Synthesis and functionalization of 4-arylamino-2-pyridone derivatives

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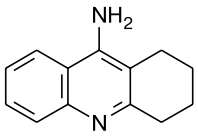
New approaches to the synthesis of the previously unknown pyrimidine, 4-amino-2-pyridone, and 4-aminopyridine derivatives were developed based on the reactions of enaminoamides with dimethylformamide dimethyl acetal. New structural modifications of 4-amino-2-pyridone derivatives were performed. Numerous compounds of this type, which are of interest for biological studies, were prepared.

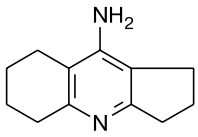
Key words: amide acetals, 3-cyano-2-oxo-5-R-4-(phenylamino)-1,2-dihydropyridines, 4-arylamino-3,5-dicyanopyridines, acidic hydrolysis, NMR spectroscopy, X-ray diffraction analysis.

Earlier, a procedure has been developed for the synthesis of various 1-alkyl- and 1-aryl-5-cyano-(2-*N*,*N*-dimethylaminovinyl)-4-oxo-1,4-dihydropyrimidines[1,2] based on the reactions of amide acetals at the primary amide amino group and at the methyl group of 3-arylamino-2-cyanocrotonamides. These pyrimidinones were found[1—4] to undergo recyclization to form 4-alkyl(aryl)amino-3-cyanopyridin-2-ones under conditions of both alkaline and acidic hydrolysis.

The aim of the present study was to synthesize new 1-arylpyrimidin-4-one derivatives containing *ortho* substituents in the phenyl ring and investigate their behavior under conditions of acidic and alkaline hydrolysis, as well as to prepare 4-arylamino-5-formyl-2-pyridones and investigate their properties. It should be emphasized that recyclization of these pyrimidinones would be expected to give substituted 4-aminopyridines, and this class of compounds is of considerable interest in searching for compounds acting on the central nervous system. It is sufficient to note that this class includes the well-known drugs tacrine and amiridine, which are used in the therapy of the neurodegenerative disease, such as Alzheimer's disease.[5—7]



Tacrine



Amiridine

Scheme 1 presents the synthesis of pyrimidinones **4a,b** by the method developed earlier.[1,4] In the first step, transamination of enaminoamide **1** with *ortho*-substituted anilines in acetic acid gives, *via* compounds **3a,b**, enaminoamides **2a,b** in high yields, and refluxing of the latter in DMF acetal (or in toluene in the presence of a threefold excess of DMF acetal) affords pyrimidinones **4a,b**.

Alkaline hydrolysis of compounds **4a,b** yields 3-cyano-4-(2-methoxyphenylamino)- and 3-cyano-4-(2,5-dimethoxyphenylamino)pyridin-2-one **5a,b**, as observed earlier in analogous reactions with various 1-alkyl- and 1-aryl-substituted pyrimidin-4-ones.[1—4] This process involves the pyrimidine ring opening accompanied by elimination of HCOOH followed by recyclization through intramolecular transamination to form 3-cyanopyridones **5**.

Acidic hydrolysis of pyrimidin-4-ones gives rise to a mixture of compounds, different products being isolated depending on the reaction conditions and the nature of substituents in the benzene ring. For example, refluxing of pyrimidinones **4a,b** in glacial acetic acid affords bicyclic compounds **6a** and **6b** in 41 and 78% yields, respectively, the pyrimidine ring remaining intact. Heating of pyrimidinone **4a** in a stronger acid (1 *M* HCl, 70 °C, 4 h) gives rise to a mixture of two products, *viz.*, *N*-formylcarbamoylpyridone **7a** and 3-carbamoylpyridone **8a**. We

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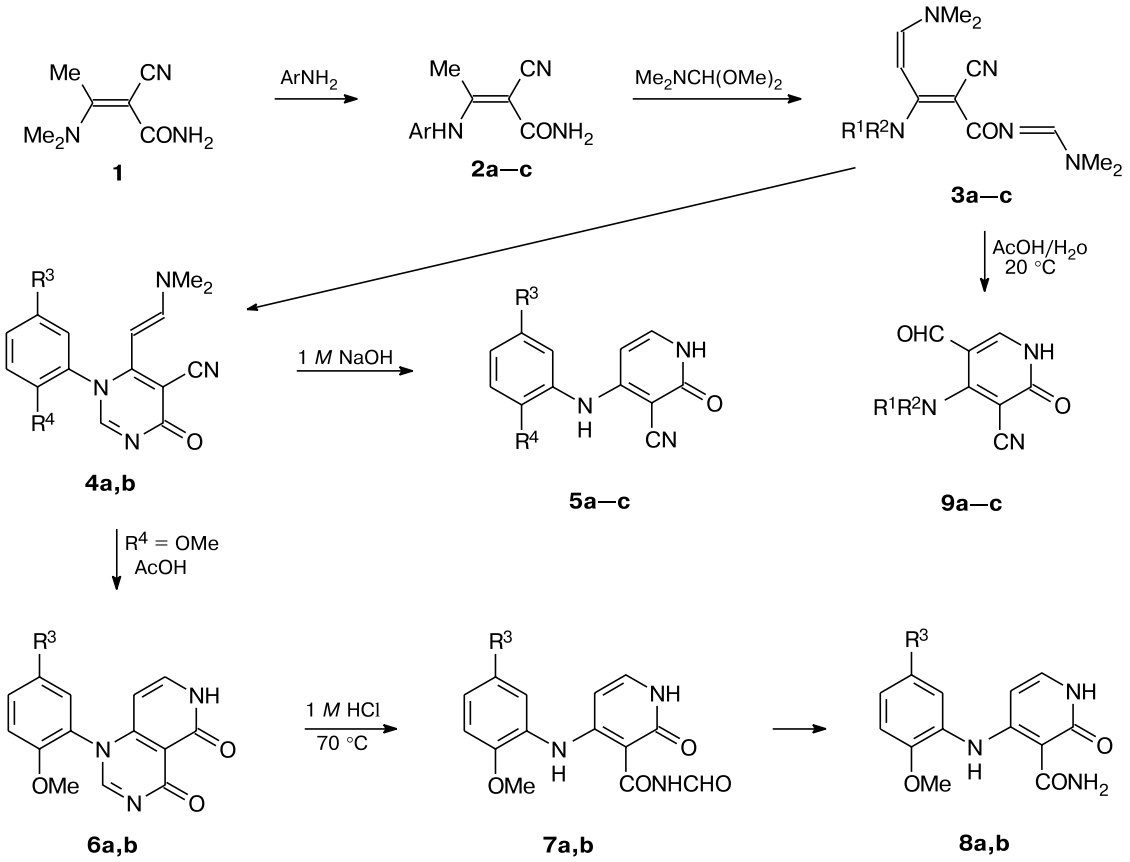
Scheme 1



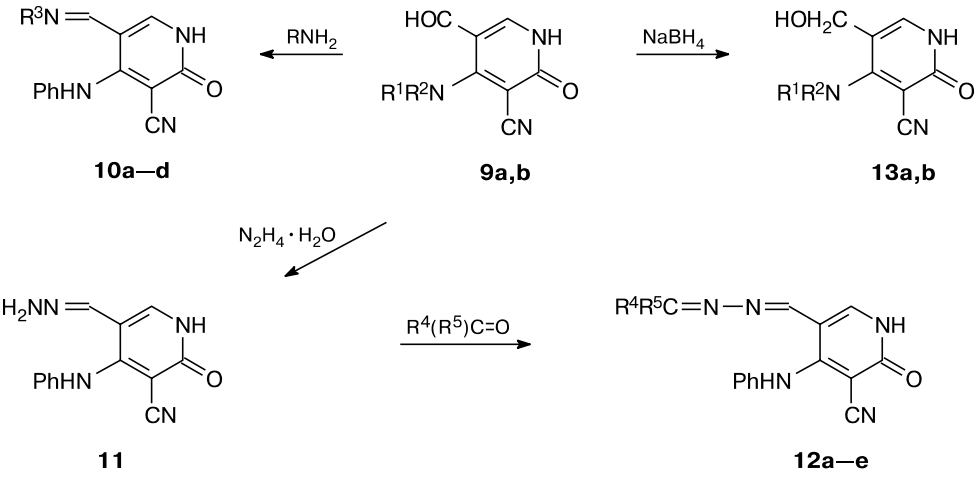
2: Ar = 2-$MeOC_6H_4$ (**a**), 2,5-$(MeO)_2C_6H_3$ (**b**), 4-ClC_6H_4 (**c**)
3, 9: R^1 = H, R^2 = Ph (**a**); R^1 = H, R^2 = 4-ClC_6H_4 (**b**); R^1 = R^2 = Me (**c**)
4—8: R^3 = H, R^4 = OMe (**a**); R^3 = R^4 = OMe (**b**); R^3 = R^4 = H (**c**)

isolated compound **7a** from this mixture in individual form in 21% yield. 3-Carbamoyl-4-(2-methoxyphenylamino)-2-pyridone (**8a**) was also prepared in 82% yield by direct hydrolysis of pyrido[4,3-*d*]pyrimidine-4,5-dione **6a** with 1 *M* KOH. Apparently, heating of pyrimidinone **4a** in 1 *M* HCl first leads to cyclization giving rise to pyrido[4,3-*d*]pyrimidine **6a** with the involvement of the enamine and cyano groups followed by the pyrimidine ring opening to form compound **7a,** which is transformed into carbamoylpyridone **8a**. Such transformations have been observed earlier[8] for 1-benzyl-substituted pyrimidinone of type **4** under both acidic and alkaline conditions.

Heating (70 °C, 1 h) of pyrimidinone **4b** containing the 2,5-dimethoxyphenyl substituent or prolonged storage of this compound at 20 °C in 1 *M* HCl also affords a mixture of products (bicyclic compound **6b**, *N*-formylcarbamoylpyridone **7b**, and an impurity of **5b** (TLC)). Storage of this mixture at 20 °C in 1 *M* KOH led to the formation of 3-carbamoylpyridone **8b** in 74% yield (see Scheme 1). *N*-Formylcarbamoylpyridone **7b**, which is an intermediate product of recyclization of pyrimidinone **4b** into carbamoylpyridone **8b**, was also isolated in individual form in 13% yield from an analogous mixture, which was prepared by moderate heating (at 70 °C for 3 h or at 40 °C for 6 h) of pyrimidinone **4b** in 99% acetic acid.

In addition, we studied the properties of 5-formyl-substituted pyridin-2-ones. Earlier, it has been found that the reactions of amide acetals with enaminoamides initially afford compounds **3** as condensation products at both the amide and methyl groups followed by cyclization to give pyridinones. It was established that it is these compounds **3** that give 4-arylamino-3-cyano-5-formylpyridin-2-ones in acidic media.[4] The drawback of this method is that compounds **3** are difficult to prepare in individual form. However, the use of *N*-(*p*-chlorophenyl)-substituted enaminoamide **2c** in the reaction with DMF acetal made it possible to isolate compound **3c**,[3] whose hydrolysis in 90% acetic acid according to the known method[4] produced 4-(4-chlorophenylamino)-3-cyano-5-formylpyridin-2-one **9b**. 5-Formyl-4-phenylamino- and 4-dimethylamino-5-formylpyridones **9a,c**[4] were synthesized analogously (see Scheme 1).

Scheme 2



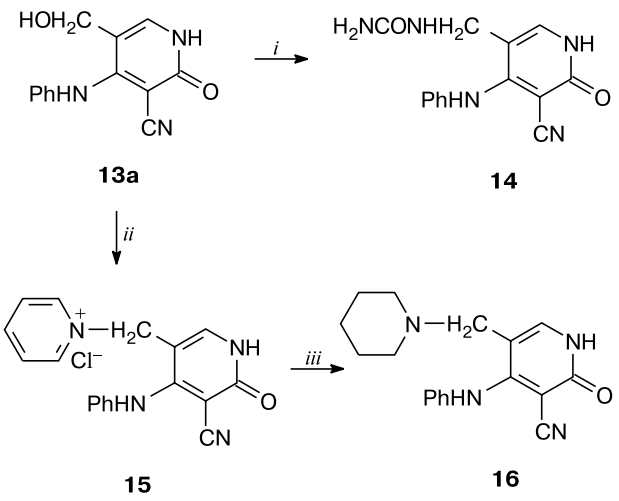
9, 13: R^1 = H, R^2 = Ph (**a**); R^1 = H, R^2 = 4-ClC_6H_4 (**b**)
10: R^3 = CH_2Ph (**a**), $(CH_2)_3COOH$ (**b**), 3,4-$(MeO)_2C_6H_3(CH_2)_2$ (**c**), Ph (**d**)
12: R^4 = Ph, R^5 = H (**a**); R^4 = 4-HOC_6H_4, R^5 = H (**b**); R^4 = 3-MeO-4-HOC_6H_3, R^5 = H (**c**); R^4 = 4-$MeOC_6H_4$, R^5 = H (**d**); $R^4 + R^5 = (CH_2)_5$ (**e**)

Earlier,[9] we have synthesized 4-(arylamino)-3-cyanopyridin-2-ones unsubstituted at position 5 of the pyridine ring and studied their biological properties. 5-Formylpyridinones prepared in our study allow one to synthesize compounds containing various substituents at position 5, which are of interest from the point of view of elucidation of structure—activity relationships. The reaction of 5-formylpyridone **9a** with amines produced Schiff bases **10a—d** (Scheme 2). The ease of the reaction is to a large extent associated with the basicity of the amine used. The reaction with γ-aminobutyric acid proceeds very slowly (product **10b** was isolated in low yield), whereas the reaction with benzylamine readily affords target product **10a** in high yield. The reaction of 5-formylpyridine **9a** with hydrazine hydrate also proceeds readily to give compound **11**, whose reactions with various aldehydes produce hydrazones **12a—e** in high yields.

The aldehyde group in 5-formylpyridines **9a,b** is reduced with $NaBH_4$ to give alcohols. These reactions afforded 4-phenylamino-substituted 5-hydroxymethylpyridones **13a,b** in 70—72% yields (see Scheme 2).

The "benzyl" alcoholic group in pyridone **13a** is rather reactive. The reaction of compound **13a** with urea in AcOH produces 5-ureidomethyl derivative **14** (Scheme 3) in high yield (89%). Various ureido derivatives can exhibit anticonvulsant and antihypoxic activities.[10,11] The transformation of 5-hydroxymethyl-4-phenylaminopyridone **13a** into the chloro derivative followed by treatment with pyridine gave pyridinium salt **15** (^{1}H NMR spectroscopic data, see the Experimental section). Such pyridinium salts were demonstrated[12] to form amino derivatives in the reactions with primary and secondary amines. However, in the reaction under consideration, the attack of the nucleophile (piperidine) unexpectedly does not occur at position 2 of the pyridinium fragment of salt **15** but leads to its replacement. As a result, 5-piperidinomethylpyridone **16** was synthesized (in 36% yield based on consumed alcohol).

Scheme 3

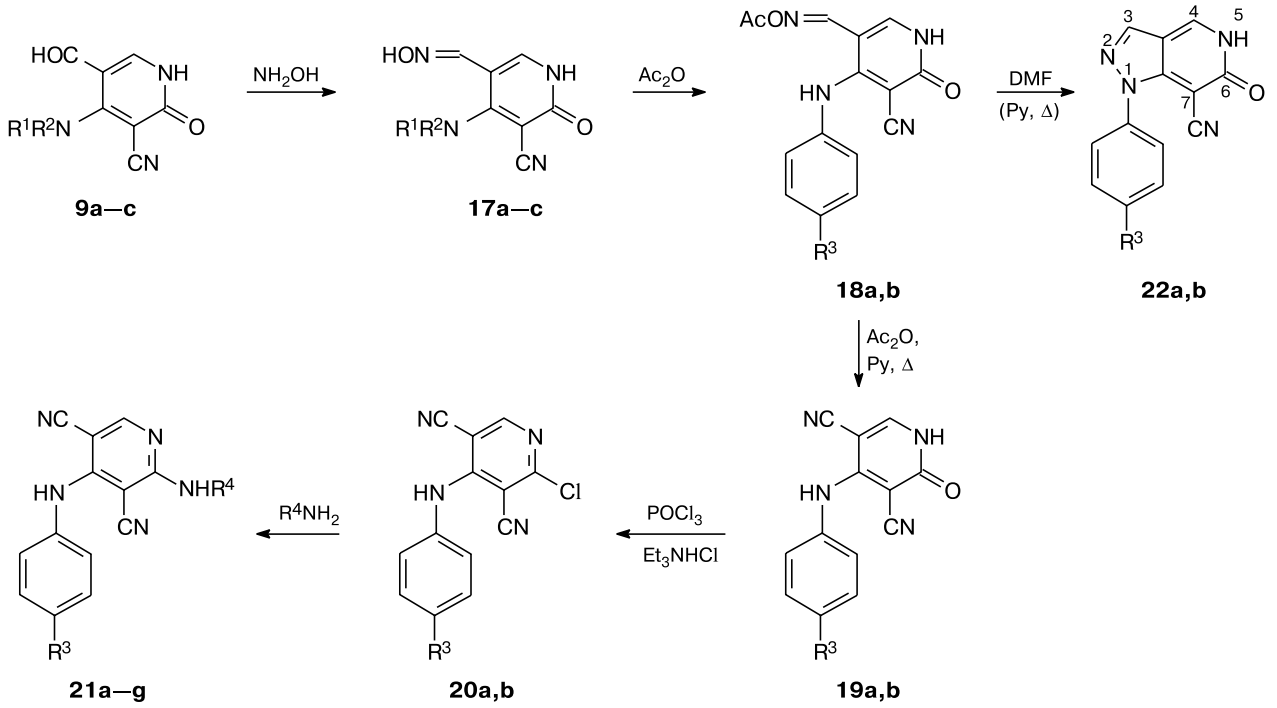


Reagents and conditions. *i*. H_2NCONH_2; *ii*. 1) $SOCl_2$, 2) pyridine; *iii*. Piperidine.

The reactions of 5-formylpyridones **9a—c** with hydroxylamine hydrochloride in pyridine under mild conditions produce oximes **17a—c** (Scheme 4).

Some cyanopyridines exhibit considerable antibradykinin, analgetic, and antihypertensive effects.[1,9] 5-Formylpyridines can be used to synthesize compounds

Scheme 4



9,17: R^1 = H, R^2 = Ph (**a**); R^1 = H, R^2 = 4-ClC_6H_4 (**b**); R^1 = R^2 = Me (**c**)
18—20, 22: R^3 = H (**a**), Cl (**b**)
21: R^3 = R^4 = H (**a**); R^3 = H, R^4 = CH_2Ph (**b**); R^3 = H, R^4 = Ph (**c**); R^3 = H, R^4 = 4-$MeOC_6H_4$ (**d**); R^3 = H, R^4 = 4-ClC_6H_4 (**e**); R^3 = H, R^4 = 4-MeC_6H_4 (**f**); R^3 = Cl, R^4 = 4-ClC_6H_4 (**g**)

containing electron-releasing substituted amino groups and two electron-withdrawing cyano groups. Alternative methods for the synthesis of such compounds are lacking, and these compounds are virtually inaccessible with the use of conventional methods of pyridine synthesis. We succeeded in preparing a series of such compounds with the use of methods for the transformation of the aldehyde moiety into the nitrile group.[13] The treatment of 4-phenylamino-substituted 5-formylpyridones with hydroxylamine hydrochloride in pyridine followed by heating of the reaction mixture in acetic anhydride afforded 3,5-dicyanopyridones **19a,b** in high yield. Apparently, the starting compounds **9a,b** are initially transformed into oximes **17a,b**, which are rapidly transformed into acetyl derivatives **18a,b** under the action of acetic anhydride. At higher temperature (110—115 °C), compounds **18a,b** eliminate the acetic acid molecule to give dicyanopyridones **19a,b**. We succeeded in synthesizing acetyl derivatives from both oximes **17a,b** and 5-formylpyridones **9a,b**. As expected, storage of these compounds in acetic anhydride at 110—115 °C afforded dicyanopyridones **19a,b**, whose reactions with phosphorus oxychloride in the presence of triethylamine hydrochloride produced 2-chloro-3,5-dicyano-4-(4-R-phenylamino)pyridines **20a,b** in high yield (see Scheme 4).

The Cl atom in these compounds is rather labile and can be replaced by the NH_2 or RNH group. This method was used to synthesize diamino derivatives of dicyanopyridones **21a—g**. The replacement of the Cl atom by the amino group was performed by the reaction of chloropyridine **20a** with ethanolic ammonia in an autoclave (see Scheme 4).

It should be noted that heating of acetyl derivatives **18a,b** in dimethylformamide or pyridine leads to their cyclization to give 7-cyano-6-oxo-1-(4-R-phenylamino)-5,6-dihydro-1*H*-pyrazolo[4,3-*c*]pyridines **22a,b**. In the case of 4-anilino-substituted **18a**, cyclization is accompanied by the formation of dicyanopyridone **19a** (which is observed by chromatography), whereas 4-chloro-substituted 5-formylpyridone undergoes only cyclization (see Scheme 4).

This cyclization is very unusual. Hence, we studied the structures of the resulting bicyclic compounds in detail by spectroscopy (the NMR spectra of compounds **22a,b** with the complete assignment of the ^1H and ^{13}C signals are given in the Experimental section).

The structure of compound **22b** was established by the HMBC (heteronuclear multiple-bond connectivity) technique. The correlations peaks at δ 8.41/112.1 (H(3)/C(3a)), 8.41/146.8 (H(3)/C(7a)), 8.73/112.1

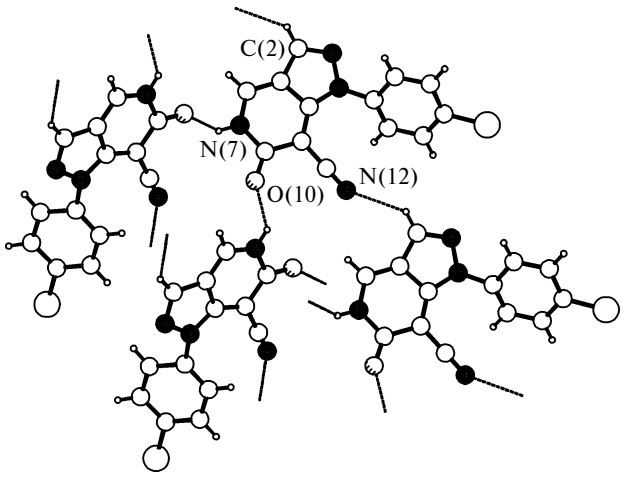


Fig. 1. Intermolecular hydrogen bonds in the crystal structure of **22b**.

(H(4)/C(3a)), 8.73/139.8 (H(4)/C(3)), 8.73/146.8 (H(4)/C(7a)), and 8.73/161.4 (H(4)/C(6)) are consistent with the proposed structure.

The NMR spectroscopic data were supported by X-ray diffraction data for bicyclic compound **22b** (see the Experimental section).

The crystal packing of compound **22b** is stabilized by intermolecular N—H...O and C—H...**N** hydrogen bonds (Fig. 1). The geometric characteristics of these bonds are given in Table 1.

As mentioned above, pyrimidinones **4** are transformed into 3-cyanopyridones **5** under the action of alkali. It is known[14] that aromatic nitriles can be transformed into aldehydes in 75% HCOOH in the presence of a large excess of a Ni—Al_2 alloy as the catalyst. The reaction with 3-cyanopyridine was documented. The yield achieved in this reaction is substantially lower than that in the reactions with aromatic nitriles (37% and 70—97%, respectively). It was of interest to study the behavior of cyano derivatives of 4-aminophenylpyridines under these conditions. Refluxing of 3-cyanopyridine **5c**, which was prepared according to a procedure described earlier,[3] in 50% HCOOH in the presence of a large excess (gram per gram of nitrile) of a Ni—Al_2 alloy as the catalyst afforded only pure formyl derivative **23** in 53% yield. The reaction

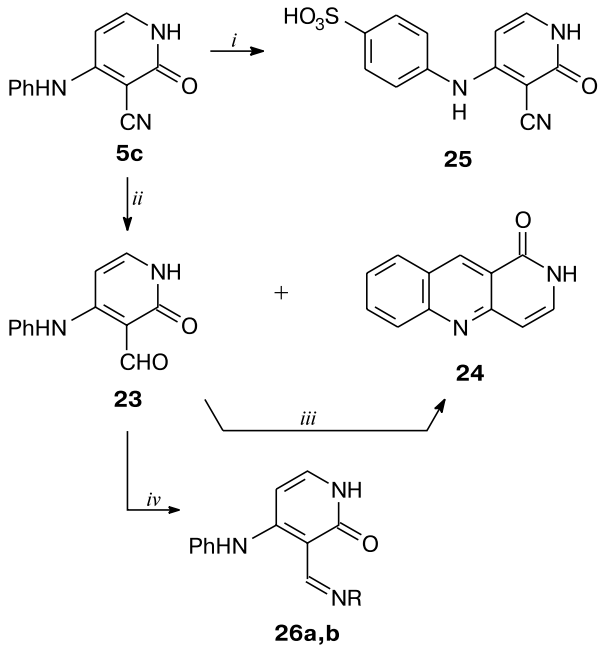
Table 1. Geometric characteristics of hydrogen bonds in compound **22b**

D—H...A	Bond length/Å			D—H...A angle /deg
	D—H	H...A	D...A	
N(7)—H(7)...O(10)^{i}	0.86	1.96	2.617(8)	133
O(18)—H(18)...O(12)^{ii}	0.93	2.46	3.210(8)	138

Note. The symmetry codes: (*i*) $-x$, $0.5 + y$, $0.5 - z$; (*ii*) $1 + x$, $1 + y$, z.

of 3-cyanopyridine **5c** in 85% HCOOH in the presence of this catalyst produced not only 3-formylpyridone **23** but also tricyclic product **24** (Scheme 5).

Scheme 5



26: R = OH (**a**), $NHC_6H_4NO_2$ (**b**)

Reagents and conditions. *i*. 63% H_2SO_4; *ii*. Raney Ni, HCOOH; *iii*. Pr^iOH + piperidine; *iv*. $HONH_2HCl$ or $NH_2NHC_6H_4NO_2$.

3-Formylpyridone **23** readily undergoes cyclization to form tricyclic compound **24** upon refluxing in isopropyl alcohol in the presence of piperidine.

Refluxing of compound **5c** (40 min) in 63% H_2SO_4 leads to hydrolysis of the nitrile group to form the carboxy group followed by decarboxylation with the simultaneous sulfonation at the *para* position of the phenyl ring to give finally compound **25** in 60% yield (see Scheme 5).

3-Formylpyridone **23** is readily involved in condensation. Refluxing in ethanol with hydroxylamine hydrochloride or *p*-nitrophenylhydrazone affords oxime **26a** and hydrazone **26b** in 63 and 68% yields, respectively.

To summarize, we developed procedures for the synthesis of various 4-aminopyridine derivatives, performed modifications of these structures, and prepared numerous compounds, which are of interest for biological studies.

Experimental

The IR spectra were recorded on a FSM-1201 instrument in Nujol mulls. The ^1H NMR spectra were measured on Bruker AC-300 and Bruker DRX-500 spectrometers in DMSO-d_6

and DMSO-d_6—CCl_4. The HMBC spectra were recorded on a Bruker DRX-500 spectrometer in DMSO-d_6. The electron impact (EI) mass spectra (70 eV) were obtained on a Finnigan SSQ-710 mass spectrometer using a direct inlet system. The electrospray—ionization (ESI) mass spectra were recorded on a Waters ZQ-2000 mass spectrometer using a direct inlet system without a chromatographic column. The course of the reactions was monitored and the purity of the compounds was checked by TLC on Merck 60 F_{254} plates (ethyl acetate—ethanol, 10 : 1, as the eluent). The melting points were determined on an Electrotermal 9100 instrument (UK). The melting points and the yields of the reaction products are given in Table 2.

Table 2. Melting points and elemental analysis data for compounds **2a,b**, **4a,b**, **5a,b**, **6a**, **7a,b**, **8b**, **9b**, **10a—c**, **11**, **12b,c,e**, **13a,b**, **14**, **17a—c**, **18a**, **19a,b**, **20a,b**, **21a—g**, **22b**, **23**, **24**, and **26a,b**

Compound	M.p./°C (solvent)	Found / Calculated (%)			Molecular formula
		C	H	N	
2a	186—187 (DMF)	62.65 / 62.33	5.76 / 5.67	18.05 / 18.17	$C_{12}H_{13}N_3O_2$
2b	177—178 (Pr^iOH)	59.73 / 59.76	5.87 / 5.79	16.06 / 16.08	$C_{13}H_{15}N_3O_3$
4a	259—262 (Pr^iOH—DMF)	65.05 / 64.85	5.59 / 5.44	18.72 / 18.91	$C_{16}H_{16}N_4O_2$
4b	205—206 (Pr^iOH—DMF)	62.51 / 62.57	5.41 / 5.56	16.90 / 17.17	$C_{17}H_{18}N_4O_3$
5a	241—242 (Pr^iOH—DMF)	64.76 / 64.72	4.64 / 4.60	17.36 / 17.42	$C_{13}H_{11}N_3O_2$
5b	275—277 (Pr^iOH—DMF)	62.06 / 61.99	4.98 / 4.83	15.15 / 15.49	$C_{14}H_{13}N_3O_3$
6a	280—284 (Pr^iOH—DMF)	61.95 / 62.45	4.07 / 4.12	14.89 / 15.61	$C_{14}H_{11}N_3O_3$
7a	208—211 (Pr^iOH—DMF)	58.72 / 58.53	4.56 / 4.56	14.44 / 14.63	$C_{14}H_{13}N_3O_4$
7b	208—211 (Pr^iOH—DMF)	57.10 / 56.78	4.69 / 4.76	13.02 / 13.24	$C_{15}H_{15}N_3O_5$
8b	280 (Pr^iOH—DMF)	58.31 / 58.13	5.44 / 5.23	14.26 / 14.53	$C_{14}H_{15}N_3O_4$
9b	290 (Pr^iOH—DMF)	57.02 / 57.05	2.65 / 2.95	15.39 / 15.35	$C_{13}H_8N_3O_2Cl$
10a	229—230 (MeOH)	73.27 / 73.17	4.84 / 4.88	17.21 / 17.07	$C_{20}H_{16}N_4O$
10b	207—209 (MeOH)	62.60 / 62.96	4.83 / 4.94	16.95 / 17.28	$C_{17}H_{16}N_4O_3$
10c	202—204 (EtOH)	68.51 / 68.66	5.58 / 5.47	13.98 / 13.93	$C_{23}H_{22}N_4O_3$
11	>320 (DMF)	61.78 / 61.66	4.54 / 4.35	27.50 / 27.67	$C_{13}H_{11}N_5O$
12b	290—292 (DMF)	66.93 / 67.23	4.49 / 4.20	19.51 / 19.61	$C_{20}H_{15}N_5O_2$
12c	292—293 (DMF)	64.98 / 65.12	4.67 / 4.39	18.26 / 18.09	$C_{21}H_{17}N_5O_3$
12e	290—291 (EtOH)	68.37 / 68.47	5.72 / 5.71	21.16 / 21.02	$C_{19}H_{19}N_5O$
13a	222—223 (Pr^iOH—DMF)	64.70 / 64.72	4.79 / 4.60	17.48 / 17.42	$C_{13}H_{11}N_3O_2$
13b	261—264 (Pr^iOH—DMF)	57.07 / 56.64	3.98 / 3.66	15.38 / 15.24	$C_{13}H_{10}N_3O_2Cl$
14	247—250 (Pr^iOH—DMF)	59.59 / 59.36	4.99 / 4.63	24.61 / 24.72	$C_{14}H_{13}N_5O_2$
17a[a]	261—263 (MeOH)	59.73 / 60.35	4.20 / 4.06	21.66 / 21.24	$C_{13}H_{10}N_4O_2 \cdot 0.25H_2O$
17b	293—294 (Pr^iOH)	54.50 / 54.28	2.91 / 2.80	19.57 / 19.48	$C_{13}H_8N_4O_2Cl$
17c	203—204 (Pr^iOH)	52.54 / 52.42	4.69 / 4.89	27.16 / 27.17	$C_9H_{10}N_4O_2$
18a	286—288 (DMF)	60.76 / 60.81	4.01 / 4.05	18.52 / 18.92	$C_{15}H_{12}N_4O_3$
19a	323—324 (MeOH)	65.74 / 66.10	3.47 / 3.39	23.41 / 23.73	$C_{13}H_8N_4O$
19b	335 (MeOH)	57.43 / 57.69	2.75 / 2.61	20.67 / 20.70	$C_{13}H_7N_4OCl$
20a[b]	192—194 (EtOH)	61.67 / 61.30	2.66 / 2.75	22.16 / 22.00	$C_{13}H_7N_4Cl$
20b	240—241 (MeOH)	53.89 / 54.01	2.20 / 2.09	19.31 / 19.38	$C_{13}H_6N_4Cl_2$
21a	225—226 (EtOH)	66.35 / 66.38	3.72 / 3.83	30.06 / 29.79	$C_{13}H_9N_5$
21b	219—220 (EtOH)	74.24 / 73.85	4.70 / 4.62	21.87 / 21.54	$C_{20}H_{15}N_5$
21c	234—236 (MeOH)	73.37 / 73.31	4.20 / 4.18	22.44 / 22.51	$C_{19}H_{13}N_5$
21d	203—204 (MeOH)	70.36 / 70.38	4.40 / 4.40	20.49 / 20.53	$C_{20}H_{15}N_5O$
21e[c]	218—220 (EtOH)	65.99 / 65.99	3.40 / 3.47	20.37 / 20.26	$C_{19}H_{12}N_5Cl$
21f	224—226 (EtOH)	73.70 / 73.85	4.51 / 4.62	21.38 / 21.54	$C_{20}H_{15}N_5$
21g	222—226 (decomp., EtOH)	59.81 / 60.02	2.77 / 2.92	18.47 / 18.42	$C_{19}H_{11}N_5Cl_2$
22b	>350 (DMF)	57.73 / 57.69	2.77 / 2.61	20.81 / 20.70	$C_{13}H_7N_4OCl$
23	241—242 ($PhCH_3$)	67.53 / 67.28	4.91 / 4.70	13.30 / 13.08	$C_{12}H_{10}N_2O_2$
24	330—331 (MeOH)	73.31 / 73.46	4.09 / 4.11	14.12 / 14.28	$C_{12}H_8N_2O$
26a	234—236 (MeOH)	62.80 / 62.87	4.85 / 4.84	18.22 / 18.33	$C_{12}H_{11}N_3O_2$
26b	361—362 (DMF)	61.61 / 61.89	4.59 / 4.33	19.93 / 20.05	$C_{18}H_{15}N_5O_3$

[a] Found (%): H_2O, 1.53. Calculated (%): H_2O, 1.74.
[b] Found (%): Cl, 14.08. Calculated (%): Cl, 13.95.
[c] Found (%): Cl, 10.42. Calculated (%): Cl, 10.27.

1-Cyano-2-(2-methoxyphenylamino)crotonamide (2a). A mixture of enaminoamide **1** (0.3 g, 0.002 mol) and *ortho*-anisidine (0.34 g, 0.028 mol) in AcOH (5 mL) was refluxed for 6 h. The reaction mixture was concentrated *in vacuo*, the residue was triturated in water, and the precipitate that formed was filtered off and washed with water. Compound **2a** was obtained in a yield of 0.3 g (67%), m.p. 186—187 °C (Pr^iOH). IR, ν/cm^{-1}: 3357, 3184 (NH); 2194 (CN); 1656 (CO); 1606 (C=C). EI MS, *m/z* (I_{rel} (%)): 231 $[M]^{+\bullet}$ (91), 214 $[M - NH_3]^{+\bullet}$ (72), 199 $[M - MeOH]^{+\bullet}$ (48), 185 $[M - CONH_2 - 2\ H]^{+\bullet}$ (39), 171 $[M - CONH_2 - CH_4]^{+\bullet}$ (54), 148 $[M - NCCH{=}CONH_2]^{+\bullet}$ (100), 123 $[M - C_6H_4OMe]^{+\bullet}$ (87), 108 $[Ph(OMe)]^{+\bullet}$ (71).

1-Cyano-2-(2,5-dimethoxyphenylamino)crotonamide (2b) was prepared analogously to compound **2a** from enaminoamide **1** and 2,5-dimethoxyaniline. The yield was 55%, m.p. 177—178 °C (Pr^iOH). ^{1}H NMR (DMSO-d_6), δ: 2.17 (s, 3 H, Me); 3.73 and 3.77 (both s, 3 H each, 2 OMe); 6.80 (br.s, 2 H, NH_2); 6.82 (dd, 1 H, H(4), J_o = 8.4 Hz, J_m = 3.0 Hz); 6.88 (br.s, 1 H, H(6)); 7.05 (d, 1 H, H(3), J_o = 8.4 Hz); 12.37 (br.s, 1 H, C(1)NH). EI MS, *m/z* (I_{rel} (%)): 261 $[M]^{+\bullet}$ (100), 229 $[M - MeOH]^{+\bullet}$ (87), 201 $[M - 2\ MeO + 2\ H]^{+\bullet}$ (45), 178 $[M - NCCH{=}CONH_2]^{+\bullet}$ (85), 153 $[H_2NC_6H_3(OMe)_2]^{+\bullet}$ (37), 138 $[C_6H_3(OMe)]^{+\bullet}$ (84).

5-Cyano-6-(2-dimethylaminovinyl)-1-(2-methoxyphenyl)-4-oxo-1,4-dihydropyrimidine (4a). A mixture of enaminoamide **2a** (0.2 g, 0.87 mol) and DMF acetal (4 mL) was refluxed for 5 h. The reaction mixture was cooled to 5 °C, and the precipitate that formed was filtered off and washed with ethanol. Compound **4a** was obtained in a yield of 0.2 g (77%), m.p. 259—262 °C (Pr^iOH—DMF, 1 : 1). ^{1}H NMR (DMSO-d_6), δ: 2.78 (br.s, 6 H, NMe_2); 3.82 (s, 3 H, OMe); 4.09 (d, 1 H, H_α, J_o = 12.9 Hz); 7.15, 7.30, 7.46, and 7.59 (all m, 1 H each, H(3′)—H(6′)); 7.87 (d, 1 H, H_β, J_o = 12.9 Hz); 8.07 (s, 1 H, H(2)). IR, ν/cm^{-1}: 3074 (NH); 2200 (CN); 1629 (CO); 1602 (C=C). EI MS, *m/z* (I_{rel} (%)): 296 $[M]^{+\bullet}$ (63), 265 $[M - MeO]^{+\bullet}$ (100), 238 $[M - MeO - CN]^{+\bullet}$ (81), 223 $[M - MeO - CN - Me]^{+\bullet}$ (52).

5-Cyano-1-(2,5-dimethoxyphenyl)-6-(2-dimethylaminovinyl)-4-oxo-1,4-dihydropyrimidine (4b) was prepared analogously to compound **4a** from enaminoamide **2b** and DMF acetal. The yield was 80%, m.p. 194—196 °C (Pr^iOH—DMF, 7 : 3). ^{1}H NMR (DMSO-d_6), δ: 2.81 (br.s, 6 H, NMe_2); 3.76 (s, 6 H, 2 OMe); 4.14 (d, 1 H, H_α, J_o = 12.9 Hz); 7.20—7.60 (m, 3 H, H(3′), H(4′), H(6′)); 7.90 (d, 1 H, H_β, J_o = 12.9 Hz); 8.08 (s, 1 H, H(2)). IR, ν/cm^{-1}: 3512, 3403, 3062 (NH); 2190 (CN); 1638 (CO). EI MS, *m/z* (I_{rel} (%)): 326 $[M]^{+\bullet}$ (45), 295 $[M - MeO]^{+\bullet}$ (100), 268 $[M - MeO - CN]^{+\bullet}$ (91), 253 $[M - MeO - CN - Me]^{+\bullet}$ (80).

3-Cyano-4-(2-methoxyphenyl)amino-2-oxo-1,2-dihydropyridin-2-one (5a). A mixture of pyrimidinone **4a** (0.3 g, 0.87 mol) and 1 *M* NaOH (7 mL) was refluxed for 1 h. The solution was acidified with concentrated HCl to pH 3. The precipitate that formed was filtered off and washed with water. Compound **5a** was obtained in a yield of 0.24 g (98%), m.p. 241—242 °C (Pr^iOH—DMF, 30 : 5). ^{1}H NMR (DMSO-d_6), δ: 3.79 (s, 3 H, OMe); 5.49 (d, 1 H, H(5), J_o = 7.4 Hz); 6.98, 7.11, 7.20, and 7.31 (all m, 1 H each, H(3′)—H(6′)); 7.24 (d, 1 H, H(6), J_o = 7.4 Hz); 8.60 (br.s, 1 H, C(4)NH); 11.04 (br.s, 1 H, N(1)H). EI MS, *m/z* (I_{rel} (%)): 241 $[M]^{+\bullet}$ (100), 226 $[M - Me]^{+\bullet}$ (47), 198 $[M - Me - CO]^{+\bullet}$ (45), 183 $[M - MeOH - CN]^{+\bullet}$ (53), 108 $[Ph(OMe)]^{+\bullet}$ (30).

3-Cyano-4-(2,5-dimethoxyphenyl)amino-2-oxo-1,2-dihydropyridin-2-one (5b) was prepared analogously to compound **5a** from pyrimidinone **4b**. The yield was 76%, m.p. 275—277 °C (Pr^iOH—DMF, 2 : 1). ^{1}H NMR (DMSO-d_6), δ: 3.72 (s, 6 H, 2 OMe); 5.53 (d, 1 H, H(5), J_o = 7.4 Hz); 6.85 (m, 2 H, H(4′), H(6′)); 7.05 (d, 1 H, H(3′), J_o = 8.4 Hz); 7.25 (d, 1 H, H(6), J_o = 7.4 Hz); 8.66 (br.s, 1 H, C(4)NH); 11.09 (br.s, 1 H, N(1)H). EI MS, *m/z* (I_{rel} (%)): 271 $[M]^{+\bullet}$ (100), 256 $[M - Me]^{+\bullet}$ (47), 228 $[M - Me - CO]^{+\bullet}$ (45).

1-(2-Methoxyphenyl)-4,5-dioxo-1,4,5,6-tetrahydropyrido[4,3-*d*]pyrimidine (6a). A solution of compound **4a** (0.3 g, 1 mmol) in glacial AcOH (4 mL) was refluxed for 7 h. The reaction mixture was cooled to 5 °C, and the precipitate that formed was filtered off and washed with ethyl acetate. Compound **6a** was obtained in a yield of 0.11 g (41%), m.p. 280—282 °C (Pr^iOH—DMF, 1 : 1). ^{1}H NMR (DMSO-d_6), δ: 3.81 (s, 1 H, OMe); 5.43 (s, 1 H, H(8), J_o = 7.2 Hz); 7.18, 7.31, and 7.51—7.69 (all m, 1 H each, 1 H, 3 H, H(7), H(3′)—H(6′)); 8.22 (s, 1 H, H(2)); 11.69 (br.s, 1 H, N(6)H). IR, ν/cm^{-1}: 3167 (NH); 1675, 1644 (CO). EI MS, *m/z* (I_{rel} (%)): 269 $[M]^{+\bullet}$ (100), 241 $[M - CO]^{+\bullet}$ (80), 213 $[M - 2\ CO]^{+\bullet}$ (78).

1-(2,5-Dimethoxyphenyl)-4,5-dioxo-1,4,5,6-tetrahydropyrido[4,3-*d*]pyrimidine (6b) was prepared analogously to compound **6a** from pyrimidinone **4b**. Acetic acid was evaporated, the residue was triturated in water, and the crystalline precipitate that formed was filtered off and washed with water and ethyl acetate. The yield was 78%, m.p. 162—165 °C (Pr^iOH—DMF, 7 : 2). Found (%): C, 56.91; H, 4.59; N, 13.11. $C_{16}H_9N_5O \cdot H_2O$. Calculated (%): C, 56.78; H, 4.76; N, 13.24. ^{1}H NMR (DMSO-d_6), δ: 3.88 and 3.90 (both s, 3 H each, 2 OMe); 5.55 (br.s, 1 H, H(8)); 7.32 (dd, 1 H, H(4′), J_o = 9.2 Hz, J_m = 2.8 Hz); 7.41 (d, 1 H, H(3′), J_o = 9.2 Hz); 7.43 (d, 1 H, H(6′), J_m = 2.8 Hz); 7.65 (br.s, 1 H, H(7)); 8.40 (s, 1 H, H(2)); 11.85 (br.s, 1 H, N(6)H). IR, ν/cm^{-1}: 3472 (OH); 3380 (NH); 1685, 1654 (CO). EI MS, *m/z* (I_{rel} (%)): 299 $[M]^{+\bullet}$ (100), 271 $[M - CO]^{+\bullet}$ (28).

***N*-Formyl-4-(2-methoxyphenyl)amino-2-oxo-1,2-dihydropyridine-3-carboxamide (7a).** A suspension of pyrimidinone **4a** (0.3 g, 1 mmol) in 1 *M* HCl (3 mL) was kept at 70 °C for 4 h. The precipitate that formed was filtered off and washed with water. Compound **8a** was obtained in a yield of 0.06 g (80%, ^{1}H NMR spectroscopic data). The aqueous mother liquor was alkalized with NaOH (sol.) to pH 8—9, and the precipitate that formed was filtered off and washed with water. A mixture of compounds **7a** and **8a** was obtained in a yield of 0.15 g (65 : 35, ^{1}H NMR spectroscopic data). The precipitate that formed was recrystallized from a 2 : 1 Pr^iOH—DMF mixture. Compound **7a** was obtained in a yield 0.06 g (21%), m.p. 208—211 °C (Pr^iOH—DMF, 2 : 1). ^{1}H NMR (DMSO-d_6), δ: 3.82 (s, 3 H, OMe); 5.93 (d, 1 H, H(5), J_o = 7.4 Hz); 7.02, 7.17, and 7.31 (all m, 1 H each, 1 H, 2 H, H(3′)—H(6′)); 7.37 (d, 1 H, H(6), J_o = 7.4 Hz); 9.25 (d, 1 H, CONHC<u>H</u>O, J_o = 9.8 Hz); 11.44 (br.s, 1 H, N(1)H); 11.57 (br.s, 1 H, C(4)NH); 13.09 (br.d, 1 H, CON<u>H</u>CHO, J_o = 9.8 Hz). IR, ν/cm^{-1}: 1700 ($CONH_2$); 1650 (CONH); 1626 (C=C, C=N). EI MS, *m/z* (I_{rel} (%)): 287 $[M]^{+\bullet}$ (96), 269 $[M - H_2O]^{+\bullet}$ (96), 259 $[M - CO]^{+\bullet}$ (95), 242 $[M - CO - OH]^{+\bullet}$ (97), 227 $[M - CO - MeO]^{+\bullet}$ (62), 213 $[M - 2\ CO - H_2O]^{+\bullet}$ (100).

***N*-Formyl-4-(2,5-dimethoxyphenyl)amino-2-oxo-1,2-dihydropyridine-3-carboxamide (7b).** A solution of pyrimidinone **4b** (0.25 g, 0.77 mmol) in glacial AcOH (2 mL) was kept at 70 °C

for 3 h and then at 40 °C for 6 h. The reaction mixture was concentrated *in vacuo*, the residue was triturated in ethyl acetate, and the precipitate that formed was filtered off and washed with ethyl acetate. A mixture of compounds **6b**, **7b**, and **8b** (TLC) was obtained in a yield of 0.12 g. The precipitate was recrystallized from a 6 : 5 Pr^iOH—DMF mixture. Compound **7b** was obtained in a yield of 0.03 g (13%), m.p. 208—211 °C (Pr^iOH—DMF, 6 : 5). ^1H NMR (DMSO-d_6), δ: 3.60 and 3.64 (both s, 3 H each, 2 OMe); 5.86 (d, 1 H, H(5), J_o = 7.4 Hz); 6.76 (m, 2 H, H(4′), H(6′)); 6.97 (d, 1 H, H(3′), J_o = 8.4 Hz); 7.26 (d, 1 H, H(6), J_o = 7.4 Hz); 9.11 (d, 1 H, CONHC<u>H</u>O, J_o = 9.8 Hz); 11.39 (br.s, 1 H, N(1)H); 11.43 (br.s, 1 H, C(4)NH); 12.98 (br.d, 1 H, CON<u>H</u>CHO, J_o = 9.8 Hz). EI MS, *m/z* (I_{rel} (%)): 317 $[M]^{+\bullet}$ (48), 299 $[M - H_2O]^{+\bullet}$ (91), 289 $[M - CO]^{+\bullet}$ (85), 271 $[M - CO - H_2O]^{+\bullet}$ (90), 257 $[M - CO - MeOH]^{+\bullet}$ (100).

4-(2-Methoxyphenyl)amino-2-oxo-1,2-dihydropyridine-3-carboxamide (8a). A solution of bicyclic compound **6a** (0.1 g, 0.37 mmol) in 1 *M* KOH (1 mL) was kept at 20 °C for 3 h. The precipitate that formed was filtered off and washed with water. Compound **8a** was obtained in a yield of 0.09 g (82%), m.p. 285—288 °C (Pr^iOH—DMF, 2 : 1). Found (%): N, 15.86. $C_{13}H_{13}N_3O_3$. Calculated (%): N, 16.21. ^1H NMR (DMSO-d_6), δ: 3.80 (s, 3 H, OMe); 5.84 (d, 1 H, H(5), J_o = 7.4 Hz); 6.95—7.25 (m, 6 H, H(3′)—H(6′), H(6), C(3)CONH); 9.84 (br.s, 1 H, C(3)CONH); 10.97 (br.s, 1 H, N(1)H); 12.31 (br.s, 1 H, C(4)NH). EI MS, *m/z* (I_{rel} (%)): 259 $[M]^{+\bullet}$ (100), 242 $[M - HO]^{+\bullet}$ (66), 213 $[M - CO - H_2O]^{+\bullet}$ (82).

4-(2,5-Dimethoxyphenyl)amino-2-oxo-1,2-dihydropyridine-3-carboxamide (8b). A suspension of pyrimidinone **4b** (0.3 g, 0.9 mmol) in 1 *M* HCl (3 mL) was kept at 20 °C for 6 days or at 70 °C for 1 h. Then 1 *M* KOH (5 mL) was added to the reaction mixture, and the mixture was kept at 20 °C for 1.5 h. The precipitate that formed was filtered off and washed with water. Compound **8b** containing a small impurity of compound **7b** (formylcarboxamide) was obtained in a yield of 0.2 g. The precipitate was recrystallized from a 3 : 2 Pr^iOH—DMF mixture. Compound **8b** was obtained in a yield of 0.07 g (27%), m.p. 208—210 °C (Pr^iOH—DMF, 7 : 5). ^1H NMR (DMSO-d_6), δ: 3.71 and 3.75 (both s, 3 H each, 2 OMe); 6.08 (d, 1 H, H(5), J_o = 7.4 Hz); 7.00 (m, 2 H, H(4′), H(6′)); 7.12 (d, 1 H, H(3′), J_o = 8.4 Hz); 7.22 (br.d, 1 H, C(3)CONH, J_{gem} = 5.0 Hz); 7.31 (d, 1 H, H(6), J_o = 7.4 Hz); 10.00 (br.d, 1 H, C(3)CONH, J_{gem} = 5.0 Hz); 11.00 (br.s, 1 H, N(1)H); 12.49 (br.s, 1 H, C(4)NH). EI MS, *m/z* (I_{rel} (%)): 289 $[M]^{+\bullet}$ (100), 271 $[M - H_2O]^{+\bullet}$ (86), 257 $[M - MeOH]^{+\bullet}$ (97).

4-(4-Chlorophenyl)amino-3-cyano-5-formyl-2-oxo-1,2-dihydropyridine (9b). A solution of compound **3b** (0.623 g, 1.8 mmol) in 90% AcOH (6 mL) was kept at 20 °C for 3 days. The precipitate that formed was filtered off and washed with ethyl acetate. Formylpyridone **9b** was obtained in a yield of 0.437 g (89%), m.p. 290 °C (decomp., Pr^iOH—DMF, 3 : 2). ^1H NMR (DMSO-d_6), δ: 7.41 (m, 4 H, C_6H_4Cl); 8.42 (s, 1 H, H(6)); 9.59 (s, 1 H, CHO); 10.52 (br.s, 1 H, N(1)H); 12.40 (br.s, 1 H, C(4)NH). IR, ν/cm^{-1}: 3198, 3130 (NH); 2219 (CN); 1691 (CO); 1646, 1586 (C=C, C=N). EI MS, *m/z* (I_{rel} (%)): 273 $[M]^{+\bullet}$ (100), 244 $[M - CHO]^{+\bullet}$ (50).

5-(Benzylimino)methyl-3-cyano-2-oxo-4-phenylamino-1,2-dihydropyridine (10a). A mixture of formylpyridone **9a** (2 g, 8 mmol), benzylamine (0.9 g, 8 mol), and a catalytic amount of *p*-TsOH in anhydrous EtOH (40 mL) was refluxed for 1.5 h. The precipitate that formed was filtered off and washed with EtOH. Compound **10a** was obtained in a yield of 2 g (82%), m.p. 229—230 °C (MeOH). IR, ν/cm^{-1}: 3315 (NH); 2208 (CN); 1675 (CO); 1644, 1635 (C=C, C=N). EI MS, *m/z* (I_{rel} (%)): 328 $[M]^{+\bullet}$ (46), 222 $[M - PhCH_2NH]^{+\bullet}$ (79), 106 $[PhCH_2{=}NH]^{+\bullet}$ (35), 106 $[PhCH_2{=}NH]^{+\bullet}$ (35), 91 $[PhCH_2]^{+\bullet}$ (100).

4-[(3-Cyano-2-oxo-4-phenylamino-1,2-dihydropyridin-5-yl)methylenamino]butyric acid (10b). γ-Aminobutyric acid (1.29 g, 12.5 mmol) was added to a solution of NaOH (0.51 g) in EtOH (25 mL), and the reaction mixture was stirred at 60 °C until complete dissolution was achieved. Formylpyridone **9a** (3 g, 12.6 mmol) was added to the resulting solution of the sodium salt of γ-aminobutyric acid in EtOH. The reaction mixture was refluxed for 5 h and cooled to 0 °C. The precipitate was filtered off and washed with EtOH. The sodium salt of compound **10b** was obtained in a yield of 1.74 g. The salt was dissolved in warm water (20 mL) and the solution was filtered from the insoluble impurity. The filtrate was acidified with concentrated HCl to pH 2—3, and the precipitate that formed was filtered off and washed with water. Compound **10b** was obtained in a yield of 0.5 g (12%), m.p. 207—208 °C (MeOH). IR, ν/cm^{-1}: 3180—3230 (NH associated); 2210 (CN); 1730, 1680 (CO); 1640, 1620, 1590 (C=C, C=N). EI MS, *m/z* (I_{rel} (%)): 324 $[M]^{+\bullet}$ (65), 222 $[M - HOOC(CH_2)_3NH]^{+\bullet}$ (100).

3-Cyano-5-[2-(3,4-dimethoxyphenyl)ethyliminomethyl]-2-oxo-4-phenylamino-1,2-dihydropyridine (10c) was prepared analogously to **10a** from formylpyridone **9a** and homoveratrylamine. The reaction time was 5.5 h. The yield was 50%, m.p. 202—204 °C (EtOH). IR, ν/cm^{-1}: 3050 (NH); 2200 (CN); 1670 (CO); 1630, 1590 (C=C, C=N). EI MS, *m/z* (I_{rel} (%)): 402 $[M]^{+\bullet}$ (47), 222 $[M - (MeO)_2C_6H_4(CH_2)_2NH]^{+\bullet}$ (50), 193 $[(MeO)_2C_6H_3(CH_2)_2N{=}CH_2]^{+\bullet}$ (43).

3-Cyano-2-oxo-4-phenylamino-5-phenyliminomethyl-1,2-dihydropyridine (10d) was prepared analogously to **10a** from formylpyridone **9a** and aniline in ethylene glycol at 135 °C. The reaction time was 2 h. The yield was 38%, m.p. 300 °C (MeOH—DMF, 5 : 1). Found (%): N, 17.48. $C_{19}H_{14}N_4O$. Calculated (%): N, 17.83. ^1H NMR (DMSO-d_6), δ: 7.24—7.43 (m, 10 H, 2 Ph); 8.14 (s, 1 H, H(1′)); 8.67 (s, 1 H, H(6)); 12.11 (br.s, 1 H, N(1)H); 12.35 (br.s, 1 H, C(4)NH). IR, ν/cm^{-1}: 3080, 3020 (NH); 2200 (CN); 1670 (CO); 1630, 1590 (C=C, C=N). EI MS, *m/z* (I_{rel} (%)): 314 $[M]^{+\bullet}$ (100), 222 $[M - PhNH]^{+\bullet}$ (91).

3-Cyano-5-hydrazinomethyl-2-oxo-4-phenylamino-1,2-dihydropyridine (11). A mixture of formylpyridone **9a** (1.2 g, 5 mmol) and hydrazine hydrate (2.5 mL) in anhydrous EtOH (5 mL) was kept at 20 °C for 1 h. The precipitate that formed was filtered off and washed with EtOH. Hydrazone **11** was obtained in a yield of 1.2 g (53%), m.p. 293—294 °C (DMF). ^1H NMR (DMSO-d_6), δ: 6.66 (br.s, 2 H, NH_2); 7.25 and 7.39 (both m, 3 H and 2 H, Ph); 7.62 (s, 1 H, H_α); 7.75 (s, 1 H, H(6)); 11.39 (br.s, 1 H, C(4)NH); 11.63 (br.s, 1 H, N(1)H). IR, ν/cm^{-1}: 3400, 3200 (NH); 2200 (CN); 1690 (CO); 1620, 1570 (C=C, C=N). ES MS, *m/z*: 254 $[M + H]^{+\bullet}$, 276 $[M + Na]^{+\bullet}$, 529 $[2\,M + Na]^{+\bullet}$. EI MS, *m/z* (I_{rel} (%)): 253 $[M]^{+\bullet}$ (50), 222 $[M - NH_2NH]^{+\bullet}$ (100).

5-Benzylidenehydrazonomethyl-2-oxo-4-phenylamino-1,2-dihydropyridine-3-carbonitrile (12a). A mixture of hydrazone **11** (0.5 g, 1.5 mmol) and benzaldehyde (3.68 g, 0.035 mol) in anhydrous EtOH (20 mL) was kept at 20 °C for 2.5 h. The precipitate that formed was filtered off and washed with EtOH.

Compound **12a** was obtained in a yield of 0.5 g (30%), m.p. 278—279 °C (EtOH). Found (%): N, 20.20. $C_{20}H_{15}N_5O$. Calculated (%): N, 20.53. ^{1}H NMR (DMSO-d_6), δ: 7.32—7.50 and 7.83 (both m, 8 H and 2 H, 2 Ph); 8.15 (s, 1 H, H(6)); 8.72 and 8.80 (both s, 1 H each, H(1′), H(4′)); 11.38 (br.s, 1 H, C(4)NH); 12.15 (br.s, 1 H, N(1)H). IR, ν/cm^{-1}: 3525, 3500, 3180 (NH); 2200 (CN); 1620 (CO); 1575 (C=C, C=N). EI MS, *m/z* (I_{rel} (%)): 341 $[M]^{+\bullet}$ (20), 222 $[M - PhCHN{=}NH]^{+\bullet}$ (63), 120 $[PhCH{=}NNH_2]^{+\bullet}$ (100).

5-[(4-Hydroxybenzylidene)hydrazonomethyl]-2-oxo-4-phenylamino-1,2-dihydropyridine-3-carbonitrile (12b) was prepared analogously to **12a**. The mixture was allowed to stand for 53 h. The yield was 67%, m.p. 283—284 °C (DMF). IR, ν/cm^{-1}: 3400, 3200 (NH); 2200 (CN); 1690 (CO); 1620, 1570 (C=C, C=N). EI MS, *m/z* (I_{rel} (%)): 357 $[M]^{+\bullet}$ (35), 222 $[M - HOC_6H_4CHN{=}NH]^{+\bullet}$ (67), 136 $[HOC_6H_4CH{=}NNH_2]^{+\bullet}$ (100).

5-[(4-Hydroxy-3-methoxybenzylidene)hydrazonomethyl]-2-oxo-4-phenylamino-1,2-dihydropyridine-3-carbonitrile (12c) was prepared analogously to **12a** but with refluxing (5 h). The yield was 53%, m.p. 292—293 °C (DMF). ^{1}H NMR (DMSO-d_6), δ: 3.80 (s, 3 H, OMe); 6.84 (d, 1 H, H(3′), J_o = 8.0 Hz); 7.24 (dd, 1 H, H(2′), J_o = 8.0 Hz, J_m = 2.0 Hz); 7.28—7.46 (m, 6 H, Ph, H(6′)); 8.09 (s, 1 H, H(6)); 8.57 and 8.76 (both s, 1 H each, H(1′), H(4′)); 9.80 (br.s, 1 H, OH); 11.45 (br.s, 1 H, C(4)NH); 12.10 (br.s, 1 H, N(1)H). IR, ν/cm^{-1}: 3300, 3180 (NH); 2200 (CN); 1660 (CO); 1580 (C=C, C=N). EI MS, *m/z* (I_{rel} (%)): 387 $[M]^{+\bullet}$ (7), 222 $[M - 3\text{-}MeO,4\text{-}OHC_6H_3CHN{=}NH]^{+\bullet}$ (100).

5-[(4-Methoxybenzylidene)hydrazonomethyl]-2-oxo-4-phenylamino-1,2-dihydropyridine-3-carbonitrile (12d) was prepared analogously to **12a**. The mixture was allowed to stand for 4 h. The yield was 69%, m.p. 280—282 °C (DMF). Found (%): C, 66.27; H, 4.57; N, 17.86; H_2O, 3.43. $C_{21}H_{17}N_5O_2 \cdot 0.65H_2O$. Calculated (%): C, 65.84; H, 4.81; N, 18.28; H_2O, 3.06. ^{1}H NMR (DMSO-d_6), δ: 3.80 (s, 3 H, OMe); 7.02, 7.33—7.42, and 7.77 (all m, 2 H each, 5 H, 2 H, Ph, C_6H_4OMe); 8.10 (s, 1 H, H(6)); 8.63 and 8.75 (both s, 1 H each, H(1′), H(4′)); 11.41 (br.s, 1 H, C(4)NH); 12.10 (br.s, 1 H, N(1)H). IR, ν/cm^{-1}: 3560, 3350 (OH); 3180 (NH); 2216 (CN); 1651 (CO); 1635, 1616 (C=C, C=N). ES MS, *m/z*: 372 $[M + H]^{+\bullet}$, 393 $[M + Na]^{+\bullet}$, 743 $[2\ M + H]^{+\bullet}$, 765 $[2\ M + Na]^{+\bullet}$.

5-Cyclohexylidenehydrazonomethyl-2-oxo-4-phenylamino-1,2-dihydropyridine-3-carbonitrile (12e) was prepared analogously to **12a** but with refluxing (3 h). The yield was 91%, m.p. 290—291 °C (anhydrous EtOH). IR, ν/cm^{-1}: 3190 (NH); 2200 (CN); 1690 (CO); 1620, 1580 (C=C, C=N). EI MS, *m/z* (I_{rel} (%)): 333 $[M]^{+\bullet}$ (50), 222 $[M - C_6H_{10}N{=}NH]^{+\bullet}$ (100).

3-Cyano-5-hydroxymethyl-2-oxo-4-phenylamino-1,2-dihydropyridine (13a). Sodium borohydride (0.726 g, 0.019 mol) was added portionwise with stirring to a suspension of formylpyridone **9a** (3 g, 12.6 mmol) in Pr^iOH (60 mL) at 50—55 °C for 3 h. The precipitate that formed was filtered off, washed with Pr^iOH, and dissolved in water (35 mL). The solution was acidified to pH 6 and kept at 20 °C for 2 h. The precipitate that formed was filtered off and washed with water. Compound **13a** was obtained in a yield of 2.15 g (70%), m.p. 222—223 °C (Pr^iOH—DMF, 50 : 1). ^{1}H NMR (DMSO-d_6), δ: 4.33 (s, 2 H, C<u>H</u>$_2$OH); 5.24 (br.s, 1 H, CH$_2$O<u>H</u>); 7.13—7.39 (m, 6 H, Ph, H(6)); 8.54 (br.s, 1 H, C(4)NH); 11.29 (br.s, 1 H, N(1)H). IR, ν/cm^{-1}: 3341 (OH); 3300 (NH); 2216 (CN); 1644, 1631 (CO). EI MS, *m/z* (I_{rel} (%)): 240 $[M - H]^{+\bullet}$ (14), 221 $[M - H_2O - 2\ H]^{+\bullet}$ (100), 193 $[M - H_2O - 2\ H - CO]$ (17).

4-(4-Chlorophenylamino)-3-cyano-5-hydroxymethyl-2-oxo-1,2-dihydropyridine (13b) was prepared from formylpyridone **9b** (0.5 g, 1.8 mmol) and $NaBH_4$ (0.069 g, 1.8 mmol) analogously to compound **13a**. The yield was 72%, m.p. 261—264 °C (Pr^iOH—DMF, 3 : 2). ^{1}H NMR (DMSO-d_6), δ: 4.34 (s, 2 H, C<u>H</u>$_2$OH); 5.25 (br.s, 1 H, CH$_2$O<u>H</u>); 7.16—7.46 (m, 6 H, Ph, H(6)); 8.62 (br.s, 1 H, C(4)NH); 11.35 (br.s, 1 H, N(1)H). IR, ν/cm^{-1}: 3405 (OH); 3273 (NH); 2208 (CN); 1646 (CO). ES MS, *m/z*: 276 $[M + H]^{+\bullet}$, 298 $[M + Na]^{+\bullet}$, 551 $[2\ M + H]^{+\bullet}$, 573 $[2\ M + Na]^+$.

3-Cyano-2-oxo-4-phenylamino-5-ureidomethyl-1,2-dihydropyridine (14). Urea (2.52 g, 0.042 mol) was added to a suspension of formylpyridone **9a** (0.4 g, 1.7 mmol) in AcOH (6 mL). The reaction mixture was heated with stirring at 90 °C until the precipitate was completely dissolved. The solution was refluxed for 13 h, cooled to 20 °C, and poured into water (20 mL). The precipitate that formed was filtered off and successively washed with water, a $NaHCO_3$ solution, and water. Compound **14** was obtained in a yield of 3.54 g (89%), m.p. 247—250 °C (MeCN—DMF, 6 : 1). ^{1}H NMR (DMSO-d_6), δ: 4.03 (d, 2 H, 2 HC(5), J_o = 6.4 Hz); 5.82 (br.s, 2 H, NH_2); 6.55 (t, 1 H, CH$_2$N<u>H</u>, J_o = 6.4 Hz); 7.13 and 7.33 (both m, 3 H and 2 H each, Ph); 7.33 (s, 1 H, H(6)); 10.26 (br.s, 1 H, C(4)NH); 11.18 (br.s, 1 H, N(1)H). IR, ν/cm^{-1}: 3429 (OH); 3348, 3188 (NH); 2199 (CN); 1632 (CO). EI MS, *m/z* (I_{rel} (%)): 283 $[M]^{+\bullet}$ (1), 266 $[M - NH_3]^{+\bullet}$ (17), 222 $[M - NH_2CONH_2 - H]^+$ (100).

3-Cyano-2-oxo-4-phenylamino-5-piperidinomethyl-1,2-dihydropyridine (16). Thionyl chloride (0.4 mL) was added dropwise to a suspension of pyridone **13a** (0.4 g, 1.66 mmol) in CH_2Cl_2 (4 mL). The reaction mixture was refluxed with stirring for 10 h, and then CH_2Cl_2 (5 mL) was added. The precipitate was triturated, filtered off, and washed with CH_2Cl_2. A chloro derivative was obtained in a yield of 0.353 g. The resulting chloro derivative (0.28 g) was stirred with Py (2 mL) at 90 °C for 6 h. The reaction mixture was cooled to 20 °C, the solution was removed by decantation, the residual oil was triturated with acetonitrile, and the precipitate was filtered off and washed with acetonitrile. Pyridinium salt **15** was obtained in a yield of 0.28 g (63%), m.p. 320—322 °C (decomp.). ^{1}H NMR (DMSO-d_6), δ: 5.97 (s, 2 H, 2 HC(6)); 7.04, 7.12, and 7.26 (all m, 2 H each, 1 H, 2 H, Ph); 7.96 (s, 1 H, H(6)); 8.08, 8.55, and 9.10 (all m, 2 H each, 1 H, 2 H, Py); 9.51 (br.s, 1 H, C(4)NH); 11.93 (br.s, 1 H, N(1)H). ES MS, *m/z*: 224 $[M - C_5H_5N]^+$, 80 $[M - C_5H_5N + H]^+$. A mixture of pyridinium salt **15** (0.28 g, 0.83 mmol) and piperidine (0.19 g, 2.2 mmol) in benzene (4 mL) was refluxed with stirring for 1 h. After cooling of the reaction mixture to 20 °C, the precipitate that formed was filtered off and triturated with petroleum ether. The precipitate was filtered off and washed with water. Compound **16** was obtained in a yield of 0.145 g (57%), m.p. 229—231 °C (MeCN). Found (%): N, 18.38. $C_{18}H_{20}N_4O$. Calculated (%): N, 18.17. ^{1}H NMR (DMSO-d_6), δ: 1.41—1.55 (m, 6 H, 2 H(3′)—H(5′)); 2.39 (br.s, 4 H, 2 H(2′), 2 H(6′)); 3.42 (s, 2 H, 2 HC(5)); 7.19—7.39 (m, 6 H, Ph, H(6)); 10.69 (br.s, 1 H, C(4)NH); 11.27 (br.s, 1 H, N(1)H). IR, ν/cm^{-1}: 3250, 3150 (NH); 2210 (CN); 1630 (CO). ES MS, *m/z*: 309 $[M + H]^+$, 331 $[M + Na]^+$, 617 $[2\ M + H]^+$, 639 $[2\ M + Na]^+$, 224 $[M - C_5H_5N]^{+\bullet}$, 86 $[C_5H_{11}N + H]^{+\bullet}$.

3-Cyano-5-hydroxyiminomethyl-2-oxo-4-phenylamino-1,2-dihydropyridine (17a). Formylpyridone **9a** (2 g, 8.4 mmol) was added to a solution of hydroxylamine hydrochloride (1.02 g, 14.7 mmol) in pyridine (8 mL). The reaction mixture was stirred at 80 °C for 2 h, cooled, and poured into water (50 mL). The precipitate that formed was filtered off and washed with water. Compound **17a** was obtained in a yield of 1.87 g (89%), m.p. 261—263 °C (MeOH). ^{1}H NMR (DMSO-d_6), δ: 7.23—7.50 (m, 5 H, Ph); 7.82 (s, 1 H, H(5′)); 8.21 (s, 1 H, H(6)); 10.37 (br.s, 1 H, C(4)NH); 11.29 (br.s, 1 H, OH); 11.86 (br.s, 1 H, N(1)H). IR, ν/cm^{-1}: 3660 (OH); 3420 (NH); 2220 (CN); 1680 (CO). ES MS, *m/z*: 237 [M + H − H_2O]$^{+\bullet}$, 255 [M + H]$^{+\bullet}$, 277 [M + Na]$^{+\bullet}$, 508 [2 M + H]$^{+\bullet}$, 531 [2 M + Na + H]$^{+\bullet}$. EI MS, *m/z* (I_{rel} (%)): 254 [M]$^{+\bullet}$ (75), 237 [M − OH]$^{+\bullet}$ (52), 236 [M − H_2O]$^{+\bullet}$ (89), 222 [M − HO − NH]$^{+\bullet}$ (100), 77 [Ph]$^{+\bullet}$(60).

4-(4-Chlorophenyl)amino-3-cyano-5-hydroxyiminomethyl-2-oxo-1,2-dihydropyridine (17b). Formylpyridone **9b** (0.5 g, 1.8 mmol) was added to a solution of hydroxylamine hydrochloride (0.21 g, 3 mmol) in pyridine (2 mL). The reaction mixture was stirred at 115 °C for 10 min, cooled, and poured into water (10 mL). The precipitate that formed was filtered off and washed with water. Compound **17b** was obtained in a yield of 0.52 g (98%), m.p. 293—294 °C (Pr^{i}OH). ^{1}H NMR (DMSO-d_6), δ: 7.25 and 7.40 (both m, 2 H each, C_6H_4Cl); 7.67 (s, 1 H, H(5′)); 8.14 (s, 1 H, H(6)); 10.34 (br.s, 1 H, C(4)NH); 11.09 (br.s, 1 H, OH); 11.80 (br.s, 1 H, N(1)H). IR, ν/cm^{-1}: 3317 (OH); 2219 (CN); 1644 (CO). ES MS, *m/z*: 289 [M + H]$^{+\bullet}$, 311 [M + Na]$^{+\bullet}$, 599 [2 M + Na]$^{+\bullet}$. EI MS, *m/z* (I_{rel} (%)): 270 [M − H_2O]$^{+\bullet}$(100), 242 [M − CO]$^{+\bullet}$ (27).

3-Cyano-4-dimethylamino-5-hydroxyiminomethyl-2-oxo-1,2-dihydropyridine (17c). Formylpyridone **9c** (0.2 g, 1 mmol) was added to a solution of hydroxylamine hydrochloride (0.11 g, 1.7 mmol) in pyridine (0.9 mL). The reaction mixture was stirred at 115 °C for 0.5 h, cooled, and poured into Pr^{i}OH (7 mL). The inorganic precipitate was filtered off, and the filtrate was concentrated to dryness. The residue was triturated with diethyl ether and heptane and decanted. Then Pr^{i}OH was added to the semicrystalline precipitate and the mixture was kept at 5 °C for 12 h. The precipitate that crystallized out was filtered off, washed with Pr^{i}OH, and dried. Compound **17c** was obtained in a yield of 0.091 g (42%), m.p. 203—204 °C (Pr^{i}OH). ^{1}H NMR (DMSO-d_6), δ: 3.13 (s, 6 H, NMe_2); 7.44 (s, 1 H, H(5′)); 7.87 (s, 1 H, H(6)); 10.85 (br.s, 1 H, OH); 11.65 (br.s, 1 H, N(1)H). IR, ν/cm^{-1}: 3169 (NH); 2216 (CN); 1635 (CO). ES MS, *m/z*: 207 [M + H]$^{+\bullet}$, 229 [M + Na]$^{+\bullet}$, 413 [2 M + H]$^+$, 435 [2 M + Na]$^+$. EI MS, *m/z* (I_{rel} (%)): 206 [M]$^{+\bullet}$ (5), 188 [M − H_2O] (100), 173 [M − H_2O − Me] (51).

5-Acetoxyiminomethyl-3-cyano-2-oxo-4-phenylamino-1,2-dihydropyridine (18a). ***A.*** Formylpyridone **9a** (0.5 g, 2 mmol) was added to a solution of hydroxylamine hydrochloride (0.24 g, 4 mmol) in pyridine (3 mL) at 90—95 °C. The reaction mixture was stirred for 0.5 h, and then acetic anhydride (1.3 mL) was slowly added. The reaction mixture was allowed to stand for 8 min, cooled, and poured into water. The precipitate that formed was filtered off, washed with water, and dried. Compound **18a** was obtained in a yield of 0.44 g (90%), m.p. 286—288 °C (MeOH). ^{1}H NMR (DMSO-d_6), δ: 2.14 (s, 3 H, COMe); 7.28 and 7.40 (both m, 3 H and 2 H each, Ph); 8.04 (s, 1 H, H(5′)); 8.66 (s, 1 H, H(6)); 10.09 (br.s, 1 H, C(4)NH); 12.20 (br.s, 1 H, N(1)H). IR, ν/cm^{-1}: 3200, 3030 (NH); 2200 (CN); 1780 (CO); 1660 (CO, ketone); 1630, 1570 (C=C, C=N). ES MS, *m/z*: 237 [M − CH_3COOH + H]$^{+\bullet}$, 297 [M + H]$^{+\bullet}$, 319 [M + Na]$^{+\bullet}$, 615 [2 M + Na]$^{+\bullet}$. EI MS, *m/z* (I_{rel} (%)): 236 [M − CH_3COOH]$^{+\bullet}$ (100), 209 [M − CH_3COOH − HCN]$^{+\bullet}$ (13), 208 [M − CH_3COOH − CO]$^{+\bullet}$ (17).

B. Compound **17a** (0.58 g, 0.002 mol) was refluxed in acetic anhydride (4 mL) for 15 min. The precipitate was filtered off and washed with water. Compound **18a** was obtained in a yield of 0.61 g (90%), m.p. 286—288 °C (DMF).

5-Acetoxyiminomethyl-4-(4-chlorophenyl)amino-3-cyano-2-oxo-1,2-dihydropyridine (18b) was prepared analogously to compound **18a** by the method *A* or *B* in 90 or 75% yield, respectively, m.p. 288 °C (decomp.). ^{1}H NMR (DMSO-d_6), δ: 2.15 (s, 3 H, COMe); 7.32 and 7.47 (both m, 2 H each, C_6H_4Cl); 8.05 (s, 1 H, H_α); 8.66 (s, 1 H, H(6)); 10.06 (br.s, 1 H, C(4)NH); 12.28 (br.s, 1 H, N(1)H). IR, ν/cm^{-1}: 3252, 3067 (NH); 2209 (CN); 1771 (CO); 1670 (CO, ketone); 1636, 1606 (C=C, C=N). ES MS, *m/z*: 331 [M + H]$^{+\bullet}$, 353 [M + Na]$^{+\bullet}$, 683 [2 M + Na]$^{+\bullet}$, 271 [M + H − CH_3COOH]$^{+\bullet}$.

3,5-Dicyano-4-phenylaminopyridine (19a). Formylpyridone **9a** (0.5 g, 2 mmol) was added to a solution of hydroxylamine hydrochloride (0.24 g, 4 mmol) in pyridine (3 mL) at 90—95 °C. The reaction mixture was stirred for 0.5 h, and then acetic anhydride (1.3 mL) was slowly added. After 8 min, pyridine (2 mL) was added. The reaction mixture was stirred at 115 °C for 2 h, cooled, and poured into water. The precipitate that formed was filtered off, washed with water, and dried. Compound **19a** was obtained in a yield of 0.44 g (90%), m.p. 323—324 °C (MeOH). ^{1}H NMR (DMSO-d_6), δ: 7.25 and 7.37 (both m, 3 H and 2 H each, Ph); 8.34 (s, 1 H, H(6)); 9.62 (br.s, 1 H, C(4)NH); 12.41 (br.s, 1 H, N(1)H). IR, ν/cm^{-1}: 3220 (NH); 2220 (CN); 1670 (CO); 1620, 1570 (C=C, C=N). ES MS, *m/z*: 237 [M + H]$^{+\bullet}$, 259 [M + Na]$^{+\bullet}$, 495 [2 M + Na]$^{+\bullet}$. EI MS, *m/z* (I_{rel} (%)): 236 [M]$^{+\bullet}$ (100), 209 [M − HCN]$^{+\bullet}$ (13), 208 [M − CO]$^{+\bullet}$ (17).

4-(4-Chlorophenyl)amino-3,5-dicyanopyridine (19b) was prepared analogously to **19a** from compound **9b**. The yield was 68%, m.p. 335 °C (decomp., MeOH). ^{1}H NMR (DMSO-d_6), δ: 7.27 and 7.42 (both m, 2 H each, C_6H_4Cl); 8.31 (s, 1 H, H(6)); 9.58 (br.s, 1 H, C(4)NH); 12.40 (br.s, 1 H, N(1)H). IR, ν/cm^{-1}: 3300 (NH); 3084, 2243, 2212 (CN); 1651 (CO). ES MS, *m/z*: 271 [M + H]$^{+\bullet}$, 293 [M + Na]$^{+\bullet}$.

2-Chloro-3,5-dicyano-4-phenylaminopyridine (20a). A mixture of compound **19a** (0.66 g, 2.8 mmol) and triethylamine hydrochloride (0.35 g, 2.5 mmol) in phosphoryl chloride (5 mL) was refluxed for 2 h, cooled, and poured into water. The precipitate that formed was filtered off and washed with water, ethanol, and diethyl ether. Compound **20a** was obtained in a yield of 0.62 g (87%), m.p. 192—194 °C (EtOH). ^{1}H NMR (DMSO-d_6), δ: 7.34 (m, 5 H, Ph); 8.61 (s, 1 H, H(6)); 10.20 (br.s, 1 H, C(4)NH). IR, ν/cm^{-1}: 3270 (NH); 2200 (CN); 1590, 1570 (C=C, C=N).

2-Chloro-4-(4-chlorophenyl)amino-3,5-dicyanopyridine (20b) was prepared analogously to **20a** from compound **19b**. The yield was 65%, m.p. 240—241 °C (MeOH). ^{1}H NMR (DMSO-d_6), δ: 7.36 and 7.47 (both m, 2 H each, C_6H_4Cl); 8.64 (s, 1 H, H(6)); 10.16 (br.s, 1 H, C(4)NH). IR, ν/cm^{-1}: 3280 (NH); 2226 (CN); 1568 (C=C, C=N).

2-Amino-3,5-dicyano-4-phenylaminopyridine (21a). A mixture of pyridine **20a** (3.35 g, 13 mmol) and a 14% ethanolic solution of ammonia (35 mL) was heated in an autoclave at

80 °C for 6 h. The precipitate was filtered off. Pyridine **21a** was obtained in a yield of 2.7 g (87%), m.p. 225—226 °C (EtOH). ^{1}H NMR (DMSO-d_6), δ: 7.20 (d, 2 H, H (2′), H(6′), J = 8.8 Hz); 7.35 (t, 3 H, H(3′)—H(5′), J = 8.8 Hz); 7.45 (br.s, 2 H, NH_2); 8.22 (s, 1 H, H(6)); 9.33 (br.s, 1 H, C(4)NH). IR, ν/cm^{-1}: 3360, 3300, 3280, 3125 (NH, NH_2); 2220 (CN); 1660 (NH, NH_2); 1590, 1550 (C=C, C=N). EI MS, m/z (I_{rel} (%)): 235 $[M]^{+\bullet}$ (100), 208 $[M - HCN]^{+\bullet}$ (27), 208 $[M - CO]^{+\bullet}$ (17).

2-Benzylamino-3,5-dicyano-4-phenylaminopyridine (21b). A mixture of compound **20a** (1.8 g, 7.1 mmol) and benzylamine (1.5 g, 0.014 mol) in anhydrous ethanol (60 mL) was stirred at 40—45 °C for 3 h. The precipitate was filtered off, washed with ethanol and diethyl ether, and dried. Pyridine **21b** was obtained in a yield of 2.1 g (91%), m.p. 219—220 °C (EtOH). IR, ν/cm^{-1}: 3360, 3280 (NH); 2200 (CN); 1590 (C=C, C=N, NH). ES MS, m/z: 326 $[M + H]^{+\bullet}$, 348 $[M + Na]^{+\bullet}$.

3,5-Dicyano-2,4-di(phenylamino)pyridine (21c) was prepared analogously to **21b** from compound **20a** (0.3 g, 1.2 mmol) and aniline (0.33 g, 3.6 mmol) in ethylene glycol (5 mL) at 100 °C. The reaction mixture was allowed to stand for 1.5 h. The yield was 91%, m.p. 234—236 °C (MeOH). IR, ν/cm^{-1}: 3360, 3300 (NH); 2200 (CN); 1590 (C=C, C=N, NH). ES MS, m/z: 312 $[M + H]^{+\bullet}$, 645 $[2 M + Na]^{+\bullet}$.

3,5-Dicyano-2-(4-methoxyphenyl)amino-4-phenylaminopyridine (21d) was prepared analogously to **21b** from compound **20a**. The reaction mixture was allowed to stand for 2 h. The yield was 98%, m.p. 203—204 °C (MeOH). IR, ν/cm^{-1}: 3360, 3260 (NH); 2200 (CN); 1600, 1560 (C=C, C=N, NH). ES MS, m/z: 342 $[M + H]^{+\bullet}$, 364 $[M + Na]^{+\bullet}$, 705 $[2 M + Na]^{+\bullet}$.

2-(4-Chlorophenyl)amino-3,5-dicyano-4-phenylaminopyridine (21e) was prepared analogously to **21b** from compound **20a** (0.35 g, 1.4 mmol) and 4-chloroaniline (0.52 g, 4.1 mmol) in ethylene glycol (5 mL) at 80 °C. The reaction mixture was allowed to stand for 2.5 h. The yield was 91%, m.p. 218—219 °C (EtOH). IR, ν/cm^{-1}: 3310, 3280 (NH); 2200 (CN); 1600, 1580, 1560 (C=C, C=N, NH). ES MS, m/z: 346 $[M + H]^{+\bullet}$, 713 $[2 M + Na]^{+\bullet}$.

3,5-Dicyano-2-(4-methylphenyl)amino-4-phenylaminopyridine (21f) was prepared analogously to **21b** from compound **20a**. The reaction mixture was allowed to stand for 3 h. The yield was 42%, m.p. 224—226 °C (EtOH). IR, ν/cm^{-1}: 3320, 3260 (NH); 2200 (CN); 1580, 1560 (C=C, C=N, NH). EI MS, m/z: 326 $[M + H]^{+\bullet}$, 348 $[M + Na]^{+\bullet}$, 650 $[2 M + H]^{+\bullet}$.

2,4-Di[(4-chlorophenyl)amino]-3,5-dicyanopyridine (21g) was prepared analogously to **21e** from compound **20b**. The yield was 70%, m.p. 222—226 °C (EtOH). ^{1}H NMR (DMSO-d_6), δ: 7.24—7.55 (m, 8 H, 2 C_6H_4Cl); 8.37 (s, 1 H, H(6)); 9.49 and 9.58 (both br.s, 1 H each, 2 NH). IR, ν/cm^{-1}: 3276 (NH); 2215 (CN); 1611, 1600 (C=C, C=N, NH). ES MS, m/z: 380 $[M + H]^{+\bullet}$.

7-Cyano-6-oxo-1-phenyl-5,6-dihydro-1*H*-pyrazolo[4,3-*c*]pyridine (22a). A solution of compound **18a** (0.2 g, 0.68 mmol) in DMF (5 mL) was refluxed for 30 min, DMF was evaporated to dryness, the residue (dark-cream-colored crystals) was triturated with ethyl acetate, and the precipitate was filtered off and washed with ethyl acetate. Compound **22a** was obtained in a yield of 0.15 g (94%), m.p. 338—340 °C (decomp., Pr^{i}OH—DMF, 1 : 1). Found (%): N, 23.49. $C_{13}H_8N_4O$. Calculated (%): N, 23.72. ^{1}H NMR (DMSO-d_6), δ: 7.55 (m, 5 H, Ph); 8.40 (s, 1 H, H(4)); 8.74 (s, 1 H, H(3)); 13.00 (br.s, 1 H, N(5)H). IR, ν/cm^{-1}: 3084 (NH); 2218 (CN); 1654 (CO); 1631 (C=C, C=N). ES MS, m/z: 237 $[M + H]^{+\bullet}$, 259 $[M + Na]^{+\bullet}$, 473 $[2 M + H]^{+\bullet}$, 495 $[2 M + Na]^{+\bullet}$.

1-(4-Chlorophenyl)-7-cyano-6-oxo-5,6-dihydro-1*H*-pyrazolo[4,3-*c*]pyridine (22b) was prepared analogously to **22a** from compound **18b**. The yield was 79%, m.p. 332—335 °C (decomp., Pr^{i}OH—DMF, 1 : 1). ^{1}H NMR (DMSO-d_6), δ: 7.62 (m, 4 H, C_6H_4Cl); 8.41 (s, 1 H, H(3)); 8.73 (s, 1 H, H(4)); 13.00 (br.s, 1 H, N(5)H). ^{13}C NMR (DMSO-d_6), δ: 73.7 (C(7)); 112.1 (C(3a)); 114.5 (CN); 128.4, 128.8, 133.6, 135.8 (C(1′)—C(6′)); 139.5 (C(3)); 140.8 (C(4)); 146.8 (C(7a)); 161.4 (C(6)). IR, ν/cm^{-1}: 3230 (NH); 2212 (CN); 1682 (CO); 1604 (C=C, C=N). ES MS, m/z: 271 $[M + H]^{+\bullet}$ 293 $[M + Na]^{+\bullet}$, 563 $[2 M + Na]^{+\bullet}$. The three-dimensional structure of molecule **22b** was established by powder X-ray diffraction. Compound **22b** crystallizes in the orthorhombic space group $P2_12_12_1$ with the unit cell parameters a = 3.879(1) Å, b = 7.633(2) Å, c = 38.83(1) Å and the unit cell volume of 1168(1) Å^3. The intensities of reflections were measured on an XPert PRO powder diffractometer using Cu-Kα_1 radiation. The crystal structure of compound **22b** was solved by the systematic search method[15] and refined by the Rietveld method using the MRIA program.[16] All structural data, including the unit cell parameters, atomic coordinates, bond angles, and bond lengths, were deposited with the Cambridge Structural Database (CCDC604040).*

3-Formyl-2-oxo-4-phenylamino-1,2-dihydropyridine (23). ***A.*** A Ni—Al_2 alloy (3 g) was added to a suspension of pyridone **5c** (3 g, 0.014 mol) in 50% HCOOH (40 mL). The reaction mixture was refluxed with stirring for 6 h and cooled to 20 °C. The precipitate that formed was filtered off and washed with a small amount of 50% HCOOH and water. The crude precipitate, which was a mixture of inorganic salts and the reaction product, was extracted with DMF (4×20 mL), and the precipitate was filtered off. The filtrate was concentrated to dryness, and the residue (the crystalline precipitate) was triturated with petroleum ether, filtered off, and washed with petroleum ether. Compound **23** was obtained in a yield of 1.62 g (53%), m.p. 251—254 °C (toluene). ^{1}H NMR (DMSO-d_6), δ: 5.88 (d, 1 H, H(5), J_o = 7.4 Hz); 7.25—7.49 (m, 6 H, Ph, H(6)); 10.03 (s, 1 H, CHO); 11.07 (br.s, 1 H, N(1)H); 11.71 (br.s, 1 H, C(4)NH). IR, ν/cm^{-1}: 3142 (OH); 1630 (CO). ES MS, m/z: 237 $[M + Na]^{+\bullet}$, 451 $[2 M + Na]^{+\bullet}$, 665 $[3 M + Na]^{+\bullet}$. EI MS, m/z (I_{rel} (%)): 213 $[M - H]^{+\bullet}$ (100), 185 $[M - CHO]^{+\bullet}$ (100). (Only a small amount of the starting compound was isolated from the mother filtrate of the reaction mixture.)

B. A Ni—Al_2 alloy (2 g) was added to a suspension of pyridone **5c** (2 g, 9.5 mmol) in 85% HCOOH (30 mL). The reaction mixture was refluxed with stirring for 20 h and cooled to 20 °C. The precipitate that formed (inorganic salts) was filtered off and washed with a small amount of 85% HCOOH. The filtrate was diluted with water (150 mL) and kept at 20 °C for 1 h. The precipitate that formed was filtered off and washed with water and petroleum ether. Compound **23** was obtained in a yield of 0.538 g (26%) (a mixture of compound **23** and the sample prepared by the method *A* showed no melting point depression).

* These data can be obtained, free of charge, on application to the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK. Fax: +44 (0) 1223 336033. E-mail: deposit@ccdc.cam.ac.uk.

1-Oxo-1,2-dihydrobenzo[*b*]-1,6-naphthyridine (24). ***A.*** A filtrate (HCOOH and washings) from the synthesis of compound **23** by the method ***B*** was concentrated to dryness, and the crystalline residue was triturated with Pr^{i}OH. Compound **24** was obtained in a yield of 0.768 g (53%), m.p. 330—331 °C (MeOH). ^{1}H NMR (DMSO-d$_6$), δ: 6.63 (d, 1 H, H(3), J_o = 7.5 Hz); 7.38 (d, 1 H, H(2), J_o = 7.5 Hz); 7.57, 7.85, 8.02, and 8.14 (all m, 1 H each, H(5)—H(8)); 9.18 (s, 1 H, H(9)); 11.07 (br.s, 1 H, N(1)H). IR, ν/cm^{-1}: 3036 (NH); 1685, 1657, 1633 (CO). ES MS, *m/z*: 197 $[M + H]^{+\bullet}$. EI MS, *m/z* (I_{rel} (%)): 196 $[M]^{+\bullet}$ (100), 168 $[M - CO]^{+\bullet}$ (52), 140 $[M - CO - HCN - H]^{+\bullet}$ (27).

B. Piperidine (0.05 mL) was added to a solution of 3-formylpyridone **23** (0.05 g, 0.23 mmol) in Pr^{i}OH (2.5 mL). The reaction mixture was refluxed for 7 h and then cooled to 20 °C. The precipitate that formed was filtered off and washed with Pr^{i}OH. Compound **24** was obtained in a yield of 0.025 g (56%). A mixture of compound **24** and the sample prepared by the method *A* showed no melting point depression.

4-(2-Oxo-1,2-dihydropyridin-4-yl)aminobenzenesulfonic acid (25). A 63% H_2SO_4 solution (2 mL) was added to pyridone **5c** (0.15 g, 0.7 mmol). The reaction mixture was refluxed for 1 h and then cooled to 20 °C. The precipitate that formed was filtered off, washed with water and Pr^{i}OH, and triturated with a $NaHCO_3$ solution. The insoluble precipitate was filtered off. The filtrate was acidified with 10% HCl to pH 4. The precipitate that formed was filtered off and washed with water. Compound **25** was obtained in a yield of 0.084 g (52%), m.p. >350 °C (MeOH). Found (%): C, 49.90; H, 3.73; N, 11.04; S, 11.63. $C_{11}H_{10}N_2O_4S$. Calculated (%): C, 49.62; H, 3.79; N, 10.52; S, 12.04. ^{1}H NMR (DMSO-d$_6$), δ: 6.22 (d, 1 H, H(3), J_m = 2.0 Hz); 6.56 (dd, 1 H, H(5), J_o = 7.2 Hz, J_m = 2.0 Hz); 7.21 and 7.68 (both m, 2 H each, $C_6H_5SO_3H$); 7.73 (d, 1 H, H(6), J_o = 7.2 Hz); 9.93 (br.s, 1 H, C(4)NH); 12.90 (br.s, 1 H, N(1)H). IR, ν/cm^{-1}: 3257 (OH); 3117 (NH); 1655, 1624 (CO). EI MS, *m/z* (I_{rel} (%)): 185 $[M - HSO_3]^{+\bullet}$ (100), 167 $[M - HSO_3 - H_2O]^{+\bullet}$ (13), 157 $[M - HSO_3 - CO]^{+\bullet}$ (20), 130 $[M - HSO_3 - CO - HCN]^{+\bullet}$ (43), 64 $[SO_2]$ (48).

3-Hydroxyiminomethyl-2-oxo-4-phenylamino-1,2-dihydropyridine (26a). Formylpyridone **23** (0.185 g, 0.86 mmol) was added to a solution of hydroxylamine hydrochloride (0.06 g, 0.87 mmol) in pyridine (0.7 mL). The reaction mixture was stirred at 60 °C for 1 h and concentrated to dryness. The residue (oil) was triturated in water (7 mL) and kept at 20 °C for 40 min. The precipitate that formed was filtered off and washed with water. Compound **26a** was obtained in a yield of 0.125 g (63%), m.p. 261—262 °C (acetonitrile). ^{1}H NMR (DMSO-d$_6$), δ: 5.97 (d, 1 H, H(5), J_o = 7.5 Hz); 7.15—7.44 (m, 6 H, Ph, H(6)); 8.50 (s, 1 H, H_α); 10.17 (br.s, 1 H, C(4)NH); 10.80 (br.s, 1 H, OH); 10.90 (br.s, 1 H, N(1)H). IR, ν/cm^{-1}: 3254 (OH); 3246 (NH); 1624 (CO). ES MS, *m/z*: 230 $[M + H]^{+\bullet}$, 252 $[M + Na]^{+\bullet}$, 212 $[M - OH]^{+\bullet}$. EI MS, *m/z* (I_{rel} (%)): 229 $[M]^{+\bullet}$ (53), 212 $[M - OH]^{+\bullet}$ (100), 197 $[M - NH - OH]^{+\bullet}$ (36).

5-(4-Nitrophenyl)hydrazonomethyl-2-oxo-4-phenylamino-1,2-dihydropyridine (26b). A mixture of 3-formylpyridone **23** (0.16 g, 0.74 mmol) and *p*-nitrophenylhydrazone (0.11 g, 0.74 mmol) in EtOH (10 mL) was refluxed in the presence of a catalytic amount of *p*-TsOH for 1.5 h. The precipitate that formed was filtered off and washed with EtOH. Compound **26b** was obtained in a yield of 0.176 g (61%), m.p. 361—362 °C (DMF). ^{1}H NMR (DMSO-d$_6$), δ: 6.10 (d, 1 H, H(5), J_o = 7.5 Hz); 6.91 and 8.09 (both m, 2 H each, $C_6H_4NO_2$); 7.20—7.53 (m, 6 H, Ph, H(6)); 8.69 (s, 1 H, H_α); 10.68 (br.s, 1 H, C(4)NH); 10.94 (br.s, 1 H, N<u>H</u>$C_6H_4NO_2$); 11.12 (br.s, 1 H, N(1)H). IR, ν/cm^{-1}: 3286, 3217, 3184 (NH); 1641 (CO). EI MS, *m/z* (I_{rel} (%)): 349 $[M]^{+\bullet}$ (33), 212 $[M - 4\text{-}NHC_6H_4NO_2]^{+\bullet}$ (100), 197 $[M - 4\text{-}NH—NHC_6H_4NO_2)]^{+\bullet}$ (64).

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