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A NITROGEN-14 NMR STUDY OF SOME OXIMES AND THEIR ISOMERIC STRUCTURES

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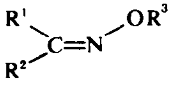
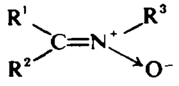
Abstract—The isomeric structures of oximes, nitrones and nitroso compounds may be readily differentiated on the basis of their nitrogen chemical shifts. The tautomeric equilibria present in oxime–nitroso systems are easily observed by means of ^{14}N NMR spectroscopy. An explanation of the range of chemical shifts found within the oxime and nitrone groups of compounds is presented, based upon the average excitation energy approximation to the paramagnetic term in the nuclear screening tensor. The increase in screening of the nitrogen found upon protonation of an oxime is analogous to that observed for pyridine-type structures and their N-oxides.

INTRODUCTION

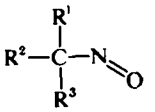
Oximes, nitrones, and nitroso compounds have mutually isomeric structures.



oxime

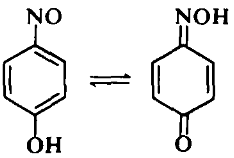


nitrone



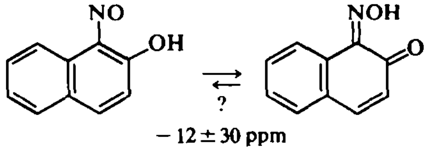
nitroso compounds

In some instances, the oxime and nitroso groups are involved in tautomeric equilibria such as that between *p*-nitrosophenol and *p*-benzoquinone mono-oxime.



It should be interesting to investigate the possibility of spectral distinction between such isomers by means of nitrogen chemical shifts. This may provide an effective method of analysis of oxime–nitroso tautomeric systems.

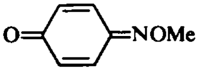
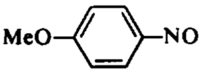
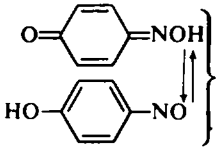
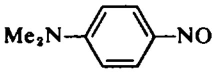
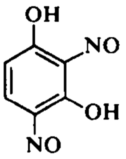
The nitroso group has been examined to some extent by both ^{14}N and ^{15}N NMR spectra.[1-3] Its nitrogen resonance is known to occur at extremely low magnetic fields as compared with other organic compounds of nitrogen. The available data are not very accurate for most of the nitroso compounds investigated but an approximate range of 400 to 500 ppm downfield from nitromethane or the NO_3^- ion may be expected. So far, there has been no reported information on the nitrogen chemical shifts of nitrones and practically no significant measurements for oximes. The only reported[1] value of 80 ± 60 ppm upfield from NO_3^- for 2-butanone oxime (60% confidence limits which approximately correspond to ±150 ppm for the 95% confidence limits used in the present work) is too inaccurate to be useful. The ^{14}N chemical shift[1] of 12 ± 30 ppm downfield from NO_3^- observed for the potentially tautomeric system of 1-nitroso-2-naphthol and 1,2-naphthaquinone-1-oxime suggests that the latter should largely prevail in the equilibrium but the lack of reliable data for the oxime group makes the conclusion rather tentative.



RESULTS AND DISCUSSION

We have investigated the ^{14}N NMR spectra of a number of molecules in order to obtain reliable estimates of the nitrogen chemical shifts for each of the isomeric groups of compounds (Table 1). For potentially tautomeric systems, model compounds have also been prepared which are not capable of tautomeric changes due to the methylation of the corresponding NOH and OH groups.

Table 1. Nitrogen-14 nuclear magnetic resonance of some oximes, nitrones, and nitroso compounds

No.	Compound	Solvent/concentration	^{14}N Chemical shift[a] p.p.m. (screening-constant scale referred to internal $MeNO_2$)	Resonance half-height width[a] Hz
1	$Me_2C{=}NOH$	Et_2O/satd.	$+48 \pm 4$	1000 ± 100
2	$Me_2C{=}NOMe$	neat; Et_2O/3M	$+8 \pm 1$	325 ± 15
3	$(Me_2C{=}NHOH)^+Cl^-$	conc. HCl/satd.	$+109 \pm 7$	1540 ± 110
4	$MeCH{=}NOH$	Et_2O/satd.	$+27 \pm 2$	800 ± 100
5	$MeCH{=}NOMe$	Et_2O/1M	-4 ± 7	420 ± 40
6	$H_2C{=}NOH$	Et_2O/1M	-2 ± 5	520 ± 80
7		Et_2O/3M	$+1 \pm 6$	355 ± 45
8		Et_2O/3M	-432 ± 10	850 ± 200
9		acetone/satd.	-52 ± 13	1140 ± 160
10		acetone/satd.	-404 ± 50[b]	?
11	PhNO	Et_2O/satd. acetone/satd.	-540 ± 3 -530 ± 4	348 ± 26 750 ± 40
12		acetone/satd.	-515 ± 10	800 ± 100
13	$PhCH{=}N(O)Me$	acetone/satd.	$+103 \pm 1$	76 ± 5
14	$PhCH{=}N(O)Bu$-t	acetone/satd.	$+74 \pm 1$	90 ± 5
15	$PhCH{=}N(O)Ph$	acetone/satd.	$+94 \pm 1$	100 ± 5
16	$PhCMe{=}N(O)Me$	acetone/satd.	$+108 \pm 1$	90 ± 5
17	Pyridine N-oxide	H_2O/3M	$+101 \pm 1$	190 ± 10
18	Pyridine N-oxide hydrochloride (N-Hydroxypyridinium ion)	conc. HCl/satd.	$+133 \pm 5$	570 ± 30

[a] Within 95% confidence limits; high-field shifts are positive on the screening-constant scale.

[b] Data from Ref 1, originally reported within 60% confidence limits, recalculated here to 95%.

The effect of O-methylation on the ^{14}N shift has been also estimated for simple oximes.

From the results shown in Table 1 the characteristic range of nitrogen chemical shifts for the oxime group, $=NOH$, may be established at about 0 to 50 ppm upfield from nitromethane (or NO_3^-). There is, however, a remarkable difference in the shifts between an oxime and its alkyl ether:

$Me_2C{=}NOH$	$Me_2C{=}NOMe$
+48 ppm	+8 ppm

The high-field displacement of the nitrogen resonance signal for the former is probably due to strong H-bonding. Apart from this, the upfield shift with increasing alkyl-substitution at the carbon atom of the oxime group

$H_2C{=}NOH$	$MeCH{=}NOH$	$Me_2C{=}NOH$
−2 ppm	+27 ppm	+48 ppm

seems to be in agreement with the observed trend in nitriles[4] where the decreasing electronegativity of group R in R—CN results in an increased magnetic screening of the nitrogen nuclei. An explanation of this may be found in a relatively simple theory of chemical shifts[4–7] involving the average excitation energy approximation since the expected decrease in the CN mobile bond order and the increased electron density at the nitrogen atom should lead in both of these cases to an increase in the diamagnetic term in the expression for the screening constant as well as to a decrease in the absolute value of the paramagnetic term. Thus, the two contributions should act in the same direction to increase the nuclear screening of nitrogen with decreasing electronegativity of the substituents at the carbon atom.

The protonation of the oxime group may occur, at least theoretically, at either the nitrogen or the oxygen atom.

$$\mathrm{Me_2C{=}NOH} \xrightarrow{H^+} \mathrm{Me_2C{=}N^+HOH}$$

$$\text{or } \mathrm{Me_2C{=}NO^+H_2}$$

In either case one should expect an upfield shift of the nitrogen resonance signal as suggested by the data for pyridine-type heterocycles and the corresponding pyridinium ions[1,5–7] or pyridine N-oxide and the corresponding N-hydroxypyridinium cation (Table 1). Such a shift is actually observed (Table 1) for acetoxime hydrochloride in aqueous HCl.

Nitrones are characterised by a range of nitrogen chemical shifts of 70 to 100 ppm upfield from nitromethane (Table 1) which is clearly different from those for the other isomeric structures. If the hydrogen atom in PhCH=N(O)R is replaced by a methyl group then an upfield shift is observed in the nitrogen NMR spectrum. This is analogous to the shifts in oximes and nitriles. An opposite effect on the shift is found when a t-Bu group replaces the methyl group in PhCH=N(O)Me. This is in agreement with the direction of the shifts observed in many classes of organic compounds including nitro derivatives, isonitriles, isocyanates, azides, pyridinium ions and other structures where the substituent is bonded directly to the nitrogen atom and the nitrogen atom constitutes a part of a system of multiple bonds. Thus, oximes and nitrones provide support for the general[4–7] conclusion that the decreasing electronegativity of substituent R results in increased nitrogen shielding for systems

R—C(multiple bond)N

whilst a deshielding is predicted for

R—N(multiple bond).

These empirical rules, apart from their practical merits, are also interesting from a theoretical point of view since they may be explained[4–7] in terms of mobile bond orders and charge densities with the assumption of no significant variation in the average excitation energy and the orbital expansion term.

The range of the nitrogen chemical shifts of the nitroso group is so remote from those for the other two isomeric structures that it is fairly easy to get reliable estimates of the tautomeric equilibrium constants for oxime–nitroso systems even if the measurements of individual shifts are not very accurate.

For the equilibrium between *p*-nitrosophenol and *p*-benzoquinone mono-oxime in a saturated acetone solution the shifts of the corresponding O-methyl derivatives may be used as the estimates of the shifts of the actual components, provided that the difference of 40 ppm in the screening constant between acetoxime and its methyl ether is algebraically added to the shift of *p*-benzoquinone mono-oxime methyl ether. Then, the molar fraction of *p*-nitrosophenol in the solute, X,

$$\underset{(\mathrm{X})}{p\text{-nitrosophenol}} \rightleftharpoons \underset{(1-\mathrm{X})}{p\text{-benzoquinone mono-oxime}}$$

may be expressed as

$$\mathrm{X} = \frac{\sigma(\text{experimental}) - \sigma(\text{oxime})}{\sigma(\text{nitroso}) - \sigma(\text{oxime})}$$

where $\sigma(\text{experimental}) = -52$ ppm, $\sigma(\text{nitroso}) = -432$ ppm, and $\sigma(\text{oxime}) = +1+48-8 = +41$ ppm. If the individual errors are considered (Table 1) then a value of

$$\mathrm{X} = 0{\cdot}20 \pm 0{\cdot}04$$

is obtained within the 95% confidence range. If the same reference values are used for the system

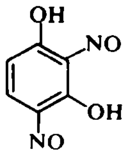
$$\underset{(\mathrm{X})}{\text{1-nitroso-2-naphthol}} \rightleftharpoons \underset{(1-\mathrm{X})}{\text{1,2-naphthoquinone-1-oxime}}$$

together with the experimental[1] value of −12 ppm, then

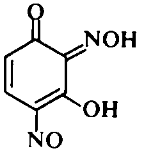
$$\mathrm{X} = 0{\cdot}14 \pm 0{\cdot}12$$

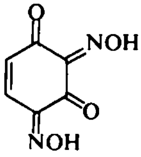
on the same significance level. The larger error reflects the uncertainty of the reported shift.

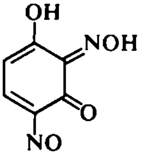
The shift of −515 ppm for 2,4-dinitrosoresorcino (Table 1) suggests that the substance in a saturated acetone solution exists mainly as such

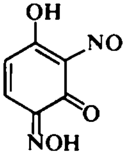


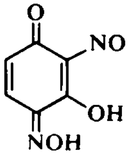
and that the other tautomeric forms











should not constitute more than 5 mole % of the solute, even if we assume the largest downfield shift observed for the NO group, that of −540 ppm for nitrosobenzene (Table 1), as an estimate of the shift for the nitroso groups in the system. It should be noted here that the value of the ^{14}N chemical shift for nitrosobenzene in a saturated solution in ether as well as the half-height width of the resonance signal are considerably different from those reported in the literature.[3]

CONCLUSIONS

It is evident from the discussion that the three isomeric structures may be easily distinguished on the basis of their nitrogen chemical shifts which have approximate ranges of

0 to +50 ppm for oximes,
+70 to 110 ppm for nitrones,
−400 to −550 ppm for nitroso compounds

referred to nitromethane or NO_3^- on the screening-constant scale. Since the difference in the shifts between the oxime and nitroso groups is about 450 ppm, the accuracy of the estimation of a tautomeric equilibrium constant does not depend critically on the precision of the spectral measurements. An uncertainty as large as 10 ppm for each of the three shifts in the expression for the molar fraction of the solute, in either tautomeric form, results in an uncertainty of about 0·04 for the fraction. The uncertainties may include not only random errors but also systematic ones, those resulting from solvent and concentration effects, calibration techniques, and the use of model compounds in the estimation of some shifts.

EXPERIMENTAL

The substances investigated were either commercially available products purified by conventional methods or were prepared according to published procedures (**2**,[8] **5**,[9] **6**,[10] **7**,[11] **8**,[12] **13**,[13] **14**,[14] **15**,[15] **16**[16]). The ^{14}N NMR spectra were recorded with a Varian HA-60 spectrometer operating at 4·33 MHz in the HR mode at room (30°C) temp. The experimental details were the same as reported elsewhere.[17] About 10–20 measurements were carried out for each substance and the results given in Table 1 are the mean values with the calculated 95% confidence limits according to the Student distribution rather than the normal distribution in order to account for the statistically low number of measurements. For broad signals, a line-shape fitting procedure was employed as before,[17] and the values of the chemical shifts and signal widths were used in the calculation of the mean, weighted by factors proportional to the standard errors of the individual mean values from each fitting procedure. The curve fitting and statistical processing of the data were performed with an ODRA-1204 computer. A rather high significance level (95%) was assumed in the calculations. For the commonly used 60% confidence range the limits would be narrower by at least a factor of two for the number of measurements involved.

The convention was adopted here which assigns the plus sign to upfield shifts of the resonance. It is theoretically sound since chemical shifts in ppm are then simply changes in the nuclear screening constant.

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