

NMR Spectra of Some Nitro-substituted N-Alkylanilines I

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NMR chemical shifts and coupling constants for a number of N-methyl- and N-ethylanilines have been determined in nitrobenzene solution.

The differences in chemical shifts between the methyl protons in the N-methyl compounds and the methylene protons in the corresponding N-ethyl compounds have been shown to depend on the substitution pattern, two *ortho* nitro groups causing an abnormally small difference.

A spin decoupling technique has been used to locate the positions of otherwise invisible amine proton resonance peaks in the N-methylaniline series.

Recent work¹ has shown that in the NMR spectrum of N-(2,4-dinitrophenyl)-ethylenediamine, the chemical shifts of the two methylene groups are different, *viz.*, 3.01 and 3.51 ppm downfield from TMS (tetramethylsilane) in nitromethane solution. In N-(2,6-dinitrophenyl)-ethylenediamine, on the other hand, the chemical shifts of the two methylene groups have the same value, 2.92 ppm. Roughly the same behaviour was shown by N-(2,6-dinitro-4-methanesulphonyl)-ethylenediamine, the chemical shift in that case being 2.99 ppm.

It was suggested¹ that in the presence of two nitro groups *ortho* to the ethylenediamine side chain in these compounds causes an upfield shift of 0.5 δ units of the "inner" methylene group from the value 3.51 in the 2,4-dinitro compound, whereas the "outer" methylene group is much less influenced by the substitution pattern. In order to prove the correctness of this explanation and to find the cause of this upfield shift, a systematic study of some N-alkylanilines was started, since these might serve as simpler models for the ethylenediamine compounds.

One obvious difficulty with the ethylenediamine compounds is the assignment of unambiguous chemical shift values to the proper methylene groups. Also, the presence of the terminal amino group can cause various chemical reactions, such as disproportionation and, possibly, intramolecular nucleophilic substitution.

The first model compounds investigated were a series of N-methylanilines. Unsubstituted N-methylaniline was commercially available, and the following substituted ones were synthesized: 2-nitro, 4-nitro, 2,4-dinitro, 2,6-dinitro, and 2,4,6-trinitro. The synthetic procedure was straightforward, namely, nucleophilic aromatic substitution with methylamine. Details are given in the Experimental part.

NMR spectra were determined in nitrobenzene because of its good solvent properties. By using nitrobenzene, the aromatic region in the NMR spectra is more or less completely swamped. In the present case, this was of little consequence since attention was focused on the chemical shifts of the methyl protons. In a study of conformation and internal rotation of nitroaromatic amines by NMR, Heidberg and co-workers² used dichloromethane as solvent, which made it possible to study the aromatic protons. Nitromethane, preferably deuterated, would have been theoretically more suitable, but some of the N-alkylanilines are not sufficiently soluble in this solvent.

At least two nitrobenzene solutions of different concentration were run with each compound. No significant change in chemical shift values caused by dilution was observed. Spectra were recorded at $38 \pm 1^\circ\text{C}$ on a Varian A-60 spectrometer.

The methyl group in all the compounds containing one or more nitro groups is split into a doublet by the amino proton. In several of the NMR spectra, the amino proton itself cannot be seen, either because it is too broad^{3a,4a} or because it falls in the region of solvent absorption, or both. However, since the spectrometer was equipped with a Varian Model V-6058 spin decoupler, the position of the amine proton could be located indirectly by noting at which separation between observing and decoupling RF fields the methyl doublet coalesces into a singlet.

The chemical shifts of the methyl groups in the N-methylanilines show considerably less variation than might be expected from a comparison with the ethylenediamine compounds. It was therefore decided to also study some N-ethylanilines, because the ethyl group would be a better model for the side chain than the methyl group.

Table 1. NMR data for N-methylanilines.

Substituents	$\delta\text{-CH}_3^a$	$\delta\text{-NH}^b$	$J\text{-NHCH}_3^c$
Unsubstituted	2.80	4.17 ^d	— ^e
2-Nitro	2.93	7.9	5.1
4-Nitro	2.90	5.4	5.1
2,4-Dinitro	3.10	8.5	5.2
2,6-Dinitro	2.87	8.4	5.5
2,4,6-Trinitro	3.04	9.2	5.6

^a In ppm downfield from TMS. Values good to ± 0.02 ppm.

^b In ppm downfield from TMS as determined by spin decoupling. Values denote center of band and are good to ± 0.2 ppm, bandwidth about 0.3 ppm.

^c In Hz. Values good to ± 0.2 Hz.

^d Directly observed.

^e No splitting observed.

RESULTS

In Table 1, the NMR information about the N-methyl compounds is presented. Similarly, Table 2 shows the data obtained for the N-ethyl series.

The syntheses of the N-ethyl compounds were analogous to those of the N-methyl compounds, ethylamine being used instead of methylamine. The same solvent, nitrobenzene, was also used for the NMR spectra of the N-ethyl compounds. Spin decoupling experiments to determine the position of the amino protons were unsuccessful in this case, mainly because of instrumental limitations.

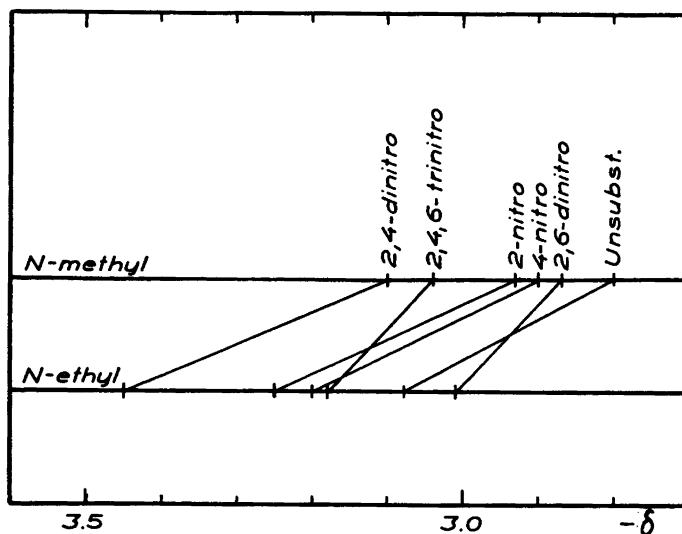


Fig. 1. Chemical shifts (ppm downfield from TMS) of methyl protons in N-methylanilines and methylene protons in N-ethylanilines.

Fig. 1 illustrates the effect of the ring substituent pattern upon the difference between the chemical shift of the methyl protons in the N-methyl series and the methylene protons in the corresponding N-ethyl compounds. Fig. 2 serves to illustrate the spin decoupling technique used for determining the positions of the amino protons.

DISCUSSION

Chemical shifts of the N-alkyl groups. It is empirically known^{3b,4b} that replacement of one proton in a methyl group by another methyl group causes a downfield shift of 0.3–0.4 ppm of the remaining protons. Fig. 1 shows that a downfield shift of 0.28–0.35 ppm upon going from N-methyl to N-ethyl ($-\text{CH}_2-$ protons) is indeed observed for all compounds that carry at most one nitro group *ortho* to the alkylamino group. The preferred conformation

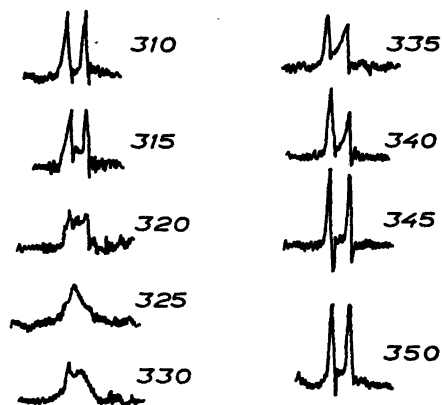


Fig. 2. NMR signal from the methyl group in N-methyl-2,4-dinitroaniline using spin decoupling. The numbers denote frequency separation in Hz between observing and decoupling fields.

of such compounds is undoubtedly that which permits a hydrogen bond between the *ortho* nitro group and the amino group, and this conformation leaves the N-alkyl group in a relatively unhindered position on the remote side of the *ortho* nitro group. On the contrary, in the compounds with *two ortho* nitro groups, the downfield shift is significantly smaller, 0.14 ppm. An explanation of this value may be that the "normal" value is partially compensated by a screening effect. It is plausible that, even allowing for some non-planarity of the molecules, the proximity of one nitro group to the alkyl group is responsible for the upfield shift. This effect would be more pronounced for ethyl than for methyl, since the terminal methyl group of the ethyl causes the two remaining methylene protons to be closer to a nitro group, on the average, than the three equivalent protons of the methyl compounds. Whether this proximity effect is caused by the anisotropy of the nitro group or by its bulkiness remains an open question. At any rate, the fact that the difference between methyl and ethyl is a function of the substitution pattern makes an explanation based purely upon inductive effects rather untenable. Steric effects have also been demonstrated to be important in this system by Heidberg and co-workers.²

Table 2. NMR data for N-ethylanilines.

Substituents	δ -CH ₂ - ^a	δ -CH ₃ - ^a	J -CH ₂ CH ₃ ^b	J -NHCH ₂ - ^b
Unsubstituted	3.08	1.20	7.1	— ^c
2-Nitro	3.25	1.28	7.3	5.1
4-Nitro	3.20	1.28	7.3	5.4
2,4-Dinitro	3.45	1.38	7.3	5.5
2,6-Dinitro	3.01	1.28	7.0	4.9
2,4,6-Trinitro	3.18	1.39	7.0	5.0

^a In ppm downfield from TMS. Values good to ± 0.02 ppm.

^b In Hz. Values good to ± 0.2 Hz.

^c No splitting observed.

The chemical shifts of the terminal methyl groups in the N-ethyl series (Table 2) seem to deserve less comment. In general, an increasing number of nitro groups causes a downfield shift.

So far, the findings in the present paper strongly support the explanation for the upfield shift upon introduction of two *ortho* nitro groups in the ethylenediamine series given in Ref. 1.

Chemical shifts of the amino protons. The values given in Table 1 for the position of the amine proton in the N-methyl compounds have been determined by spin decoupling, except for the unsubstituted compound. First, as is apparent from Fig. 2, the uncertainty in determining the center of the amine band is of the order of ± 10 Hz or ± 0.2 ppm. This is not surprising, however, since the amine peaks themselves are quite broad, as was pointed out previously.

Another point to consider is the Bloch-Siegert effect,⁵ which causes the difference frequency as observed by spin decoupling to be smaller than the real difference. Its size in field-sweep experiments (the method used in this work) has been deduced by Anderson and Freeman⁶ and is given by the expression $(\gamma H_2)^2/2(\omega_A - \omega_X)$. In this expression, γ is the magnetogyric ratio for protons, H_2 the decoupling field strength and $\omega_A - \omega_X$ the difference in real resonance frequencies of the protons involved. In the present case, the correction turns out to be almost insignificant (less than 0.01 δ units.) Indeed, in one case, N-methyl-4-nitroaniline, spin decoupling gave $\delta_{\text{NH}} = -5.40$, whereas in the non-decoupled NMR spectrum, a broad hump was observed at $\delta = -5.35$, in good agreement with the first value.

The chemical shifts of the amine protons were found to be largely independent of the concentration. The temperature dependence was not investigated.

The actual values of chemical shift may depend on a number of factors and will be discussed in a forthcoming paper.

In the N-ethylaniline series, no corresponding experiments could be successfully performed because of the electronic limitations of the equipment. At the sample concentrations that could be obtained, the noise level was prohibitively high.

Coupling constants. The coupling constants for $-\text{NHCH}_3$ (Table 1) and $-\text{NHCH}_2-$ (Table 2) are all of the same magnitude, about 5 Hz. The small variations observed are certainly outside the experimental error, but no attempt will be made here to rationalize them. It is very satisfying that the values found for the N-methyl compounds agree with those obtained in dichloromethane solution by Heidberg and co-workers² for 2,4-dinitro-, 2,6-dinitro-, and 2,4,6-trinitrosubstitution. The remaining compounds in this work were not studied by Heidberg and co-workers.

Finally, the coupling constants within the N-ethyl groups (Table 2) are of the usual size, about 7 Hz.

EXPERIMENTAL

Melting points have been determined on a Kofler micro hot stage.

N-Methylaniline and *N-ethylaniline* were good commercial samples, redistilled *in vacuo* before use.

N-Methyl-2-nitroaniline * was prepared from 2-nitroanisole and methylamine by heating in methanol solution in a sealed tube at 120° for 6 h. Yield after recryst. from dilute methanol 60 %, m.p. found 34–34.5°, lit. 35°.

N-Methyl-4-nitroaniline * was prepared from 4-nitrofluorobenzene and excess methylamine in methanol-water solution (2:1 by vol.) by keeping at room temperature for 24 h. Yield after recryst. from ethanol 40 %, m.p. found 152°, lit. 151.6–151.9°.

N-Methyl-2,4-dinitroaniline * was prepared from 2,4-dinitrochlorobenzene and excess methylamine in ethanol-water solution (1:1 by vol.) in an instantaneous reaction. Yield after recryst. from glacial acetic acid 93 %, m.p. found 179°, lit. 178°.

N-Methyl-2,6-dinitroaniline * was prepared from 2,6-dinitrochlorobenzene and excess methylamine in ethanol-water solution (1:1 by vol.) by boiling under reflux for 5 min. Yield after recryst. from ethanol 89 %, m.p. found 108°, lit. 106°.

N-Methyl-2,4,6-trinitroaniline * was prepared from 2,4,6-trinitroanisole and excess methylamine in methanol solution in an instantaneous reaction. Yield after recryst. from ethanol-benzene solution (1:1 by vol.) 85 %, m.p. found 116°, lit. 115°.

N-Ethyl-2-nitroaniline * was prepared from 2-nitrochlorobenzene and excess ethylamine in methanol solution by boiling under reflux for 72 h. Isolation of the product was effected by evaporation of the methanol *in vacuo* and extraction with ether. The ether solution was washed with water and dried with Drierite, and the ether was removed *in vacuo*. The product is a liquid at room temperature but solidifies completely when placed in a deep-freeze at –15°. Yield 90 %. According to the literature, the melting point of the compound is below room temperature.

N-Ethyl-4-nitroaniline * was prepared from 4-nitrofluorobenzene and excess ethylamine in methanol solution by boiling under reflux for 2 h. Yield after two recrystallizations from ethanol 70 %, m.p. found 95–96°, lit. 96°.

N-Ethyl-2,4-dinitroaniline * was prepared from 2,4-dinitrochlorobenzene and excess ethylamine in methanol solution by refluxing for 10 min. Yield after recryst. from ethanol 90 %, m.p. found 115°, lit. 113–114°.

N-Ethyl-2,6-dinitroaniline was prepared from 2,6-dinitrochlorobenzene and excess ethylamine in ethanol solution by boiling under reflux for 10 min. Yield after two recrystallizations from ethanol 76 %, m.p. found 88°, lit. 85–86°.

N-Ethyl-2,4,6-trinitroaniline * was prepared from 2,4,6-trinitroanisole and excess ethylamine in methanol solution in an instantaneous reaction. Yield after recryst. from methanol 45 %, m.p. found 84–84.5°, lit. 84°.

NMR experiments. The spectra were recorded on a Varian A-60 spectrometer equipped with a Varian Model V-6058 spin decoupler. The temperature of the probe was $38 \pm 1^\circ\text{C}$. Of each sample, two different solutions in nitrobenzene, usually 10 and 5 % by weight, were run. The solvent also contained 0.75 % by weight tetramethylsilane as internal standard. In no case was a significant concentration dependence of the chemical shifts observed.

Coupling constants were determined by superimposing suitable audio sidebands from a generator similar to the Hewlett-Packard Model 200 CD, the frequency of which was accurately measured with a Hewlett-Packard Model 5233 L digital frequency counter. Interpolation could then be made on the chart paper.

The author wishes to thank Prof. Lars Melander and Dr. Robert E. Carter for valuable criticism. Fil.kand. Kjell Nordfält has assisted in preparing some of the compounds, and ing. Reine Torberntsson in recording NMR spectra.

Financial aid from the *Swedish Natural Science Research Council* is gratefully acknowledged.

* Compounds marked with an asterisk are described in Beilstein's *Handbuch der Org. Chemie*, from which the melting points have been obtained.

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Received September 4, 1965.