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"COMPLETE" NUCLEAR MAGNETIC RESONANCE SPECTRUM OF 4,6-DIAMINO-3,5-DICYANO-2-CYANOMETHYLPYRIDINE

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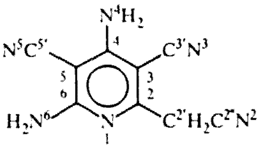
The structure of the molecule of 4,6-diamino-3,5-dicyano-2-cyanomethylpyridine is confirmed by the ^{13}C NMR spectrum which, together with the ^{1}H and ^{15}N NMR spectra (the "complete" NMR spectrum), allows almost unambiguous assignment (with the exception of the virtually coinciding paired signals of the atoms of carbon and nitrogen of the 3- and 5-CN groups). The applicability of the method of increments in the ^{13}C NMR was shown in the assignment of the signals of the carbon atoms in pyridine derivatives. The ratio of the chemical shifts of the nitrogen and hydrogen atoms of the amino groups, known from the literature for aminobenzenes, was confirmed.

In the work [1], describing the detailed synthesis of 4,6-diamino-3,5-dicyano-2-cyanomethylpyridine (I) by the trimerization of malononitrile in dimethylformamide in the presence of anhydrous $ZnCl_2$, no reference is made to NMR methods as a means of identifying the product obtained.



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Meanwhile, the pentasubstituted pyridine (I) represents material which, although difficult, is tempting for investigation by NMR methods. The results of such an investigation will undoubtedly be found useful in widening the scope of spectral–structural correlations available to chemists.

The present work presents data of the ^{1}H, ^{13}C, and ^{15}N NMR spectra (the "complete" NMR spectrum) of compound (I) and examines possibilities for the assignment of all the signals in them.

The PMR spectrum of the solution of the substituted pyridine (I) in DMSO-D_6 at 200 MHz shows singlets at 4.2 ppm (CH_2), 7.3 ppm (4-NH_2), and 7.45 ppm (6-NH_2) besides the group of signals of the solvent ($\delta_H = 2.50$ ppm) and the water contained in it ($\delta_H \cong 3$ ppm). The assignment of the signals of the 4-NH_2 and 6-NH_2 groups can be performed by the selective transfer of polarization to the signals of the corresponding carbon atoms according to the method modified by Yu. A. Strelenko [2]. The line of the protons of the 6-NH_2 group is markedly shifted to low field, and is broadened 25% more strongly than the line of the protons of the 4-NH_2 group when excess water is present in the DMSO-D_6 [the molar ratio of H_2O:(I) = 7:1]. This feature may be determined by the more stable intermolecular hydrogen bonds of the protons of the amino group at the position 6 and, thereby, by the greater time of correlation of the quadrupole interaction of the nucleus of the main nitrogen isotope ^{14}N with the protons. When repeatedly tested in markedly more dried DMSO [the corresponding ratio of H_2O:(I) = 1:1], the relative broadening of the line of the 6-NH_2 group increased by a factor of almost 2.5; this confirms the hypothesis expressed and indicates the requirement to account not only for the structural features of the investigated molecule, but also its interaction with the solvent, in the interpretation of the spectra.

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TABLE 1. Calculation of the Chemical Shifts of the Carbon Atoms of the Pyridine Ring in Compound (I) in the δ_C Scale According to the Scheme of Increments of the Substituents

Atom	CS of pyridine	Increments					Sum of increments	Calculated CS	Measured CS	Difference
		2-CH_2CN	3-CN	5-CN	4-NH_2	6-NH_2				
$C_{(2)}$	150,6	9,3	3,1	3,1	0,9	-0,9	15,5	166,1	159,0	-7,1
$C_{(3)}$	124,5	-1,1	-13,3	0,2	-13,8	-10,6	-38,6	85,9	81,6	-4,3
$C_{(4)}$	136,4	0,8	3,9	3,9	19,6	2,3	30,5	166,9	158,3	-8,6
$C_{(5)}$	124,5	-2,5	0,2	-13,3	-13,8	-14,7	-44,1	81,4	71,1	-10,3

TABLE 2. Exact Values of the ^{13}C NMR Spectral Parameters Obtained by the Method of SPT (A), with the Simultaneous Selective Decoupling of the Protons, and by the Method of the Work [2] (B)

Atom	δ_C	$^2J_{CH}$, Hz	$^3J_{CH}$, Hz	Interacting nucleus (method of observation)
$C_{(2)}$	158,95	6,2		2-CH_2 (A) with decoupling of 4-NH_2
$C_{(3)}$	81,55		2,5	2-CH_2 (A) with decoupling of 4-NH_2
			6,3	4-NH_2 (A) with decoupling of 2-CH_2
$C_{(4)}$	158,28	2,2		4-NH_2 (B)
$C_{(5)}$	71,11		6,3	4-NH_2 (A)
			4,5	6-NH_2
$C_{(6)}$	161,63			6-NH_2
$C_{(2')}$	25,99			
$C_{(2'')}$	116,51	9,6		2-CH_2 (B)
$C_{(3')}$	114,72*			
$C_{(5')}$	115,26*			

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*Assignment may be changed.

TABLE 3. Summary of Data on the NMR of Nitrogen Obtained by Different Experimental Methods

Atom	δ_N	$^1J_{NH}$, Hz	$^{2,3}J_{NH}$, Hz	Interacting proton	Method of observation
N^1	244,0		≅5	2-CH_2	INEPT-5*
N^2	233,9		≅5	2-CH_2	INEPT-5
N^3	279,5†				
N^4	88,1	≅90		4-NH_2	INEPT-90; SPT
N^5	277,5†				
N^6	105,0	≅90		6-NH_2	INEPT-90

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*INEPT-J gives the sequence adjusted to the transfer of polarization in the spectrum with the indicated J_{NH}.

†Assignment may be changed.

The ^{13}C NMR spectra, taken under conditions indicated above using the regime of the complete noise decoupling from the protons, also contain all the expected nine signals of the carbon atoms in (I) besides the group of signals of the deuterated DMSO (39.5 ppm). Only the assignment of the line of the methylene carbon $C_{(2)}$ at the δ_C = 25.99 ppm is evident from them (all the refined assignments are presented according to data obtained on the AMX-300 instrument). The remaining eight lines fall into three clearly marked groups: three lines in the region of δ_C = 160 ppm, three lines in the region of δ_C = 115 ppm, and two lines at the δ_C = 81.55 and 71.11 ppm. Such distinct separation of the signals according to the range of chemical shifts allowed confidence in its successful application for assignments of the semiquantitative method of increments of the substituents (cf., e.g., [3]). In the case under consideration, this method should be applied to the assignment of the signals of the carbon atoms of pyridine. Data on the values of the increments of different substotuents at different positions of the pyridine ring are in the classic handbook [3] (Table 4.11, page 127) and, partially, in the later monograph [4] (Table 3.81, page 400). We took the increments of cyanomethyl to be equal to the increments of methyl. The scheme for the calculation of the proposed chemical shifts is presented in Table 1. The results of such a calculation clearly show that the signals of the $C_{(2)}$, $C_{(4)}$, and $C_{(6)}$ atoms occur at low field as a result of the deshielding ipso-influences of the NH_2 and CH_2CN groups and the deshielding ortho-influence of the CN groups, and the shielding ipso-influence of the CN substituents and the ortho–para-influences of the NH_2 groups shift the lines of the $C_{(3)}$ and $C_{(5)}$ atoms to high field.

It is impossible to consider such an assignment as rigid but, as can be seen from Table 1, it is entirely correct qualitatively, i.e., it predicts the order of sequence of the lines correctly with the increase in the values of the shift, although the formal possibility of improving the "agreement of calculation with the experiment" always remains by means of the change in the increments or calculation of bilinear contributions (e.g., the contribution of the pair of ortho–ortho-substituting NH_2 groups at the positions 4 and 6 to the shift of the carbon at the position 5). The parameters for the model of increments may, strictly speaking, only be selected if the simultaneous satisfactory description of the data is obtained for the corresponding (sufficiently large) number of experiments.

The presence of the marked $^2J_{CH}$ SSCCs for the protons of the methylene group with the carbon atoms $C_{(2)}$ and $C_{(2'')}$ allows the assignment of their lines in taking the spectrum "without decoupling" (the monoresonance of carbon). That is shown by triplets at 159.4 ppm ($^2J_{CH}$ = 6.5 Hz) and 116.9 ppm ($^2J_{CH}$ = 10.0 Hz) correspondingly.

The refined data for the NMR parameters of carbon, obtained by methods of the selective transfer of polarization (SPT) [5] (as a rule, by the simultaneous selective decoupling of the protons or by analogy with the work [2]), are brought together in Table 2. The assignments were performed unambiguously, and may only be mutually changed in the case of the $C_{(3')}$ and $C_{(5')}$ signals (marked in Table 2). However, the differences between the chemical shifts of these atoms are insignificant.

Only three lines are reliably observed for the nitrogen of the CN groups [$N_{(2)}$, $N_{(3)}$, $N_{(5)}$] in the ^{15}N NMR spectra with the direct prolonged buildup. It was found to be impossible to separate the last two signals, having practically the same shift and not having appreciable SSCCs with protons, as was marked in Table 3. Experiments on ^{15}N NMR were performed on the AMX-300 spectrometer. The INEPT method [6] was employed with adjustment to one or the other range of values of J_{NH}. The data are brought together in Table 3.

To sum up, the results of the measurements by the methods of ^1H, ^{13}C, and ^{15}N NMR form almost a closed body of data, which also makes it practically unambiguous (the "complete" NMR spectrum).

The necessary (if they will in fact be necessary) specifications concerning the assignments of the signals of the carbon and nitrogen atoms of the CN groups require either isotopic labels or two-dimensional experiments to show the interactions in pairs of uncommon isotopes ($^{13}C-{}^{13}C$ and $^{13}C-{}^{15}N$ [7, 8]). Regrettably, there is not sufficient information in the literature pertaining to the ^{15}N NMR of substituted pyridines. Data on the NMR of aromatic amines [9], obtained using the solution of DMSO, indicate the markedly lower (by a factor of not more than 72) δ_N of the NH_2 group in aminobenzenes by comparison with the δ_N in aminopyridines. By analogy, also, the δ_H of amino groups in aminobenzenes are less (by a factor of not more than 6) than the corresponding values in aminopyridines. The previously found correlation between the δ_N and δ_H of amino groups [9] also occurs in our case: both values increase with the increase in the ionization potential of the group and, it can be added, with the increase in the stability of the hydrogen bond with the main solvent.

EXPERIMENTAL

The synthesis of compound (I) was performed by the method similar to that described in the work [1]. The spectra were taken on the Bruker WP-200 and AMX-300 spectrometers for solutions of (I) in DMSO-D_6 [the practically saturated solution at 30°C contained up to 10% by weight of (I)], with which inserts were filled for plotting on the WP-200, and the standard NMR ampul of the spectrometer of the external diameter 5 mm was filled for measurements on the AMX-300.

The ^1H NMR spectra and the ^{13}C chemical shifts, presented in Table 1, were obtained on the Bruker WP-200 instrument (200 MHz for ^1H, and 50 MHz for ^{13}C).

The data presented in the Tables 2 and 3 were obtained on the Bruker AMX-300 spectrometer in the ranges of 75 MHz for ^{13}C and 30 MHz for ^{15}N in the Institute of Organic Chemistry of the Russian Academy of Sciences (RAN). Standard impulse sequences of the company Bruker were utilized. We are grateful to Yu. A. Strelenko for having performed these measurements.

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