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# $^1$H NMR SPECTRA OF SOME NITRO DERIVATIVES OF 2-ALKYLAMINO-, 2-PHENYLAMINO-, 2-PIPERIDYL-; 2-MORPHOLYL-, 2-(N-ALKYL-N-NITROSOAMINO)-, AND 2-ALKYLNITRAMINO-4(or 6)-METHYLPYRIDINES

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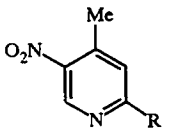
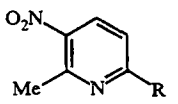
*$^1$H NMR spectra of some N-substituted 2-amino-3-nitro- and 2-amino-5-nitropyridines were measured and interpreted. Chemical shift assignments were based on existing chemical shift rules for substituted pyridines and spectral comparison with compounds of similar structure. The splitting of the methyl group signal of the methylamino group into a doublet testifies that the investigated compounds exist in the amino form. Some* ortho-*amino- and* ortho-*alkylaminonitropicolines were found to give splitting of the amino signals due to intramolecular hydrogen bonding and steric hindrance.*

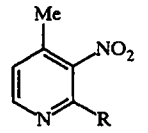
$^1$H NMR spectra of some nitrated alkylaminopyridines have been investigated by different research groups [1-4]. As a part of our studies in this field we present here the $^1$H NMR chemical assignments for new 2-substituted nitropicolines (**1-33**) and discuss the hydrogen bonding ability of *ortho*-aminonitropicolines.



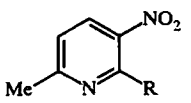
**1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21**



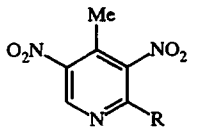
**2, 4, 6, 8, 10, 12, 14, 16, 18, 20**



**22, 24, 25, 27, 28, 29, 31**



**23, 26, 30**



**32, 33**

Compounds of this type have found application as new nucleophilic substitution or transacylation catalysts [5-8], and as intermediate compounds for fungicides [9], herbicides [10], insecticides [11], and bactericides [12]. Especially, the presence of nitro group in a molecule is essential for meaningful antifungal activity in these compounds [13, 14]. They form complexes with nickel [15], copper [16, 17], and cobalt salts [18]. Besides, from a theoretical point of view, it is interesting to learn how the presence of three (2-alkylamino, 5- or 3-nitro, 4- or 6-methyl) or four (2-alkylamino, 4- or 6-methyl, 3- and 5-nitro) substituents that have different electronegativity and are situated in various positions of the pyridine ring, influence the shielding of alkylamino- as well as ring protons.

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TABLE 1. $^1H$ NMR Chemical Shifts, $\delta$, and Coupling Constants, J, Hz, for 2-R-4-Me-5-$NO_2$- and 2-R-6-Me-5-$NO_2$-Pyridines in DMSO-$D_6$ (A) or $CDCl_3$ (B)

| Compound | R | Solvent | 3-H | 4-H | 6-H | 4-$CH_3$ | 6-$CH_3$ | $J_{34}$ | Other signals |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| 1 | $NHCH_3$ | A | 6,57 | | 9,03 | 2,68 | | | 8,03 (NH), 3,08 ($NCH_3$) d ($J$ = 6,5) |
| | | B | 6,13 | | 8,93 | 2,53 | | | 5,47 (NH), 2,97 ($NCH_3$) d ($J$ = 6,5) |
| 2 | | A | 6,57 | 8,23 | | | 2,80 | 9 | 8,17 (NH), 3,03 ($NCH_3$) d ($J$ = 5) |
| | | B | 6,37 | 8,30 | | | 2,80 | 9 | 5,90 (NH), 3,07 ($NCH_3$) d ($J$ = 5) |
| 3 | $NHCH_2CH_3$ | A | 6,50 | | 9,00 | 2,62 | | | 8,03 (NH), 3,10 ($NCH_2$) m ($J$ = 6,5), 1,27 ($CH_3$) t ($J$ = 6,5) |
| | | B | 6,13 | | 8,93 | 2,53 | | | 5,60 (NH), 3,33 ($NCH_2$) m ($J$ = 6,5), 1,27 ($CH_3$) t ($J$ = 6,5) |
| 4 | | A | 6,57 | 8,26 | | | 2,80 | 9 | 8,17 (NH), 3,52 ($NCH_2$) m ($J$ = 6), 1,28 ($CH_3$) t ($J$ = 7) |
| | | B | 6,37 | 8,25 | | | 2,77 | 9 | 5,77 (NH), 3,47 ($NCH_2$) m ($J$ = 6), 1,28 ($CH_2$) t ($J$ = 7) |
| 5 | $NHCH_2CH_2CH_3$ | A | 6,56 | | 8,97 | 2,57 | | | 8,00 (NH), 3,40 ($NCH_2$) m ($J$ = 6,5), 1,70 ($CH_2$) m ($J$ = 6,5), 0,97 ($CH_3$) t ($J$ = 6,5) |
| | | B | 6,13 | | 8,90 | 2,53 | | | 5,60 (NH), 3,17 ($NCH_2$) m ($J$ = 6,5), 1,60 ($CH_2$) m ($J$ = 6,5), 0,93 ($CH_3$) t ($J$ = 6,5) |
| 6 | | A | 6,50 | 8,21 | | | 2,70 | 9 | 8,10 (NH), 3,40 ($NCH_2$) q ($J$ = 7), 1,60 ($CH_2$) m ($J$ = 7), 1,0 ($CH_3$) t ($J$ = 6) |
| | | B | 6,25 | 8,22 | | | 2,75 | 9 | 5,58 (NH), 3,33 ($NCH_2$) q ($J$ = 7), 1,60 ($CH_2$) m ($J$ = 7), 0,96 ($CH_3$) t ($J$ = 6) |
| 7 | $N(CH_3)_2$ | A | 6,60 | | 8,90 | 2,53 | | | 3,20 (CH3) |
| 8 | | B | 6,23 | | 8,97 | 2,57 | | | 3,17 ($CH_3$) |
| | | A | 6,80 | 8,40 | | | 2,80 | 10 | 3,30 ($CH_3$) |

TABLE 1 (continued)

| Compound | R | Solvent | 3-H | 4-H | 6-H | 4-$CH_3$ | 6-$CH_3$ | $J_{34}$ | Other signals |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| 9 | $NC_5H_{10}$ | A | 6,87 | | 8,97 | 2,60 | | | 3,83 (4H), 1,70 (6H) |
| | | B | 6,33 | | 9,00 | 2,53 | | | 3,53 (4H), 1,63 (6H) |
| 10 | | A | 6,90 | | 8,30 | | 2,80 | 10 | 3,80 (4H), 1,70 (6H) |
| | | B | 6,47 | | 8,20 | | 2,75 | 10 | 3,71 (4H), 1,67 (6H) |
| 11 | $NC_4H_8O$ | A | 6,90 | | 8,93 | 2,60 | | | 3,73 (8H) |
| | | B | 6,40 | | 9,00 | 2,63 | | | 3,76 (8H) |
| 12 | | A | 6,90 | 8,40 | | | 2,80 | 10 | 3,80 (8H) |
| 13 | $NHC_6H_5$ | A | 6,98 | | 9,17 | 2,77 | | | 10,18 (NH), 8,00, 7,86, 7,70, 6,46 (5H, Ph) |
| | | B | 6,57 | | 8,93 | 2,50 | | | 7,83 (NH), 7,33 (5H) |
| 14 | | A | 6,97 | 8,40 | | | 2,87 | 9 | 10,17 (NH), 8,00, 7,86, 7,66, 7,56, 7,00 (5H) |
| | | B | 6,70 | 8,28 | | | 2,75 | 9 | 10,20 (NH), 7,40 (5H) |
| 15 | $NNO_2CH_3$ | A | 8,17 | | 9,33 | 2,83 | | | 3,55 ($CH_3$) |
| | | B | 7,73 | | 9,00 | 2,60 | | | 3,70 ($CH_3$) |
| 16 | | A | 8,07 | 8,80 | | | 2,80 | 9 | 3,93 ($CH_3$) |
| | | B | 7,94 | 8,52 | | | 2,93 | 9 | 3,96 ($CH_3$) |
| 17 | $NNO_2CH_2CH_3$ | A | 8,15 | | 9,37 | 2,83 | | | 4,40 (CH2) q ($J$ = 6), 1,43 ($CH_3$) t ($J$ = 6,5) |
| | | B | 7,73 | | 9,00 | 2,60 | | | 3,60 ($CH_2$) q ($J$ = 6), 1,27 ($CH_3$) t ($J$ = 6,5) |
| 18 | | A | 7,92 | 8,68 | | | 2,87 | 9 | 4,37 ($CH_2$), 1,38 ($CH_3$) |
| 19 | $NNOCH_3$ | A | 8,27 | | 9,27 | 2,73 | | | 3,57 ($CH_3$) |
| | | B | 8,03 | | 9,17 | 2,70 | | | 3,50 ($CH_3$) |
| 20 | | A | 8,13 | 8,70 | | | 2,90 | 9 | 3,58 ($CH_3$) |
| | | B | 8,05 | 8,50 | | | 2,90 | 9 | 3,53 ($CH_3$) |
| 21 | $NNOCH_2CH_3$ | A | 8,23 | | 9,27 | 2,73 | | | 4,27 ($CH_2$) q ($J$ = 6,5), 1,10 ($CH_3$) t ($J$ = 6,5) |
| | | B | 8,03 | | 9,17 | 2,70 | | | 4,27 ($CH_2$) q ($J$ = 6,5), 1,07 ($CH_3$) t ($J$ = 6,5) |

TABLE 2. $^1H$ NMR Chemical Shifts, δ, and Coupling Constants, J, Hz, for 2-R-4-$CH_3$-3-$NO_2$- and 2-R-6-$CH_3$-3-$NO_2$-Pyridines in DMSO-$D_6$ (A) or $COCl_3$ (B)

| Compound | R | Solvent | 4-H | 5-H | 6-H | 4-$CH_3$ | 6-$CH_3$ | $J_{45}$ | $J_{56}$ | Other signals |
|---|---|---|---|---|---|---|---|---|---|---|
| 22 | $NHCH_3$ | A | | 6,75 | 8,32 | 2,53 | | | 5 | 7,65 (NH), 3,10 ($NCH_3$) d ($J$ = 5) |
| | | B | | 6,50 | 8,17 | 2,50 | | | 5 | 7,57 (NH), 3,07 ($NCH_3$) d ($J$ = 5) |
| 23 | | A | 8,33 | 6,67 | | | 2,52 | 8 | | 8,60 (NH), 3,13 ($NCH_3$) d ($J$ = 6) |
| | | B | 8,30 | 6,47 | | | 2,43 | 8 | | 8,30 (NH), 3,13 ($NCH_3$) d ($J$ = 6) |
| 24 | $NHCH_2CH_3$ | A | 8,40 | 6,73 | | | 2,53 | 8 | | 8,73 (NH), 3,72 ($NCH_2$) m ($J$ = 6), 1,33 ($CH_3$) t ($J$ = 6) |
| | | B | 8,30 | 6,47 | | | 2,42 | 8 | | 8,30 (NH), 3,63 ($NCH_2$) m ($J$ = 6), 1,25 ($CH_3$) t ($J$ = 6) |
| 25 | $NHC_6H_5$ | A | | 7,05 | 8,37 | 2,50 | | | 5 | 9,20 (NH), 7,80, 7,69, 7,58, 7,30 (5H, Ph) |
| | | B | | 6,67 | 8,17 | 2,50 | | | 5 | 9,17 (NH), 7,50, 7,35, 7,26 (5H, Ph) |
| 26 | | A | 8,47 | 6,90 | | | 2,50 | 9 | | 10,17 (NH), 7,88, 7,67, 7,56, 7,43, 7,33 (5H) |
| | | B | 8,50 | 6,67 | | | 2,50 | 9 | | 10,25 (NH), 7,83, 7,75, 7,42, 7,25 (5H) |
| 27 | $NNO_2CH_3$ | A | | 7,77 | 8,83 | 2,57 | | | 5 | 3,72 ($NCH_3$) |
| | | B | | 7,40 | 8,50 | 2,50 | | | 5 | 3,67 ($NCH_3$) |
| 28 | $NNO_2CH_2CH_3$ | A | | 7,88 | 8,85 | 2,57 | | | 5 | 4,22 ($CH_2$) q ($J$ = 6,5), 1,33 ($CH_3$) t ($J$ = 6,5) |
| | | B | | 7,47 | 8,60 | 2,50 | | | 5 | 4,17 ($CH_2$) q ($J$ = 6,5), 1,30 ($CH_3$) t ($J$ = 6,5) |
| 29 | $NNOCH_3$ | A | | 7,77 | 8,83 | 2,53 | | | 5 | 3,60 ($NCH_3$) |
| | | B | | 7,17 | 8,40 | 2,33 | | | 5 | 3,42 ($NCH_3$) |
| 30 | | A | 8,55 | 7,70 | | | 2,70 | 8 | | 3,58 ($NCH_3$) |
| | | B | 8,17 | 7,25 | | | 2,63 | 8 | | 3,53 ($NCH_3$) |
| 31 | $NNOCH_2CH_3$ | B | | 7,20 | 8,43 | 2,40 | | | 5 | 4,17 ($CH_2$) q ($J$ = 6,5), 1,10 ($CH_3$) t ($J$ = 6,5) |

TABLE 3. $^1H$ NMR Chemical Shifts, $\delta$, and Coupling Constants, J, Hz, for 2-R-3,5-$(NO_2)_2$-4-$CH_3$-Pyridines in DMSO-$D_6$ (A) or $CDCl_3$ (B)

| Compound | R | Solvent | 6-H | 4-$CH_3$ | Other signals |
|---|---|---|---|---|---|
| 32 | $NHCH_3$ | A | 9,01 | 2,54 | 8,20 (NH), 3,07 ($NCH_3$) d ($J$ = 5) |
| | | B | 8,97 | 2,57 | 6,93 (NH), 3,13 ($NCH_3$) d ($J$ = 5) |
| 33 | $NHCH_2CH_3$ | A | 9,01 | 2,50 | 8,03 (NH), 3,53 ($NCH_2$) m ($J$ = 6), 1,27 ($CH_3$) t ($J$ = 7) |
| | | B | 8,97 | 2,57 | 6,90 (NH), 3,63 ($NCH_2$) m ($J$ = 7; 2), 1,27 ($CH_3$) t ($J$ = 7) |

## EXPERIMENTAL

Syntheses of the investigated compounds have been described in previous publications [19] (compounds **2, 4, 14, 16, 18, 23-26**); [20] (compounds **6, 8, 10, 12**); [21] (compounds **1, 3, 13, 15, 17, 22, 27, 28, 32, 33**); [22] (compounds **5, 9, 11**); [23] (compounds **19-21, 29-31**).

The $^1H$ NMR spectra were obtained with a Tesla BS 598 A, 100-MHz NMR spectrometer at temperature 25°C. $CDCl_3$ and DMSO-$D_6$ were used as solvents and TMS as an internal standard.

The chemical shift values obtained, as well as coupling constants, are presented in Tables 1-3.

## RESULTS AND DISCUSSION

Introduction of an alkyl group in place of a hydrogen atom in the 2-amino group of the 5-nitro derivatives studied produces a downfield shift of amino group proton signals from 7.30 ppm [3] to 8.03 ppm for 4-$CH_3$ derivatives and from 7.36 ppm [3] to 8.17 ppm for 6-$CH_3$ derivatives (Table 1), whereas deshielding of the ring protons changes in a significantly smaller degree (0.13-0.26 ppm). The greater paramagnetic shifts of the ring protons are caused by the piperidyl and morpholyl substituents (0.51-0.54 ppm) (Table 1) due to the inductive effect of the heteroatom present in the 2-substituent.

The greatest paramagnetic changes in chemical shifts of the amino group protons are caused by the phenyl group in 3-nitro derivatives (2.07-2.27 ppm) (Table 2, compound **25**) in spite of the steric hindrance (3-$NO_2$ group). The effect of the 3-nitro group on deshielding of the proton of the alkylamino group as well as those of the ring protons is significantly smaller than that of 5-nitro derivatives because of the steric hindrance, especially in the 4-methyl derivatives (Table 2). The large nitro group, situated between the bulky 2-substituent and 4-methyl group, loses its coplanarity with the ring.

The great deshielding effect of H-5 in 3-nitro derivatives (1.02-1.15 ppm) (Table 2) is observed when alkylnitramino or N-alkyl-N-nitrosoamino substituents are placed in position 2 instead of the alkylamino group according to their strong electron-withdrawing ability. In 3-nitro derivatives, creating a hydrogen bond between the proton of the alkylamino group and the 3-nitro group is possible. However, in the 4-methyl derivatives there is no such possibility because of the lack of coplanarity between the amino and nitro groups. In the 6-methyl derivatives the signal of the proton of the 2-alkylamino group is recorded as a broadened singlet.

Passing from 2-alkylamino-4-methyl-3-nitropyridines to their 3,5-dinitro derivatives results in a significant deshielding of H-6 (8.32-9.01 ppm) (Table 3). This value is close to that characteristic of 5-nitro derivative (9.03 ppm). The dominant influence of the 5-nitro group on the proton in position 6, and the lack of effect of the 3-nitro group is due to its noncoplanarity.

It is worthwhile to note that splitting of the signal of the methyl protons of the 2-methylamino group into two signals in the spectra of the compounds studied proves their existence in the amino form. 2-Substituted 5-nitro and analogous 3-nitro derivatives were studied as AB splitting patterns. The values of $J_{34}$ = 9-10 (Table 1), $J_{45}$ = 8-9, and $J_{56}$-5 Hz (Table 2) change with the electronegativity of the 2-substituent and the order of the bond between carbons 3 and 4, 4 and 5, and 5 and 6.

The $^1H$ NMR spectra recorded in two different solvents ($CDCl_3$ and DMSO-$D_6$) show that the effect of DMSO-$D_6$ on the chemical shift of protons of alkylamino groups is significant in comparison to the chemical shift of protons of the pyridine ring.

On passing from $CDCl_3$ to DMSO-$D_6$, the shielding effect of NH protons in the spectra of 5-nitro derivatives increases from 8.17 to 5.57 ppm for 6-methyl derivatives and from 8.03 to 5.47 ppm for 4-methyl derivatives (Table 1) due to formation of hydrogen bonds between the proton of the alkylamino group and the oxygen atom of the solvent. The lack of change in deshielding of amino group protons in the spectra of 3-nitro derivatives irrespective of the kind of solvent gives one more evidence of the steric hindrance in these compounds as well as of the intramolecular hydrogen bond between 2-amino and 3-nitro groups.

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