; IR $\nu$/cm$^{-1}$: 3398, 3321 (NH), 2220 (CN). $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 0.93 (d, $J$=6.6 Hz, 6H, CH(*CH*$_3$)$_2$), 1.42–1.50 (m, 2H, CH*CH*$_2$), 1.65 (sp, $J$=6.6 Hz, 1H, *CH*(CH$_3$)$_2$), 1.87–1.93 (m, 4H, (CH$_2$)$_2$), 2.36 (s, 3H, NCH$_3$), 2.56 (t, $J$=6.0 Hz, 2H, N*CH*$_2$CH$_2$), 2.73 (t, $J$=6.0 Hz, 2H, NCH$_2$*CH*$_2$), 3.32–3.40 (m, 2H, NH*CH*$_2$), 3.35 (s, 2H, NCH$_2$), 3.52–3.58 (m, 4H, N(CH$_2$)$_2$), 5.71 (t, $J$=5.7 Hz, 1H, NH). Anal. Calcd for $C_{19}H_{29}N_5$: C 69.69; H 8.93; N 21.39. Found: C 69.59; H 9.01; N 21.25%.

*4.5.7. 3-[(2-Aminoethyl)amino]-7-methyl-1-pyrrolidin-1-yl-5,6,7,8-tetrahydro-2,7-naphthyridine-4-carbonitrile (**3n**).* Reaction of compound **2a** with ethylendiamine gave a pale yellow solid; mp 161–163 °C; IR $\nu$/cm$^{-1}$: 3480, 3350, 3320 (NH, NH$_2$), 2215 (CN). $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 1.26 (br, 2H, NH$_2$), 1.87–1.93 (m, 4H, (CH$_2$)$_2$), 2.35 (s, 3H, NCH$_3$), 2.55 (t, $J$=6.0 Hz, 2H, *CH*$_2$NH$_2$), 2.74 (t,

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*J*=5.9 Hz, 2H, NC*H*$_2$CH$_2$), 2.77 (t, *J*=5.9 Hz, 2H, NCH$_2$*CH*$_2$), 3.33 (s, 2H, NCH$_2$), 3.37 (q, *J*=5.8 Hz, 2H, NH*CH*$_2$), 3.52–3.59 (m, 4H, N(CH$_2$)$_2$), 5.97 (br t, *J*=5.5 Hz, 1H, NH). Anal. Calcd for $C_{16}H_{24}N_6$: C 63.97; H 8.05; N 27.98. Found: C 63.85; H 8.15; N 28.18%.

*4.5.8. 3-{[2-(Dimethylamino)ethyl]amino}-7-methyl-1-pyrrolidin-1-yl-5,6,7,8-tetrahydro-2,7-naphthyridine-4-carbonitrile (**3o**).* Reaction of compound **2a** with 2-(dimethylamino)ethylamine gave a gray solid; mp 149–151 °C; IR $\nu$/cm$^{-1}$: 3393, 3335 (NH), 2222 (CN). $^1$H NMR (300 MHz, DMSO-*d*$_6$) $\delta$ 1.88–1.94 (m, 4H, (CH$_2$)$_2$), 2.24 (s, 6H, N(CH$_3$)$_2$), 2.35 (s, 3H, NCH$_3$), 2.47 (t, *J*=6.5 Hz, 2H, *CH*$_2$N(CH$_3$)$_2$), 2.55 (t, *J*=6.0 Hz, 2H, NC*H*$_2$CH$_2$), 2.74 (t, *J*=6.0 Hz, 2H, NCH$_2$*CH*$_2$), 3.33 (s, 2H, NCH$_2$), 3.43 (td, *J*=6.5, 5.1 Hz, 2H, NH*CH*$_2$), 3.53–3.60 (m, 4H, N(CH$_2$)$_2$), 5.71 (br t, *J*=5.1 Hz, 1H, NH). Anal. Calcd for $C_{18}H_{28}N_6$: C 65.82; H 8.59; N 25.59. Found: C 65.91; H 8.47; N 25.70%.

*4.5.9. 3-[(3-Methoxypropyl)amino]-7-methyl-1-pyrrolidin-1-yl-5,6,7,8-tetrahydro-2,7-naphthyridine-4-car-bonitrile (**3p**).* Reaction of compound **2a** with 3-methoxypropylamine gave a white solid; mp 109–111 °C; IR $\nu$/cm$^{-1}$: 3372 (NH), 2184 (CN). $^1$H NMR (300 MHz, DMSO-*d*$_6$) $\delta$ 1.76–1.85 (m, 2H, NHCH$_2$*CH*$_2$), 1.87–1.93 (m, 4H, (CH$_2$)$_2$), 2.35 (s, 3H, NCH$_3$), 2.55 (t, *J*=6.0 Hz, 2H, NC*H*$_2$CH$_2$), 2.74 (t, *J*=6.0 Hz, 2H, NCH$_2$*CH*$_2$), 3.29 (s, 3H, OCH$_3$), 3.33 (s, 2H, NCH$_2$), 3.38–3.45 (m, 4H, NH*CH*$_2$ and CH$_2$O), 3.53–3.59 (m, 4H, N(CH$_2$)$_2$), 5.91 (br t, *J*=5.9 Hz, 1H, NH). Anal. Calcd for $C_{18}H_{27}N_5O$: C 65.62; H 8.26; N 21.26. Found: C 65.73; H 8.15; N 21.37%.

*4.5.10. 3-{[3-(Dimethylamino)propyl]amino}-7-methyl-1-pyrrolidin-1-yl-5,6,7,8-tetrahydro-2,7-naphthyridine-4-carbonitrile (**3q**).* Reaction of compound **2a** with 3-(dimethylamino)-1-propylamine gave a light-yellow solid; mp 138–140 °C; IR $\nu$/cm$^{-1}$: 3343 (NH), 2219 (CN). $^1$H NMR (300 MHz, DMSO-*d*$_6$) $\delta$ 1.69 (q, *J*=6.4 Hz, 2H, NHCH$_2$*CH*$_2$), 1.87–1.93 (m, 4H, (CH$_2$)$_2$), 2.20 (s, 6H, N(CH$_3$)$_2$), 2.34 (t, *J*=6.5 Hz, 2H, *CH*$_2$N(CH$_3$)$_2$), 2.35 (s, 3H, NCH$_3$), 2.55 (t, *J*=6.0 Hz, 2H, NC*H*$_2$CH$_2$), 2.73 (t, *J*=6.0 Hz, 2H, NCH$_2$*CH*$_2$), 3.32 (s, 2H, NCH$_2$), 3.41 (td, *J*=6.4, 5.2 Hz, 2H, NH*CH*$_2$), 3.52–3.58 (m, 4H, N(CH$_2$)$_2$), 6.54 (br t, *J*=5.2 Hz, 1H, NH). Anal. Calcd for $C_{19}H_{30}N_6$: C 66.63; H 8.83; N 24.54. Found: C 66.51; H 8.75; N 24.41%.

*4.5.11. 1,3-Bis[(2-hydroxypropyl)amino]-7-methyl-5,6,7,8-tetrahydro-2,7-naphthyridine-4-carbonitrile (**3r**).* Reaction of compound **2g** with 1-amino-2-propanol gave a brown solid; mp 193–195 °C; IR $\nu$/cm$^{-1}$: 3324 (NH), 2192 (CN). $^1$H NMR (300 MHz, DMSO-*d*$_6$) $\delta$ 1.09 (d, *J*=6.3 Hz, 3H, CH*CH*$_3$), 1.09 (d, *J*=6.3 Hz, 3H, CH*CH*$_3$), 2.40 (s, 3H, NCH$_3$), 2.53–2.62 (m, 2H, NC*H*$_2$CH$_2$), 2.62–2.70 (m, 2H, NCH$_2$*CH*$_2$), 3.04–3.19 (m, 4H, NCH$_2$, 2NH*CH*$_2$), 3.42–3.53 (m, 2H, NH*CH*$_2$), 3.73–3.88 (m, 2H, 2*CH*CH$_3$), 4.45 (d, *J*=4.1 Hz, 1H, OH), 4.52 (d, *J*=4.3 Hz, 1H, OH), 5.73–5.83 (m, 1H, NH), 5.88–5.98 (m, 1H, NH). Anal. Calcd for $C_{16}H_{25}N_5O_2$: C 60.17; H 7.89; N 21.93. Found: C 60.04; H 7.98; N 22.02%.

*4.5.12. 1-[(2-Hydroxypropyl)amino]-7-methyl-3-pyrrolidin-1-yl-5,6,7,8-tetrahydro-2,7-naphthyridine-4-car-bonitrile (**3s**).* Reaction of compound **2g** with pyrrolidine gave a light-yellow solid; mp 177–179 °C; IR $\nu$/cm$^{-1}$: 3332, 3140 (NH), 2182 (CN). $^1$H NMR (300 MHz, DMSO-*d*$_6$) $\delta$ 1.08 (d, *J*=6.3 Hz, 3H, CH*CH*$_3$), 1.89–2.00 (m, 4H, (CH$_2$)$_2$), 2.40 (s, 3H, NCH$_3$), 2.53–2.61 (m, 2H, NC*H*$_2$CH$_2$), 2.64–2.72 (m, 2H, NCH$_2$*CH*$_2$), 3.08 (dt, *J*=14.2, 1.3 Hz, 1H, NCH$_2$), 3.12 (ddd, *J*=13.3, 7.3, 4.8 Hz, 1H, NH*CH*$_2$), 3.13 (dt, *J*=14.2, 1.3 Hz, 1H, NCH$_2$), 3.48 (ddd, *J*=13.3, 6.2, 3.6 Hz, 1H, NH*CH*$_2$), 3.62–3.72 (m, 4H, N(CH$_2$)$_2$), 3.76–3.88 (m, 1H, *CH*CH$_3$), 4.40 (d, *J*=4.3 Hz, 1H, OH), 5.85 (dd, *J*=6.2, 4.8 Hz, 1H, NH). Anal. Calcd for $C_{17}H_{25}N_5O$: C 64.73; H 7.99; N 22.20. Found: C 64.61; H 8.10; N 22.11%.

*4.5.13. 1-[(2-Hydroxypropyl)amino]-7-methyl-3-morpholin-4-yl-5,6,7,8-tetrahydro-2,7-naphthyridine-4-carbonitrile (**3t**).* Reaction of compound **2g** with morpholine gave a yellow solid; mp 185–187 °C; IR $\nu$/cm$^{-1}$: 3389, 3308 (NH), 2219 (CN). $^1$H NMR (300 MHz, DMSO-*d*$_6$) $\delta$ 1.08 (d, *J*=6.2 Hz, 3H, CH*CH*$_3$), 2.41 (s, 3H, NCH$_3$), 2.53–2.63 (m, 2H, NC*H*$_2$CH$_2$), 2.66–2.76 (m, 2H, NCH$_2$*CH*$_2$), 3.17 (ddd, *J*=13.3, 7.3, 4.9 Hz, 1H, NH*CH*$_2$), 3.11 (d, *J*=14.7 Hz, 1H, NCH$_2$), 3.16 (d, *J*=14.7 Hz, 1H, NCH$_2$), 3.44 (ddd, *J*=13.3, 6.1, 4.2 Hz, 1H, NH*CH*$_2$), 3.43–3.53 (m, 4H, N(CH$_2$)$_2$), 3.65–3.77 (m, 4H, O(CH$_2$)$_2$), 3.76–3.88 (m, 1H, *CH*CH$_3$), 4.41 (d, *J*=4.4 Hz, 1H, OH), 6.11 (dd, *J*=6.1, 4.9 Hz, 1H, NH). Anal. Calcd for $C_{17}H_{25}N_5O_2$: C 61.61; H 7.60; N 21.13. Found: C 61.51; H 7.52; N 21.21%.

### 4.6. General procedure for the synthesis of compounds 4a–g

A. A mixture of compound **2** (5 mmol) and the corresponding amine (25 mmol) was refluxed for 5 h. The reaction mixture was cooled, water (50 ml) was added, and the separated crystals were filtered off, washed with water, dried, and recrystallized from ethanol.
B. A mixture of compound **3** (5 mmol) and the corresponding amine (25 mmol) was refluxed for 4.5 h. The product was isolated as in method A.

*4.6.1. 8-[(2-Hydroxyethyl)amino]-2-methyl-6-pyrrolidin-1-yl-3,4-dihydro-2,7-naphthyridin-1(2H)-one (**4a**).* Reaction of compound **2a** or **3a** with 2-aminoethanol gave a white solid; mp 147–149 °C; IR $\nu$/cm$^{-1}$: 3401, 3312 (NH), 1605 (CO). $^1$H NMR (300 MHz, DMSO-*d*$_6$) $\delta$ 1.92–2.04 (m, 4H, (CH$_2$)$_2$), 2.74 (t, *J*=6.6 Hz, 2H, NC*H*$_2$CH$_2$), 2.95 (s, 3H, NCH$_3$), 3.39 (t, *J*=6.6 Hz, 2H, NCH$_2$*CH*$_2$), 3.42–3.52 (m, 6H, N(CH$_2$)$_2$ and NH*CH*$_2$), 3.58 (m, 2H, *CH*$_2$OH), 4.46 (t, *J*=4.8 Hz, 1H, OH), 5.35 (s, 1H, CH), 9.08 (t, *J*=5.1 Hz, 1H, NH). Anal. Calcd for $C_{15}H_{22}N_4O_2$: C 62.05; H 7.64; N 19.30. Found: C 62.12; H 7.52; N 19.43%.

*4.6.2. 8-[(2-Hydroxypropyl)amino]-2-methyl-6-pyrrolidin-1-yl-3,4-dihydro-2,7-naphthyridin-1(2H)-one (**4b**).* Reaction of compound **2a** or **3a** with 1-amino-2-propanol gave a lactic solid; mp 166–168 °C; IR $\nu$/cm$^{-1}$: 3393, 3320 (NH), 1600 (CO). $^1$H NMR (300 MHz, DMSO-*d*$_6$) $\delta$ 1.10 (d, *J*=6.3 Hz, 3H, CH$_3$), 1.94–2.03 (m, 4H, (CH$_2$)$_2$), 2.74 (t, *J*=6.6 Hz, 2H, NC*H*$_2$CH$_2$), 2.88 (s, 3H, NCH$_3$), 3.28 (ddd, *J*=13.5, 6.8, 5.4 Hz, 1H, NH*CH*$_2$), 3.39 (t, *J*=6.6 Hz, 2H, NCH$_2$*CH*$_2$), 3.44 (ddd, *J*=13.5, 6.2, 4.1 Hz, 1H, NH*CH*$_2$), 3.38–3.50 (m, 4H, N(CH$_2$)$_2$), 3.74–3.86 (m, 1H, CH), 4.64 (d, *J*=4.3 Hz, 1H, OH), 5.34 (s, 1H, CH), 9.12 (dd, *J*=6.2, 5.4 Hz, 1H, NH). $^{13}$C NMR (75 MHz, DMSO-*d*$_6$) $\delta$: 21.1, 25.5, 29.1, 34.9, 46.9, 47.6, 49.5, 70.1, 93.3, 95.0, 150.3, 157.1, 159.9, 167.5. MS: *m*/*z* ($I_{отн,\ \%}$), [M$^+$] 304. 304 (22), 259 (100), 229 (5). Anal. Calcd for $C_{16}H_{24}N_4O_2$: C 63.13; H 7.95; N 18.41. Found: C 63.22; H 7.87; N 18.52%.

*4.6.3. 8-{[2-(Diethylamino)ethyl]amino}-2-methyl-6-pyrrolidin-1-yl-3,4-dihydro-2,7-naphthyridin-1(2H)-one (**4c**).* Reaction of compound **2a** or **3c** with 2-diethylaminoethylamine gave a white solid; mp 117–119 °C; IR $\nu$/cm$^{-1}$: 3399, 3350 (NH), 1601 (CO). $^1$H NMR (300 MHz, DMSO-*d*$_6$) $\delta$ 1.03 (t, *J*=7.1 Hz, 6H, N(CH$_2$*CH*$_3$)$_2$), 1.93–2.02 (m, 4H, (CH$_2$)$_2$), 2.55 (q, *J*=7.1 Hz, 4H, N(*CH*$_2$CH$_3$)$_2$), 2.59 (t, *J*=6.6 Hz, 2H, NCH$_2$), 2.73 (t, *J*=6.6 Hz, 2H, NC*H*$_2$CH$_2$), 2.94 (s, 3H, NCH$_3$), 3.38 (t, *J*=6.6 Hz, 2H, NCH$_2$*CH*$_2$), 3.38–3.52 (m, 6H, N(CH$_2$)$_2$ and NH*CH*$_2$), 5.30 (s, 1H, CH), 8.92 (t, *J*=5.5 Hz, 1H, NH). Anal. Calcd for $C_{19}H_{31}N_5O$: C 66.05; H 9.04; N 20.27. Found: C 66.13; H 9.11; N 20.19%.

*4.6.4. 2-Methyl-6-pyrrolidin-1-yl-8-[(tetrahydrofuran-2-ylmethyl)amino]-3,4-dihydro-2,7-naphthyridin-1(2H)-one (**4d**).* Reaction of compound **2a** or **3d** with 2-tetrahydrofurfurylamine gave a gray solid; mp 158–160 °C; IR $\nu$/cm$^{-1}$: 3415, 3360 (NH), 1605 (CO). $^1$H NMR (300 MHz, DMSO-*d*$_6$) $\delta$ 1.60–1.72 and 1.80–1.95 (both m, 1H

and 3H, CH$CH_2CH_2$), 1.94–2.03 (m, 4H, $(CH_2)_2$), 2.74 (t, $J$=6.6 Hz, 2H, N$CH_2CH_2$), 2.95 (s, 3H, $NCH_3$), 3.39 (t, $J$=6.6 Hz, 2H, $NCH_2CH_2$), 3.42–3.58 (m, 6H, $N(CH_2)_2$ and NH$CH_2$), 3.62–3.72 and 3.81–3.91 (both m, 1H and 1H, $OCH_2$), 3.95–4.06 (m, 1H, OCH), 5.32 (s, 1H, CH), 9.00 (t, $J$=5.6 Hz, 1H, NH). Anal. Calcd for $C_{18}H_{26}N_4O_2$: C 65.43; H 7.93; N 16.96. Found: C 65.39; H 7.88; N 16.89%.

*4.6.5. 8-[(2-Hydroxypropyl)amino]-2-methyl-6-morpholin-4-yl-3,4-dihydro-2,7-naphthyridin-1(2H)-one (**4e**).* Reaction of compound **2b** or **3e** with 1-amino-2-propanol gave a lactic solid; mp 143–145 °C; IR $\nu$/cm$^{-1}$: 3408, 3316 (NH), 1604 (CO). $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 1.12 (d, $J$=6.2 Hz, 3H, $CH_3$), 2.75 (t, $J$=6.6 Hz, 2H, N$CH_2CH_2$), 2.96 (s, 3H, $NCH_3$), 3.27 (ddd, $J$=13.3, 6.6, 5.3 Hz, 1H, NH$CH_2$), 3.38 (ddd, $J$=13.3, 5.9, 4.8 Hz, 1H, NH$CH_2$), 3.40 (t, $J$=6.6 Hz, 2H, $NCH_2CH_2$), 3.46–3.56 (m, 4H, $N(CH_2)_2$), 3.63–3.73 (m, 4H, $O(CH_2)_2$), 3.74–3.86 (m, 1H, CH), 4.33 (d, $J$=4.6 Hz, 1H, OH), 5.61 (s, 1H, CH), 9.06 (dd, $J$=5.9, 5.3 Hz, 1H, NH). MS: $m/z$ ($I_{отн,\ \%}$), [M$^+$] 320. 320 (19), 275 (100), 245 (4). Anal. Calcd for $C_{16}H_{24}N_4O_3$: C 59.98; H 7.55; N 17.49. Found: C 59.85; H 7.46; N 17.38%.

*4.6.6. 8-[(2-Hydroxyethyl)amino]-2-methyl-6-piperidin-1-yl-3,4-dihydro-2,7-naphthyridin-1(2H)-one (**4f**).* Reaction of compound **2c** or **3f** with 2-aminoethanol gave a brown solid; mp 138–140 °C; IR $\nu$/cm$^{-1}$: 3400, 3330 (NH), 1603 (CO). $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 1.54–1.65 (m, 6H, $(CH_2)_3$), 2.73 (t, $J$=6.6 Hz, 2H, N$CH_2CH_2$), 2.95 (s, 3H, $NCH_3$), 3.39 (t, $J$=6.6 Hz, 2H, $NCH_2CH_2$), 3.41–3.51 (m, 2H, NH$CH_2$), 3.52–3.62 (m, 6H, $CH_2$OH, $N(CH_2)_2$), 4.28 (d, $J$=5.3 Hz, 1H, OH), 5.59 (s, 1H, CH), 8.99 (t, $J$=5.6 Hz, 1H, NH). Anal. Calcd for $C_{16}H_{24}N_4O_2$: C 63.13; H 7.95; N 18.41. Found: C 63.24; H 7.86; N 18.50%.

*4.6.7. 8-{[1-(Hydroxymethyl)propyl]amino}-2-methyl-6-piperidin-1-yl-3,4-dihydro-2,7-naphthyridin-1(2H)-one (**4g**).* Reaction of compound **2c** or **3g** with 2-amino-1-butanol gave a white solid; mp 109–111 °C; IR $\nu$/cm$^{-1}$: 3360, 3290 (NH), 1602 (CO). $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 0.96 (t, $J$=7.5 Hz, 3H, $CH_3$), 1.45–1.76 (m, 8H, $CH_2CH_3$, $(CH_2)_3$), 2.73 (t, $J$=6.6 Hz, 2H, N$CH_2CH_2$), 2.95 (s, 3H, $NCH_3$), 3.39 (t, $J$=6.6 Hz, 2H, $NCH_2CH_2$); 3.42–3.58 (m, 6H, $N(CH_2)_2$ and OH$CH_2$), 3.91–4.02 (m, 1H, CH), 4.21 (dd, $J$=5.6, 4.6 Hz, 1H, OH), 5.58 (s, 1H, CH), 8.92 (d, $J$=7.6 Hz, 1H, NH). Anal. Calcd for $C_{18}H_{28}N_4O_2$: C 65.03; H 8.49; N 16.85. Found: C 65.11; H 8.40; N 16.72%.

### 4.7. General procedure for the synthesis of compounds 4h–m

The A method of preparation of compounds **4a**–**g** was used.

*4.7.1. 8-{[1-(Hydroxymethyl)propyl]amino}-2-methyl-6-pyrrolidin-1-yl-3,4-dihydro-2,7-naphthyridin-1(2H)-one (**4h**).* Reaction of compound **2a** with 2-amino-1-butanol gave a white solid; mp 126–128 °C; IR $\nu$/cm$^{-1}$: 3239 (NH), 1610 (CO). $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 0.97 (t, $J$=7.4 Hz, 3H, $CH_3$), 1.45–1.60 and 1.61–1.74 (both m, 1H and 1H, $CH_2CH_3$), 1.94–2.02 (m, 4H, $(CH_2)_2$), 2.74 (t, $J$=6.7 Hz, 2H, N$CH_2CH_2$), 2.95 (s, 3H, $NCH_3$), 3.39 (t, $J$=6.7 Hz, 2H, $NCH_2CH_2$), 3.40–3.52 (m, 6H, $N(CH_2)_2$ and OH$CH_2$), 3.93–4.04 (m, 1H, CH), 4.47 (t, $J$=5.1 Hz, 1H, OH), 5.33 (s, 1H, CH), 9.00 (d, $J$=7.2 Hz, 1H, NH). Anal. Calcd for $C_{17}H_{26}N_4O_2$: C 64.12; H 8.23; N 17.60. Found: C 64.21; H 8.35; N 17.52%.

*4.7.2. 8-[(2-Hydroxypropyl)amino]-2-methyl-6-piperidin-1-yl-3,4-dihydro-2,7-naphthyridin-1(2H)-one (**4i**).* Reaction of compound **2c** with 1-amino-2-propanol gave a light-yellow solid; mp 182–184 °C; IR $\nu$/cm$^{-1}$: 3360, 3280 (NH), 1600 (CO). $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 1.12 (d, $J$=6.3 Hz, 3H, $CH_3$), 1.54–1.71 (m, 6H, $(CH_2)_3$), 2.73 (t, $J$=6.6 Hz, 2H, N$CH_2CH_2$), 2.95 (s, 3H, $NCH_3$), 3.26 (ddd, $J$=13.3, 6.6, 5.3 Hz, 1H, NH$CH_2$), 3.39 (ddd, $J$=13.3, 6.1, 4.5 Hz, 1H, NH$CH_2$), 3.41 (t, $J$=6.6 Hz, 2H, $NCH_2CH_2$), 3.50–3.60 (m, 4H, $N(CH_2)_2$), 3.74–3.86 (m, 1H, CH), 4.33 (d, $J$=4.6 Hz, 1H, OH), 5.59 (s, 1H, CH), 9.04 (dd, $J$=6.1, 5.5 Hz, 1H, NH). Anal. Calcd for $C_{17}H_{26}N_4O_2$: C 64.12; H 8.23; N 17.60. Found: C 64.19; H 8.31; N 17.71%.

*4.7.3. 2-Methyl-8-[(2-morpholin-4-ylethyl)amino]-6-piperidin-1-yl-3,4-dihydro-2,7-naphthyridin-1(2H)-one (**4j**).* Reaction of compound **2c** with 2-morpholinoethylamine gave a yellow solid; yield 73%; mp 141–143 °C; IR $\nu$/cm$^{-1}$: 3415, 3310 (NH), 1604 (CO). $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 1.54–1.71 (m, 6H, $(CH_2)_3$), 2.39–2.51 (m, 4H, $N(CH_2)_2$), 2.54 (t, $J$=6.6 Hz, 2H, NH$CH_2CH_2$), 2.73 (t, $J$=6.6 Hz, 2H, N$CH_2CH_2$), 2.95 (s, 3H, $NCH_3$), 3.39 (t, $J$=6.6 Hz, 2H, $NCH_2CH_2$), 3.49 (td, $J$=6.6, 5.3 Hz, 2H, NH$CH_2$), 3.52–3.62 (m, 4H, $N(CH_2)_2$), 3.57–3.67 (m, 4H, $O(CH_2)_2$), 5.58 (s, 1H, CH), 8.92 (d, $J$=5.3 Hz, 1H, NH). Anal. Calcd for $C_{20}H_{31}N_5O_2$: C 64.32; H 8.37; N 18.75. Found: C 64.43; H 8.42; N 18.66%.

*4.7.4. 8-[(2-Hydroxypropyl)amino]-2-methyl-6-(4-methylpiperidin-1-yl)-3,4-dihydro-2,7-naphthyridin-1(2H)-one (**4k**).* Reaction of compound **2d** with 1-amino-2-propanol gave a lactic solid; yield 71%; mp 146–148 °C; IR $\nu$/cm$^{-1}$: 3420, 3345 (NH), 1600 (CO). $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 0.96 (d, $J$=6.2 Hz, 3H, $(CH_2)_2CHCH_3$), 1.12 (d, $J$=6.2 Hz, 3H, OHCH$CH_3$), 1.10–1.21 and 1.55–1.72 (both m, 2H and 3H, $CH(CH_2)_2$), 2.73 (t, $J$=6.6 Hz, 2H, N$CH_2CH_2$), 2.79 (td, $J$=12.5, 2.2 Hz, 2H), and 4.32 (td, $J$=12.5, 2.9 Hz, 2H, $N(CH_2)_2$), 2.95 (s, 3H, $NCH_3$), 3.25 (ddd, $J$=13.2, 6.6, 5.3 Hz, 1H, NH$CH_2$), 3.39 (t, $J$=6.6 Hz, 2H, $NCH_2CH_2$), 3.41 (ddd, $J$=13.2, 6.0, 4.4 Hz, 1H, NH$CH_2$), 3.74–3.86 (m, 1H, OH$CH$), 4.34 (d, $J$=4.5 Hz, 1H, OH), 5.60 (s, 1H, CH), 9.03 (br dd, $J$=6.0, 5.3 Hz, 1H, NH). $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$: 21.0, 21.5, 28.5, 30.7, 33.3, 34.0, 44.3, 46.7, 47.7, 65.8, 91.2, 94.6, 149.4, 157.7, 157.9, 165.8. MS: $m/z$ ($I_{отн,\ \%}$), [M$^+$] 332. 332 (27), 287 (100), 257 (7), 98 (2). Anal. Calcd for $C_{18}H_{28}N_4O_2$: C 65.03; H 8.49; N 16.85. Found: C 65.14; H 8.39; N 16.79%.

*4.7.5. 6-(4-Benzylpiperidin-1-yl)-8-{[1-(hydroxymethyl)propyl]amino}-2-methyl-3,4-dihydro-2,7-naphthyri-din-1(2H)-one (**4l**).* Reaction of compound **2e** with 2-amino-1-butanol gave a white solid; yield 76%; mp 159–161 °C; IR $\nu$/cm$^{-1}$: 3400, 3319 (NH), 1601 (CO). $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 0.96 (t, $J$=7.4 Hz, 3H, $CH_3$), 1.15–1.29 (m, 2H), 1.45–1.59 (m, 1H), and 1.62–1.87 (m, 4H, $CH_2CHCH_2$, $CH_2CH_3$), 2.53 (d, $J$=7.2 Hz, 2H, $CH_2$Ph), 2.69–2.77 (m, 4H, N$CH_2CH_2$, $N(CH_2)_2$), 2.95 (s, 3H, $NCH_3$), 3.39 (t, $J$=6.6 Hz, 2H, $NCH_2CH_2$), 3.37–3.55 (m, 2H, HO$CH_2$), 3.88–4.00 (m, 1H, NH$CH$), 4.21 (dd, $J$=5.6, 4.6 Hz, 1H, OH), 4.28–4.40 (m, 2H, $N(CH_2)_2$), 5.58 (s, 1H, CH), 7.07–7.16 and 7.18–7.26 (both m, 3H and 2H, Ph), 8.92 (d, $J$=7.6 Hz, 1H, NH). Anal. Calcd for $C_{25}H_{34}N_4O_2$: C 71.06; H 8.11; N 13.26. Found: C 71.14; H 8.21; N 13.34%.

*4.7.6. 6-[4-(Diphenylmethyl)piperazin-1-yl]-8-[(2-hydroxyethyl)amino]-2-methyl-3,4-dihydro-2,7-naphthy-ridin-1(2H)-one (**4m**).* Reaction of compound **2f** with 2-aminoethanol gave a brown solid; yield 74%; mp 108–110 °C; IR $\nu$/cm$^{-1}$: 3402, 3326 (NH), 1600 (CO). $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 2.40–2.46 (m, 4H, $CHN(CH_2)_2$), 2.73 (t, $J$=6.6 Hz, 2H, N$CH_2CH_2$), 2.95 (s, 3H, $NCH_3$), 3.38 (t, $J$=6.6 Hz, 2H, $NCH_2CH_2$), 3.40 (q, $J$=5.4 Hz, 2H, NH$CH_2$), 3.51 (td, $J$=5.4, 5.0 Hz, 2H, OH$CH_2$), 3.54–3.59 (m, 4H, $N(CH_2)_2$), 4.25 (s, 1H, CH), 4.26 (t, $J$=5.0 Hz, 1H, OH), 5.56 (s, 1H, CH), 7.15 (tt, $J$=7.2, 1.4 Hz, 2H, 4′-CH, Ph), 7.22–7.28 (m, 4H, 3′,5′-CH, Ph), 7.39–7.43 (m, 4H, 2′,6′-CH, Ph), 8.97 (t, $J$=5.4 Hz, 1H, NH). $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$: 28.5, 34.0, 42.6, 44.0, 46.7, 51.2, 60.5, 75.4, 91.2, 95.3, 126.4, 127.3, 128.0, 142.1, 149.6, 157.4, 158.2, 165.8. Anal. Calcd for $C_{28}H_{33}N_5O_2$: C 71.31; H 7.05; N 14.85. Found: C 71.25; H 7.12; N 14.96%.

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