SYNTHESIS OF N-(2-PYRIDYL)CYANOACETAMIDES AND 4-AMINO-2H-PYRIDO-[1,2-a]PYRIMIDIN-2-ONES FROM ETHYL CYANOACETATE AND 2-AMINOPYRIDINE

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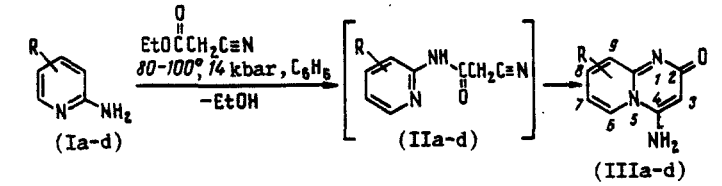
The reaction of 2-aminopyridine and 2-aminopicolines with ethyl cyanoacetate under high pressures results in the formation of 4-amino-4H-pyrido[1,2-a]pyrimidin-2-ones. Depending on the structure of the initial pyridine base, heating of a mixture of the above reagents under low vacuum gives either the same products or their isomeric N-(2-pyridyl)cyanoacetamides. The mutual transformations of the synthesized isomers were studied; it was found that cyanoacetamides are readily cyclized by the action of an alcoholic solution of HCl into pyrido[1,2-a]pyrimidin-2-ones, while the latter, during sublimation or heating in DMSO, undergo opening of the pyrimidine ring.

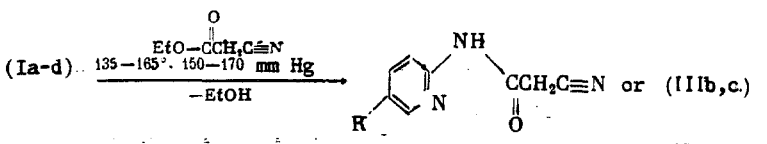
Derivatives of pyrido[1,2-a]pyrimidine are popular subjects of investigation, attracting attention due to their diverse biological activity (cf. [1]). The most common methods of preparation of these compounds are based on the use of 2-aminopyridine (AP) as a dinucleophile in reactions with C_3-synthones (esters of malonic, ethoxymethylenemalonic, 2-bromocrotonic, propionic acids, etc. [1-6]). It seemed that the reaction of AP with cyanoacetic acid esters could also be used as a simple path for building up a pyrido[1,2-a]pyrimidine system, but no information was given in the literature on this subject.

It was reported in [7] that on heating AP with ethyl cyanoacetate (ECA) to 180-200°C, N-(2-pyridyl)cyanoacetamide (PCA) was isolated, the yield of which however was not indicated. Our attempts to repeat this reaction under the same conditions showed that it is accompanied by strong resinification and PCA is obtained in low and variable yields. According to the data in [8], the corresponding cyanoacetamide is also obtained from ECA and 2-amino-6-methylpyridine in a yield of only 16%. However, the dialkylboryl derivatives of AP react readily with ECA even at 20°C, but in this case, instead of the PCA, the ethyl ester of 3-amino-2-cyano-4-[-N-(2-pyridyl)carbamoyl]crotonic acid is formed, corresponding in its structure to the addition product of a molecule of ECA to the C≡N group of PCA [9].

We found that 4-amino-2H-pyrido[1,2-a]pyrimidin-2-ones (IIIa-d) can be directly obtained from ECA and AP (Ia) or 2-aminopicolines (Ib-d) at high pressures (see preliminary communication [10]). Under optimal conditions – heating the reagents in benzene at 80-100°C and a pressure of 14 kbar – the resulting (IIIa-d), which can be readily isolated from the reaction mixture by treatment with DMF, reaches yields of 40-85% (scheme (1)). At lower pressures, and also on changing the temperature in either direction, the yields of (III) sharply decrease



(1)



(2)

(I), (II): R = H (a); 3-Me (b); 4-Me (c); 5-Me (d); (III): R = H (a); 9-Me (b); 8-Me (c); 7-Me (d).

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It is most probable that cyanoacetamides (IIa-d) are intermediately formed from (Ia-d) and ECA and further cyclize into (IIIa-d). It has recently been reported that high pressures are used in the syntheses of amides from carboxylic acid esters and amines [11], while the ability of (IIa-d) to undergo cyclization under a pressure of 14 kbar was confirmed by us in special experiments.

The use of benzene as a solvent is important in the synthesis of (IIIa-d). Attempts to replace it with ether or acetonitrile, and also to carry out the reaction without a solvent were unsuccessful. It can be assumed that under the conditions of process (1), benzene exists in the solid state. In such a case, we can assume that the reaction of (Ia-d) with ECA proceeds in the micropores of the solid phase. This favors an intramolecular cyclization of the intermediately formed amides (II) and restricts intermolecular processes leading to resinification.

The experimental results prompted us to return to the problem of the reaction of aminopyridines (Ia-d) with ECA without the use of high pressures. It was found that by carrying out the reaction with the simultaneous distillation of ethanol that separates out at 150-170 mm Hg, it is possible to lower the process temperature to 135-165°C, and thus substantially reduce the resinification of the reaction mixture. Under these conditions, cyanoacetamides (IIa, d) were synthesized from (Ia-d) and ECA in a yield of 50% (scheme (2)). It was unexpectedly found that the reaction of (Ib) with ECA under similar conditions does not lead to the formation of (IIb), but of the corresponding pyrido[1,2-a]pyrimidine (IIIb) isolated in a yield of 60%. A parallel action of (Ic) on ECA under these conditions gives (IIIc) but in a low yield, since in this case substantial resinification of the reaction mixture cannot be avoided.

Thus, the results of the reaction of (Ia-d) with ECA are substantially dependent on the structure of the initial (I) and on the reaction conditions. In this connection, the problem of the mutual transformations of the isomeric compounds (II) and (III) also becomes important.

The study of the thermal stability of compounds (IIa-d) and (IIIa-d) showed that the former are thermodynamically more stable. Vacuum sublimation of the condensed heterocycles (IIIa-d) leads completely to opening of the pyrimidine ring, i.e., to the formation of cyanoacetamides (IIa-d)

$$\begin{array}{c}(\text{IIIa}-\text{d})\xrightarrow[(1\ \text{mm Hg})]{\sim 140^\circ\ (\text{for (IIIb)}\sim 230^\circ)}(\text{IIa}-\text{d})\\(\text{IIb})\xrightarrow{\Delta,\ \text{Py or Et}_3\text{N}}(\text{IIIb})\end{array} \qquad (3)$$

Compound (IIIa) converts completely in the course of 3 h into (IIIa-d) leads completely any visible signs of melting. The study of the IR spectra of (IIIa) in KBr, carried out in a cuvette with a variable degree of heating of the sample showed that the isomerization already begins at 120°C, while at 140°C it proceeds at a significnat rate. The opening of the pymidine ring in (IIIc) occurs under the same conditions, but substantially more slowly. Compound (IIIb) was found to be much more stable to heating; in its IR spectrum no noticeable changes were observed up to 170-180°C (for the sublimation of (IIIb) in vacuo with conversion into (IIb), the compound must be heated at ≥230°C).

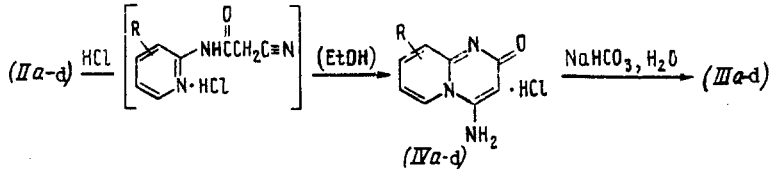
Samples of compounds (IIIa-d) which were stored for several months in a crystalline state, practically did not undergo any changes. However, in DMSO-d_6 solutions, according to the PMR spectral data, a slow transformation of (IIIa-d) into (IIa-d) takes place. For example, (IIIa, c, d) isomerize completely at ~20°C in the course of 5-6 weeks. Increase in the temperature substantially accelerates the process, while at ~100°C, the conversion of (IIIa, c, d) into (IIa, c, d) takes 1 h. In the case of (IIIb), the isomerization does not proceed so fast, and after 4 h of heating at 100°C, about 10% of the initial isomer still remains (during a more prolonged heating of the solution, further isomerization of (IIIb) is accompanied by side processes).

It has recently been discovered that in solutions, (2-pyridyl)aminomethylenemalononitrile is present in an equilibrium with its bicyclic isomer – 4-imino-3-cyano-4H-pyrido[1,2-a]-pyrimidine [12]. The mutual transformations of these compounds belong to ring-chain tautomerism processes and depend on the temperature, nature of solvent and time.

The poor solubility of compounds (IIIa-d) in most organic solvents and the tendency to autocondensation of (IIa-d) do not make it possible to solve unequivocally the question

of the existence of a ring-chain tautomerism (III) ⇄ (II). In any case, not only the transformations of (III) into (II) are possible but also the reverse process. Thus, cyanoacetamide (IIb) cyclizes on heating in the presence of triethylamine, pyridine or (Ib), so that (IIIb) that is formed can be isolated in a yield of 70-80% (see scheme (3)). Using PMR spectroscopy, a partial isomerization of (IIa, c, d) was observed in Py-d_5 solutions, which however cannot be used for preparative purposes, since it proceeds slowly and is accompanied by side reactions.

We succeeded in finding a convenient method for the preparation of (IIIa-d) from cyanoacetamides (IIa-d) consisting in treatment of the latter with a solution of HCl in ethanol. The hydrochlorides (IVa-d) thus formed readily convert into free bases (IIIa-d) by the action of an aqueous $NaHCO_3$ solution

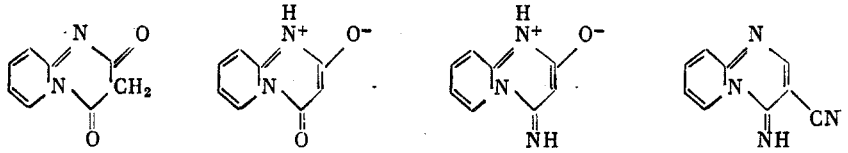


(4)

Both (IIa-d) and (IIIa-d) are soluble in water, but while the former are well soluble in DMF and DMSO and on heating in MeCN, the latter are insoluble in most organic solvents. Therefore, compounds (III) can be readily purified from the impurity of (II) by washing with DMF. Compounds (IIIa-d) can be recrystallized from 75% EtOH (thus (IIIa) precipitates in the form of a monohydrate, which loses water on heating in vacuo).

Cyanoacetamides (IIa-d) crystallize from MeCN or EtOH. In their IR spectra, taken in KBr, bands of stretching vibrations of the associated NH groups are observed in the 3290-3120 cm^{-1} range, a medium intensity band at 2270 cm^{-1} (νC≡N), an intense band at 1680 cm^{-1} (νC=O), and also bands with frequencies at about 1600 and 1580 cm^{-1} characteristic for the pyridine fragment. In the PMR spectra of (IIa-d) in DMSO-d_6, the CH_2 group signal appears in the form of a singlet with a chemical shift (CS) of 3.95-4.00 ppm.

The bicyclic compound (IIIa) can be regarded in a sense as a nitrogenous analog of the so-called "malonyl-α-aminopyridine" (MAP), a product of the reaction of AP with malonic ester. Originally MAP was described as having the dioxo form (V) [2], but in fact, this compound has a betaine structure (VI) [13], which in particular, was confirmed by x-ray investigation [14]. Correspondingly, also in the case of (III) the possibility of an alternative structure of (VII) similar to (VI) should be considered. However, the data of the IR



and PMR spectra indicate a structure with the amino group. Thus, in the PMR spectrum of (IIIa) in DMSO-d_6 one singlet is observed from two NH protons. The position of the H^6 signal with CS of 8.18 ppm corresponds to structure (III) but not to (VII), since in the latter case we should expect a considerable shift to the weak field because of the descreening action of the C=NH group. (Thus, for example, in the spectrum of compound (VIII) in DMSO-d_6, the H^6 signal has a CS of 9.30 ppm [12].)

In the IR spectra of (IIIá-d) run in KBr, the νC=O band appears in a narrow interval of 1675-1690 cm^{-1}, while the stretching vibrations of the NH_2 group are observed in the form of a series of broad bands in the 3050-3410 cm^{-1} region. The intense absorption with a frequency at 1630 cm^{-1} can be attributed to deformational vibrations of the NH_2 group, probably overlapped by the vibration bands of a conjugated system of multiple C=C and C=N bonds.

Compounds (IIIa-d) form salts (IVa-d) by the action of an aqueous or alcoholic HCl. The protonation clearly occurs at the cyclic N^1 atom. In the IR spectra of the salts an intense absorption of νC=O is observed with a frequency at 1690 cm^{-1}, while in the PMR spectra a shift of the H^6 is observed to a weak field (CS ~ 8.90 ppm) compared with the free bases.

Thus, the bicyclic compounds (IIIa-d) can be obtained from (Ia-d) and ECA, with and without the use of high pressures. N,N-dialkyl derivatives of 4-amino-2H-pyrido[1,2-a]-pyrimidin-2-one have recently been synthesized by the reaction of AP with reagents prepared by mixing N,N-dialkylethoxycarbonylacetamides with $POCl_3$ [15]. However, together with the above reaction products, the yield of which varies from 10 to 48%, small amounts of their isomers containing the dialkylamino group at the 2-position and a carbonyl group in the 4-position are also formed. The N-phenyl-N-alkyl derivatives of compound (IIIa) were obtained in a similar way [16], but this method cannot be used for the synthesis of compounds of type (III) with an unsubstituted amino group.

Cyanoacetamides (IIa-d) are of interest as potential ligands and reagents in organic synthesis.

EXPERIMENTAL

The ^1H NMR spectra (δ, ppm) (J, Hz) and ^{13}C NMR spectra (δ, ppm) (J, Hz) were recorded in DMSO-d_6 on "Bruker WM-250" (250 MHz) and "Bruker AM-300" (300 MHz) spectrometers. The IR spectra were run on "Specord M-80", "Perkin-Elmer-577" and UR-20 spectrophotometers in KBr. The mass spectra (m/z) were obtained on a "Varian MAT CH 6" mass-spectrometer with direct introduction of the samples into the ionic source.

The "pure" grade solvents and ECA were made absolute. The initial 2-aminopyridine and 2-aminopicolines (Ia-d) were additionally purified by distillation under vacuum. The experiments using high pressures were carried out on a "cylinder-piston" type apparatus in Teflon ampuls, as shown in [17].

Synthesis of 4-Amino-2H-pyrido[1,2-a]pyrimidin-2-ones (IIIa-d) from ECA and (Ia-d) at High Pressures. A mixture of 5-6 mmoles of (Ia-d) and 5-6 mmoles of ECA in 1.2-1.5 ml of C_6H_6 was held in a Teflon ampul for 5 h at 14 kbar pressure and at 80°C. The reaction mixture was treated with ether (2 × 10 ml) and filtered off, and then the precipitate on the filter was treated with DMF (2 × 5 ml) and filtered again. The residue of (IIIa-d) was washed with ether and dried under vacuum (1 mm) for 3-5 h.

4-Amino-2H-pyrido[1,2-a]pyrimidin-2-one (IIIa). Yield 40%, mp 160-162°C ($EtOH/H_2O$). PMR spectrum: 8.18 d.d (1H, H^6, J = 7.0, 1.4), 7.57 d.d.d (1H, H^8, J = 8.5, 6.6, 1.4), 7.08 d.d (1H, H^9, J = 8.5, 1.5), 6.89 d.d.d (1H, H^7, J = 7.0, 6.6, 1.5), 6.84 br.s (2H, NH_2), 5.50 s (1H, H^3). ^{13}C NMR spectrum: 169.37 (C^2), 91.52 d (164, C^3), 150.98 (C^4), 127.91 d (187, C^6), 112.90 d (172, C^7), 136.24 d (167, C^8), 124.92 d (171, C^9), 150.73 br.s (C^{10}). Mass spectrum, m/z: 161 [M^+]. IR spectrum (ν, cm^{-1}): 3398, 3300, 3055 (NH): 1675 (C=O). Found: C 59.56; H 4.48; N 26.50%. $C_8H_7N_3O$. Calculated: C 59.62; H 4.38; N 26.08%.

4-Amino-9-methyl-2H-pyrido[1,2-a]pyrimidin-2-one (IIIb). Yield 65% (after recrystallization from 75% EtOH), mp 219-220°C (dec.) PMR spectrum: 8.06 d (1H, H^6), 7.48 d (1H, H^8), 6.81 m (3H, H^7 and NH_2), 5.50 s (1H, H^3); 2.27 s (3H, Me). Mass spectrum, m/z: 175 [M^+]. IR spectrum (ν, cm^{-1}): 3390, 3280, 3070 (NH): 1676 (C=O). Found: C 61.61; H 5.13; N 23.87%. $C_9H_9N_3O$. Calculated: C 61.70; H 5.18; N 23.99%.

4-Amino-8-methyl-2H-pyrido[1,2-a]pyrimidin-2-one (IIIc). Yield 60%, mp 162-163°C ($EtOH/H_2O$). PMR spectrum: 8.07 d (1H, H^6, J = 7.3), 6.88 d (1H, H^9, J = 1.9), 6.79 s (2H, NH_2); 6.78 d.d (3H, H^7, J = 7.3, 1.9), 5.43 s (1H, H^3), 2.29 s (3H, Me). ^{13}C NMR spectrum: 168.58 d (5, C^2), 90.07 d (164, C^3), 149.97 (C^4), 126.00 d (186, C^6), 121.44 d (168, C^7), 146.29 (C^8), 114.29 d (170, C^9), 149.36 (C^{10}), 20.44 q (128, Me). Mass spectrum, m/z: 175 [M^+]. IR spectrum (ν, cm^{-1}) 3410, 3280, 3055 (NH): 1675 (C=O). Found: C 61.45; H 5.40; N 23.51%. $C_9H_9N_3O$. Calculated: C 61.70; H 5.18; N 23.99%.

4-Amino-7-methyl-2H-pyrido[1,2-a]pyrimidin-2-one (IIId). Yield 49%, mp 172-173°C ($EtOH/H_2O$). PMR spectrum: 8.11 d.q (1H, H^6, J = 1.8; 1.1), 7.76 d.d (1H, H^8, J = 9.3, 1.8), 7.27 d (1H, H^9, J = 9.3), 5.71 s (1H, H^3); 2.25 s (3H, Me). Mass spectrum, m/z: 175 [M^+]. IR spectrum (ν, cm^{-1}) 3405, 3250, 3050 (NH); 1688 (C=O). Found: C 61.45; H 5.18; N 24.04%. $C_9H_9N_3O$. Calculated: C 61.70; H 5.18; N 23.99%.

Reaction of ECA and (Ia-d) without Using High Pressures. N-(2-Pyridyl)cyanoacetamide (IIa). A 4.0 g portion (43 mmoles) of (Ia) and 7.2 g (64 mmoles) of ECA were placed in a distillation apparatus. The mixture was held for 5 h under vacuum (~170 mm) on an oil bath at 135-140°C, whereby ethanol was distilled off. A 15 ml portion of EtOH was added to the residue, the precipitate was filtered off, and washed with 5 ml of EtOH and ether (3 × 10 ml). Yield, 3.5 g (51%) of (IIa), mp 155-156°C (cf. [7]: mp 159-160°C). PMR spectrum:

10.82 br.s (1H, NH), 8.33 d.d (1H, H^6, J = 4.4, 2.0), 8.01 d (1H, H^3, J = 8.3); 7.82 d.d (1H, H^4, J = 6.4, 2.0), 7.14 d.d (1H, H^5, J = 6.4, 4.4), 3.98 s (2H, CH_2). ^{13}C NMR spectrum: 151.23 (C^2), 113.45 d (170, C^3), 138.31 d (164, C^4), 119.88 d (166, C^5), 148.00 d (179, C^6), 161.86 t (6.8, C=O), 115.58 t (10.2, CN), 26.63 t (136, CH_2). Mass spectrum, m/z: 161 [M^+]. IR spectrum (ν, cm^{-1}) 3265, 3205, 3120 (NH); 2270 (C≡N); 1682 (C=O).

N-(5-Methyl-2-pyridyl)cyanoacetamide (IId). In a similar way as in the case of (IIa), by heating 2.0 g (18.5 mmoles) of (Id) and 2.1 g (18.5 mmoles) of ECA at 160-165°C on an oil bath and under vacuum (150-155 mm) for 2 h, 1.64 g (51%) of (IId) was obtained, mp 186-187°C. PMR spectrum: 10.72 br.s (1H, NH), 8.17 d (1H, H^6, J = 2.4), 7.91 d (1H, H^3, J = 8.2), 7.63 d.d (1H, H^4, J = 8.2, 2.4), 3.95 s (2H, CH_2), 2.24 s (3H, Me). ^{13}C NMR spectrum: 149.11 (C^2), 113.03 d (170, C^3), 138.71 d (161, C^4), 128.95 q (6, C^5), 147.84 d (176, C^6), 161.62 (C=O), 115.74 (CN), 26.59 t (136, CH_2), 17.25 q (127, 5-Me). Mass spectrum, m/z: 175 [M^+]. IR spectrum (ν, cm^{-1}) 3290, 3200, 3130 (NH); 2270 (C≡N), 1680 (C=O). Found: C 61.94; H 5.47; N 23.93%. $C_9H_9N_3O$. Calculated: C 61.70; H 5.18; N 23.99%.

Synthesis of (IIIb). In a similar way as in the case of (Ia), by heating 2.5 g (23 mmoles) of (Ib) and 4.0 g (35 mmoles) of ECA at 160-165°C under vacuum (160-165 mm) for 3 h, 2.45 g (60%) of the bicyclic compound (IIIb) was obtained (identified from IR and PMR spectra and by comparison with the spectra of samples obtained under high pressure).

Synthesis of (IIIc). In a similar way, by heating 1.5 h (14 mmoles) of (Ic) and 1.6 g (14 mmoles) of ECA at 160-165°C under vacuum (160-165 mm) for 2.5 h, 0.42 g (17%) of compound (IIIc) was obtained.

Isomerization of (IIIa-d) into (IIa-d). Synthesis of (IIa). Vacuum sublimation (1 mm) of 0.14 g (0.8 mmole) of (IIIa) at 150°C gave 0.08 g (57%) of (IIa).

Synthesis of (IId). In a similar way, by sublimation of 0.06 g (0.3 mmole) of (IIId) under vacuum (2 mm) at 150-155°C, 0.05 g (83%) of compound (IId) was obtained.

N-(3-Methyl-2-pyridyl)cyanoacetamide (IIb). In a similar way, by sublimation of (IIIb) at 230°C (1 mm), compound (IIb) was obtained in a 90% yield, mp 216-217°C. PMR spectrum: 10.38 br.s (1H, NH), 8.26 d (1H, H^6), 7.70 d (1H, H^4), 7.23 d.d (1H, H^5), 3.97 s (2H, CH_2), 2.17 s (3H, Me). Mass spectrum, m/z: 175 [M^+]. IR spectrum (ν, cm^{-1}): 3252, 3195, 3120 (NH); 2260 (C≡N), 1662 (C=O). Found: C 61.44; H 5.07; N 24.40%. $C_9H_9N_3O$. Calculated: C 61.70; H 5.18; N 23.99%.

N-(4-Methyl-2-pyridyl)cyanoacetamide (IIc). In a similar way, by sublimation of (IIIc) at 150-155°C (1 mm), compound (IIc) was obtained in a 80% yield, mp 108-109°C. PMR spectrum: 10.82 br.s (1H, NH), 8.18 d (1H, H^6, J = 5.1), 7.84 d (1H, H^3, J = 1.3), 7.00 d.d (1H, H^5, J = 5.1, 1.3), 3.98 s (2H, CH_2), 2.32 s (3H, Me). ^{13}C NMR spectrum: 151.37 (C^2), 113.89 d (167, C^3), 149.18 (C^4), 120.96 d (164, C^5), 147.69 d (178, C^6), 161.83 t (6.7, C=O), 115.72 t (10.3, CN), 26.71 t (136, CH_2), 20.86 q (127, Me). Mass spectrum, m/z: 175 [M^+]. IR spectrum (ν, cm^{-1}): 3268, 3225, 3162 (NH); 2270, 2260 (C≡N), 1678 (C=O). Found: C 61.46; H 5.20; N 24.35%. $C_9H_9N_3O$. Calculated: C 61.70; H 5.18; N 23.99%.

Cyclization of (IIb) into (IIIb) in the Presence of Pyridine. A mixture of 0.1 g (0.5 mmole) of (IIb), 3 ml of C_6H_6 and 1 ml of pyridine was boiled for 6 h. The precipitate was filtered, washed with ether (2 × 10 ml) and dried. Yield 0.07 g (70%) of (IIIb).

Cyclization of (IIa-d) into (IIIa-d) by the Action of HCl in EtOH. A 15 mmole portion of a 3.5 M solution of HCl in EtOH was added to a suspension of 15 mmoles of (IIa-d) in 5 ml of EtOH. The mixture was boiled for 1 h, the precipitate of hydrochloride (IV) was filtered, washed with EtOH (2 × 5 ml), ether (2 × 10 ml) and dried in vacuo.

4-Amino-2H-pyrido[1,2-a]pyrimidin-2-one Hydrochloride (IVa). Yield, 90%, mp 266-267°C (dec.). PMR spectrum: 13.48 br.s (1H, HCl), 8.91 d (1H, H^6), 8.58 br.s (2H, NH_2), 8.23 d.d (1H, H^8), 7.68 d (1H, H^9), 7.61 d.d (1H, H^7), 6.00 br.s (1H, H^3). ^{13}C NMR spectrum: 163.91 br.s (C^2), 89.09 d (171, C^3), 149.29 m (C^4), 129.16 d (191, C^6), 118.08 d (174, C^7), 141.88 d (171, C^8), 120.76 d (175, C^9), 152.56 br.s (C^{10}). Mass spectrum, m/z: 161 [$(M-HCl)^+$]. IR spectrum (ν, cm^{-1}): 3380, 3250, 3080 (NH), 1690 (C=O). Found: C 48.40; H 4.25; N 21.30; Cl 17.91%. $C_9H_8N_3ClO$. Calculated: C 48.61; H 4.08; N 21.26; Cl 17.96%.

4-Amino-8-methyl-2H-pyrido[1,2-a]pyrimidin-2-one Hydrochloride (IVc). Yield, 75%, mp 252-253°C (dec.). PMR spectrum: 13.32 br.s (1H, HCl), 8.82 d (1H, H^6), 8.48 br.s (2H, NH_2), 7.51 d (1H, H^7), 7.46 s (1H, H^9), 5.89 br.s (1H, H^3), 2.53 s (3H, Me). Mass spectrum, m/z:

175 [$(M-HCl)^+$]. IR spectrum (ν, cm^{-1}): 3360, 3300, 3070 (NH), 1665 (C=O). Found: C 51.17; H 4.86; N 19.85; Cl 16.71%. $C_9H_{10}N_3ClO$. Calculated: C 51.06; H 4.76; N 19.85; Cl 16.77%.

4-Amino-7-methyl-2H-pyrido[1,2-a]pyrimidin-2-one Hydrochloride (IVd). Yield, 87%, mp 245-246°C (dec.). PMR spectrum: 9.83 br.s (1H, HCl), 8.99 s (1H, H^6), 8.68 br.s (2H, NH_2), 8.11 d (1H, H^8), 7.63 d (1H, H^9), 6.04 br.s (1H, H^3), 2.41 s (3H, Me). Mass-spectrum, m/z: 175 [$(M-HCl)^+$]. IR spectrum (ν, cm^{-1}): 3355, 3240, 3165, 3080 (NH); 1665 (C=O). Found: C 51.42; H 4.72; N 19.81; Cl 16.62%. $C_9H_{10}N_3ClO$. Calculated: C 51.06; H 4.76; N 19.85; Cl 16.77%. (4-Amino-9-methyl-2H-pyrido[1,2-a]pyrimidin-2-one hydrochloride (IVb) was further used for the preparation of (IIIb) without additional examination.)

Separation of (IIIa-d) from Salts (IVa-d). The free bases were obtained by neutralization of the aqueous solutions of the corresponding (IVa-d) with an equimolar amount of $NaHCO_3$. The precipitates of (IIIa-d) were washed with ethanol (2 × 5 ml), ether (2 × 10 ml), and were dried in vacuo. The yield of (IIIa) was 86%, (IIIc) 86%, (IId) 85%. The yield of (IIIb) (based on (IIb)) was 77%. According to spectral characteristics and melting points, the samples of the compounds obtained were identical with the corresponding (IIIa-d) obtained by the above-described methods.

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