

EFFECT OF LANTHANIDE SHIFT REAGENTS ON $^1\text{H-NMR}$ SPECTRA OF AMINOPYRIDINES

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The effect of $\text{Eu}(\text{dpm})_3$ and $\text{Pr}(\text{dpm})_3$ on the proton spectra of 2-amino-, 3-amino- and 4-aminopyridines has been studied by the $^1\text{H-NMR}$ spectroscopy in tetrachloromethane and deuteriochloroform at 25°C . Relative changes of the induced chemical shifts of pyridine carrying electron-donor substituents (amino group) are the same as the values given in literature for pyridine ring with electron-acceptor substituents.

Pyridine¹ and its derivatives (pyridine oxide², lutidines³, 3-fluoropyridine⁴, 2-, 3- and 4-substituted pyridines⁵) belong among the substances for which the effect of lanthanide shift reagents was intensively studied. Shifts of the α -protons are comparable with those of amines⁶. Sanders and Williams⁷ arranged an order according to intensity of interaction with $\text{Eu}(\text{dpm})_3$ ($\text{dpm} = 2,2,6,6\text{-tetramethyl-3,5-heptanedionate}$) for the compounds of the type $-\text{CH}_2-\text{R}$ as follows: amine > hydroxyl > ketone > aldehyde > ether > ester > nitrile.

Aminopyridines represent thus compounds containing two very efficient groups *viz.* heteroatom and amino group. In this report we present the results of study of effects of $\text{Eu}(\text{dpm})_3$ and $\text{Pr}(\text{dpm})_3$ on 2-aminopyridine (*I*), 3-aminopyridine (*II*) and 4-aminopyridine (*III*) in tetrachloromethane and deuteriochloroform. Content of imino forms^{8,9} is negligible in the compounds *I* and *III*, the compound *II* is present in its amino form only.

EXPERIMENTAL

2-Aminopyridine (*I*), 3-aminopyridine (*II*) and 4-aminopyridine (*III*) were commercial chemicals which were crystallized and dried in vacuum. $\text{Eu}(\text{dpm})_3$ and $\text{Pr}(\text{dpm})_3$ were commercial reagents (Merck). Tetrachloromethane and deuteriochloroform (99.8% D) were kept over molecular sieves.

Two methods were used in the measurements: *A*) According to Armitage and coworkers¹⁰ the measured substance was weighed and added gradually to solution of the shift reagent (4 to 9 mmol/l) in tetrachloromethane or deuteriochloroform, and, after dissolution, spectra were recorded, and changes in chemical shifts were evaluated. The ratio $[\text{aminopyridine}]/[\text{La}(\text{dpm})_3]$ varied within 8 to 35. The shift value ΔM_1 (for the ratio $[\text{aminopyridine}]/[\text{La}(\text{dpm})_3] = 1$) was obtained from the slope of dependence $1/\Delta_1$ (where $\Delta_1 = \delta_{\text{La}1} - \delta_1$) vs concentration of the

respective aminopyridine using the least squares method. *B*) Weighed amounts of $\text{Eu}(\text{dpm})_3$ were gradually added to 0.1M solution of the aminopyridines in deuteriochloroform, spectra were recorded, and the changes in chemical shifts were evaluated. The values ΔM_i were obtained by the least squares method from the slope of the linear dependences (up to the ratio of $[\text{Eu}(\text{dpm})_3]/[\text{aminopyridine}] = 0.7$) of Δ_i vs ratio $[\text{Eu}(\text{dpm})_3]/[\text{aminopyridine}]$.

The spectra were measured at 60 MHz at 25°C with a JNM-3 H-60 apparatus (Jeol) using TMS as reference substance. The chemical shifts were determined by calibration by the side band method with the accuracy ± 0.03 ppm.

The spectra of the compounds *I* to *III* were interpreted according to ref.¹¹.

RESULTS

The compounds *I* and *II* were measured in tetrachloromethane by the method (*A*). The compound *III* is very little soluble in this solvent. The concentration dependences of $1/\Delta_i$ were linear. The ΔM_i values are given in Table I.

In deuteriochloroform all the three compounds were measured by the method (*A*). However, the concentration dependence of $1/\Delta_i$ was linear in the case of the compound *II* only. The ΔM_i values are given in Table II. The non-linearity of the concentration dependence of $1/\Delta_i$ for the compounds *I* and *III* (Fig. 1 and 2) both in the case of $\text{Eu}(\text{dpm})_3$ and $\text{Pr}(\text{dpm})_3$ indicates a specific interaction of these compounds with solvent.

Therefore, all the three compounds were measured in deuteriochloroform by the method (*B*). In this case the concentration dependences of Δ_i were linear up to the ratio $[\text{Eu}(\text{dpm})_3]/[\text{aminopyridine}] = 0.7$; the ΔM_i values are given in Table II.

Changes of chemical shift of the protons of amino group were insignificant in all the cases.

From the results it follows, that pyridine heteroatom forms such a stable complex with the shift reagent that interaction of the reagent with amino groups does not practically make itself felt. Thus *e.g.* ΔM of the protons H(3) and H(5) of the com-

TABLE I
Survey of ΔM_i Values of the Protons of 2-Aminopyridine (*I*) and 3-Aminopyridine (*II*) in CCl_4 Solution in the Presence of Shift Reagents $\text{La}(\text{dpm})_3$

| Compound | La | H(2) | H(3) | H(4) | H(5) | H(6) |
|-----------|----|-------|-------|-------|-------|-------|
| <i>I</i> | Eu | — | 7.9 | 6.2 | 5.6 | 20.4 |
| | Pr | — | -15.3 | -9.5 | -13.4 | -44.7 |
| <i>II</i> | Eu | 21.5 | — | 8.7 | 8.7 | 19.2 |
| | Pr | -39.6 | — | -14.2 | -15.9 | -35.4 |

pond *III* are practically identical with those of H(3) of the compound *I* and H(5) of the compound *II*. Certainly it is impossible to use formation of complex of amino group with the shift reagent for explanation of small increase of ΔM of the protons *ortho* to amino group as compared with ΔM of the protons symmetrically bound to them with respect to the pyridine heteroatom.

Practically the same mutual ratios of M_i were observed both with 2-substituted pyridines⁵ ($-\text{CH}_3$; $-\text{CN}$; $-\text{Cl}$; $-\text{CH}=\text{CH}_2$; 3-pentyl-) and $\text{Eu}(\text{fod})_3$ ($\text{fod} = = 6,6,7,7,8,8,8\text{-heptafluoro-2,2-dimethyl-3,5-octanedionate}$) and with 3-substituted

TABLE II
Survey of ΔM_i Values of the Protons of 2-Aminopyridine (*I*), 3-Aminopyridine (*II*) and 4-Aminopyridine (*III*) in CDCl_3 Solutions in the Presence of Shift Reagents $\text{La}(\text{dpm})_3$

| Compound | La | H(2) | H(3) | H(4) | H(5) | H(6) |
|------------|-----------------|-------|------|-------|-------|-------|
| <i>I</i> | Eu | — | 8.2 | 7.3 | 6.9 | 25.1 |
| <i>II</i> | Eu | 21.8 | — | 6.7 | 7.8 | 19.4 |
| | Eu ^a | 22.0 | — | 7.3 | 8.2 | 19.4 |
| | Pr ^a | -32.7 | — | -12.9 | -15.2 | -28.4 |
| <i>III</i> | Eu | 25.3 | 8.4 | — | 8.4 | 25.3 |

^a The values obtained by the method of addition of the compound *II* to solution of the shift reagent of constant concentration.

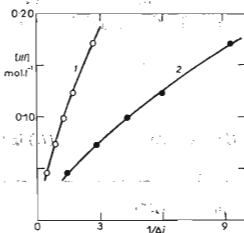


FIG. 1

Dependence of $1/\Delta_i$ H(2,6) (1) and H(3,5) (2) on Concentration of 4-Aminopyridine at Constant $\text{Eu}(\text{dpm})_3$ Concentration (4.5 mmol/l) in CDCl_3

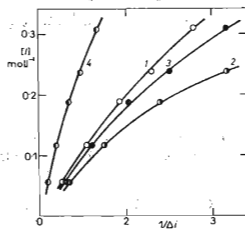


FIG. 2

Dependence of $1/\Delta_i$ H(3) (1), H(4) (3), H(5) (2) and H(6) (4) on Concentration of 2-Aminopyridine at Constant $\text{Pr}(\text{dpm})_3$ Concentration (8.0 mmol/l) in CDCl_3

pyridines (3-cyano-⁵ with Eu(fod)₃ and 3-fluoro-⁴ with Eu(dpm)₃). Hence, the effect is not due to electron-donor or -acceptor properties of substituents neither to their ability to form complex with shift reagents. Obviously, the reason is the Fermi contact action of the lanthanide atom transferred through the bonds of the pyridine ring. This possibility for pyridine derivatives and isoquinoline was proved by Gansow and coworkers¹² on the basis of complete disagreement between experimental ΔM_i ¹³C with the values calculated with the use of position of europium atom derived from the proton spectra according to the McConnell–Robertson equation¹³ for pure pseudocontact interaction.

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