

## NUCLEAR OVERHAUSER EFFECT AND $^1\text{H-NMR}$ SPECTRUM OF 1,2-DIMETHOXY-4-HYDROXY-5-NITROBENZENE\*

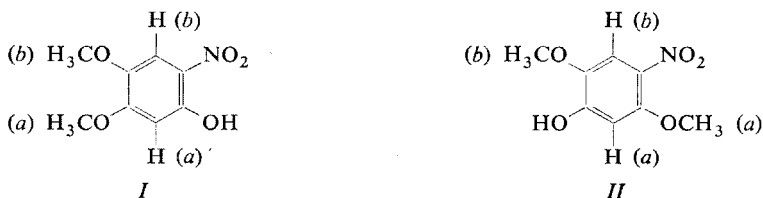
J. DĚDINA and J. SCHRAML

*Institute of Chemical Process Fundamentals,  
Czechoslovak Academy of Sciences, 165 02 Prague 6*

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$^1\text{H-NMR}$  spectrum lines are assigned and 1,2-dimethoxy-4-hydroxy-5-nitrobenzene identified through the combined use of Nuclear Overhauser Effect (NOE), intramolecular hydrogen bond shift, and application of direct additivity rules to the shifts of aromatic protons. The results allow to differentiate the above compound from its isomer (1,4-dimethoxy-2-hydroxy-5-nitrobenzene) by NMR even in cases when small amounts of compounds are available and only  $\text{CH}_3$  lines are visible in the spectrum. NOE data on 1,2-dimethoxy-4-hydroxy-5-nitrobenzene and guaiaicol are presented.

In connection with the study of nitrophenols<sup>1-3</sup> a problem of NMR differentiation and identification of isomers *I* and *II* has arisen. The two compounds are, in some reactions, produced in their mixtures, other reactions which were found to yield only one of the isomers are accompanied by rearrangements so that the other than the expected isomer can be (and in fact is<sup>3</sup>) formed.



Since the direct additivity rules are well applicable to the chemical shifts of aromatic protons in polysubstituted benzenes<sup>4</sup> it is clear from the comparison of formulas *I* and *II* that  $^1\text{H-NMR}$  spectra of the isomers could differ only in the chemical shifts of  $\text{OH}$  and  $\text{OCH}_3$  protons. Indeed, of the two sample compounds (samples *A* and *B*) we obtained<sup>3</sup>, the spectrum of the sample *A* showed two  $\text{CH}_3\text{O}$  proton lines (at  $\delta = 3.88$  and  $\delta = 3.95$ ) while that of *B* consisted of only one such line

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( $\delta = 3.92$ ). Because of limited quantity of the sample *B* available, proton of hydroxy group could not be detected in its spectrum. In the solution of the sample *A* hydroxyl proton appeared at  $\delta = 11.02$ , aromatic protons gave two single lines at  $\delta = 7.45$  and  $\delta = 6.52$ .

With the present knowledge of the trends in  $\text{CH}_3\text{O}$  proton chemical shifts it is not possible to identify the samples *A* and *B* with their corresponding structures *I* or *II* on the basis of the difference in these shifts.

The chemical shift of the OH proton is well out of the range (around  $\delta = 4.5$ ) in which the lines of substituted phenols occur<sup>5</sup>. Other cases of appreciably less shielded OH proton were noted in molecules in which strong intramolecular hydrogen bonding was expected<sup>5</sup>. *ortho*-Nitrophenol is a classical example of a compound with such a bonding. Chemical shift of OH proton in *ortho*-nitrophenol is  $\delta = 10.6$ , so it is very similar to that of sample *A* (under the identical conditions). *Ortho* arrangement of nitro and hydroxy groups is the essential feature of the structure *I*. Under the same conditions the chemical shift of OH proton in guaiacol (*o*-methoxyphenol), which would be a model compound for the structure *II*, is  $\delta = 5.4$ . It follows from these comparisons that the sample *A* has structure *I*.

With the structure determined, the remaining problem is to assign the other lines in the spectrum. It should be emphasized, however, that the following assignments would remain valid had the sample structure *II*. The chemical shifts of aromatic protons H(*a*) and H(*b*) can be calculated on the basis of direct additivity rule which holds for polysubstituted benzenes<sup>4</sup>. Using the published values of shielding contributions<sup>4</sup> of the groups present in *I* the following chemical shifts were calculated: H(*a*)  $\delta = 6.46$  and H(*b*)  $\delta = 7.57$  (with benzene at  $\delta = 7.27$ ). It is therefore beyond

TABLE I  
Nuclear Overhauser Effects in 1,2-Dimethoxy-4-hydroxy-5-nitrobenzene<sup>a</sup>

NMR line <sup>b</sup> irradiated	Observed		
	H( <i>b</i> ) (7.45)	H( <i>a</i> ) (6.52)	OH (11.02)
$\text{CH}_3^c$ (3.95)	$3.5 \pm 4.2$	$21.4 \pm 4.4$	$0.4 \pm 2.8^d$
$\text{CH}_3^c$ (3.88)	$22.7 \pm 3.9$	$1.1 \pm 4.1$	$1.2 \pm 3.4^d$
OH (11.02)	$1.9 \pm 3.8$	$0.2 \pm 3.0$	—

<sup>a</sup> NOE values are given as percentage of enhancement of the integrated intensity of the observed line when the irradiated line is being saturated, errors indicate 95% confidence limits for *t*-distribution. <sup>b</sup> Lines are denoted by their assignment and by their position in the spectrum ( $\delta$  in parenthesis). <sup>c</sup> In order to avoid saturation of the other  $\text{CH}_3$  line the amplitude of saturating field ( $H_2$ ) was 0.6 Hz. <sup>d</sup> Determined from the line heights.

any doubts that of the two lines of aromatic protons that at lower field ( $\delta = 7.45$ ) corresponds to the proton H(b) while that at higher field ( $\delta = 6.52$ ) to H(a) proton. The two CH<sub>3</sub>O lines can be assigned through nuclear Overhauser effect (NOE) measurements.

The results of such measurements of sample *A* are summarized in Table I. The values of  $F_{H(a)}^{CH_3}$  (3.95) and  $F_{H(b)}^{CH_3}$  (3.88)\* clearly indicate (for the necessary theoretical background of NOE applications see ref.<sup>6</sup>) that the line at  $\delta = 3.95$  corresponds to methyl protons which are sterically close to H(a) ring proton (and remote to H(b) proton) and that at  $\delta = 3.88$  corresponds to CH<sub>3</sub>(b) methyl protons which are close to H(b) ring proton.

Large relative error prohibits to quote the NOE measurements on OH proton line as supporting evidence for the proposed structure of the sample. In compound *I* both NOEs observed on OH line ( $F_{OH}^{CH_3(a)}$  and  $F_{OH}^{CH_3(b)}$ ) should be zero, but in compound *II* only  $F_{OH}^{CH_3(a)}$  would be zero while  $F_{OH}^{CH_3(b)}$  would be similar as it is in guaiacol. According to our measurements in guaiacol  $F_{OH}^{CH_3} = 4.9 \pm 2.4$  (and  $F_{H(arom)}^{CH_3} = 6.2 \pm 1.4$ ).

The values measured in sample *A* are neither significantly different from zero nor from guaiacol's value. For the same reason, the experimental ratio of  $F_{H(a)}^{OH}/F_{H(a)}^{CH_3}$  which is  $0.01 \pm 0.15$  cannot be used for determination of the sterical position of the hydrogen atom of the hydroxyl group. The value is, however, close to the value of this ratio (0.00) calculated<sup>7</sup> for OH proton situated in the ring plane with O—H bond directed towards nitrogroup. (For the other position in which the proton is also in the ring plane but the O—H bond is pointing to H(a) hydrogen atom the theoretical ratio is  $0.2^7$ .)

## EXPERIMENTAL

The measurements of <sup>1</sup>H-NMR spectra and NOE were performed on a modified Tesla BS 477 spectrometer operating at 60 MHz. Through the measurements internal lock employing the line of hexamethyldisilane was used. Unless otherwise noted NOE values were determined from at least ten independent measurements of integrated intensities (by electronic built-in integrator).

The samples were degassed by bubbling gaseous nitrogen through the solutions before measurements. The measured samples were 0.3M solutions of the studied compounds in 0.1M solutions of hexamethyldisilane in CDCl<sub>3</sub> (Merck, Uvasol quality, isotopic purity 99%). Hexamethyldisilane, prepared in this laboratory, was used instead of tetramethylsilane since the higher boiling point of the former ensures better reproducibility of sample preparation. Guaiacol (Koch & Light) and *o*-nitrophenol (Lachema, Brno) were used as supplied without any further purification.

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\* The symbol  $F_B^A$  stands for the value of NOE observed on the line *B* when line *A* is saturated.

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