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^{14}N NMR STUDY OF SOME SYDNONES, SYDNONIMINES AND RELATED STRUCTURES

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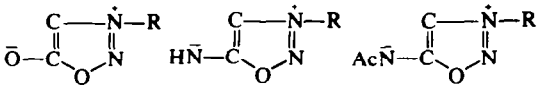
Abstract—^{14}N NMR spectra indicate that the sydnones, their hydrochlorides, the N-acetylsydnonimines, their hydrochlorides and the sydnonimine hydrochlorides studied exist as such in solution. The sydnonimines themselves are involved in a more complicated equilibrium; neutral solutions contain only the corresponding isomeric alkyl-cyanomethyl-nitrosoamine molecules which upon acidification are turned into cyclic cations, representing true sydnonimine structure, protonated at the exocyclic N atom.

Sydnones and sydnonimines are thought of as betaine type ring structures which are formally derived from 5-alkoxy (or aryloxy)- and 5-alkylamino (or arylamino)-1,2,3-oxadiazoles as internal salts.

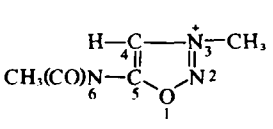


sydnone sydnonimine N-acetylsydnonimine

However there have been controversial spectroscopic[1,2] and theoretical[3-6] data concerning their actual structure. It seems probable that nitrogen NMR will be useful in the structural determination of such molecules since a great deal of ^{14}N experimental data have already been accumulated on heterocyclic structures.[7]

RESULTS AND DISCUSSION

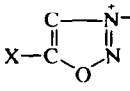
In order to determine the approximate ranges of nitrogen NMR signals in sydnonimine structures, the ^{14}N NMR spectrum of 3-methyl-N-acetylsydnonimine was measured (in acetone 1:3 V/V) together with those for the same molecule labelled with ^{15}N at N-3 (synthesis from $CH_3{}^{15}NH_2{\cdot}HCl$), N-2 (from $Na^{15}NO_2$), and N-6 (from $KC^{15}N$); respectively. This has led to an unambiguous assignment of the three signals which appear in the ^{14}N spectra of the unlabelled compound.



nitrogen	chemical shift from external nitromethane (ppm)	^{14}N signal half-height width (Hz)
N-2	+27 ± 5	450 ± 50
N-3	+109 ± 1	46 ± 4
N-6	+205 ± 8	500 ± 50

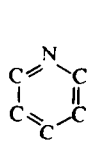
The assignment is based on the assumption that the structure is actually as shown above, which is demonstrated to be correct in the following argument.

The ^{14}N NMR spectra (Table 1) of the sydnones, their hydrochlorides, the N-acetylsydnonimines, their hydrochlorides and the sydnonimine hydrochlorides show sharp signals in the range +78 – +108 ppm.

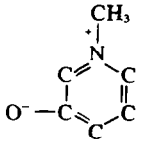


X = O⁻, OH, (NAc)⁻, NHAc, NH₂
R = Me, Et, i-Pr, n-Pr, Ph etc.

These shifts indicate that they represent the "cationic" N atoms in the betaine type structures, as deduced from the following comparison

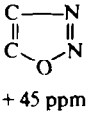


+63 ± 2 ppm[7]

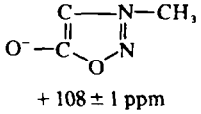


+179 ± 1 ppm[8]

and



+45 ppm



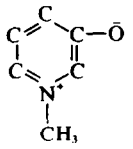
+108 ± 1 ppm

The chemical shift of N-3 in 1,2,3-oxadiazole was calculated from the shift for 1,3-oxazole[7] and additivity rules for azoles.[9]

The so called β-effect, observed as a downfield shift in the series where R = Me, Et, i-Pr, t-Bu, indicates that the signal corresponds to the N-3 nitrogen atom. This is a general rule for N atoms which are directly bonded to alkyl groups.[7]

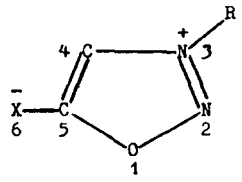
The relatively long quadrupolar relaxation times and the resulting rather narrow ^{14}N signals are also typical for N atoms which bear a formal positive charge, as is observed in nitroalkanes, azine N-oxides, azinium ions, isonitriles, etc.[7]

The proton resonance spectra provide additional support for the cyclic structure. In the region of chemical shifts characteristic of aromatic structures, particularly that of N-methyl-3-oxypyridyl-betaine, there is always a



singlet and the presence of the $\overset{+}{N}{-}CH_3$ moiety is also evident from the three-proton signals with chemical

Table 1. Chemical shifts of N-3 nitrogen atoms in sydnones, sydnonimines and related structures



No.	Compound (R =)	Nitrogen chemical shift[a] in ppm (±1)	Signal half-height width in Hz
	Sydnones (X = O)		
1	Me-	+108[b]	24±2[b]
2	Et-	+97[b]	29±2[b]
		+96[e]	106±4[e]
3	i-Pr-	+84[b]	35±2[b]
4	Pr-	+98[b]	44±2[b]
		+97[e]	122±4[e]
5	Bu-	+98[b]	47±2[b]
		+101[d]	58±2[d]
6	i-Bu-	+99[b]	38±2[b]
		+97[e]	195±5[e]
7	s-Bu-	+87[b]	36±2[b]
		+86[e]	125±5[e]
8	t-Bu-	+79[c]	28±3[c]
9	cyclohexyl-	+86[b]	43±2[b]
10	Ph-CH_2-	+96[b]	50±3[b]
11	Ph-	+98[c]	28±2[c]
		+94[f]	43±2[f]
12	p-Cl-C_6H_4-	+100[c]	46±3[c]
13	p-Br-C_6H_4-	+100[c]	39±2[c]
14	p-NO_2-C_6H_4-	+102[c]	36±3[c]
15	3-pyridyl-	+103[c]	36±2[c]
16	Ph- ; Br- at C-4	+100[c]	92±4[c]
17	Ph- ; NO_2- at C-4	+101[b]	80±4[b]
	Acetylsydnonimines (X = N-$COCH_3$)		
18	Me-	+27±5 (N-2)[c]	450±50[c]
		+109[c]	46±4[c]
		+205±8 (N-6)[c]	500±50[c]
19	Et-	+97[b]	65±3[b]
		+97±2[g]	340±30[g]
20	i-Pr-	+86[c]	75±3[c]
21	Pr-	+98[b]	75±3[b]
22	Bu-	+98[c]	65±3[c]
23	Ph-	+97±2[b]	240±20[b]

Table 1. (*Contd.*)

No.	Compound (R =)	Nitrogen chemical shift[a] in ppm (±1)	Signal half-height width in Hz
	Sydnone hydrochlorides (X = O ; + HCl)		
24	Me–	+94±5[h]	270±30[h]
25	Et–	+88±5[h]	290±30[h]
26	i-Pr–	+83±5[h]	300±30[h]
	Sydnonimine hydrochlorides (X = NH ; + HCl)		
27	Me–	+106±2[g]	150±15[g]
28	Et–	+95±3[g]	190±20[g]
29	i-Pr–	+87±4[g]	230±20[g]
30	Ph-CH_2–	+94±2[g]	250±20[g]
31	Ph–	+96±4[g]	260±30[g]
	Acetylsydnonimine hydrochlorides (X = N-$COCH_3$; + HCl)		
32	Me–	+104±5[g]	250±20[g]
33	Et–	+92±3[g]	300±20[g]
34	i-Pr–	+84±4[g]	380±40[g]

a – all shifts are referred to external neat nitromethane; positive values correspond to upfield shifts; b – in acetone 1:3 v/v; c – in acetone 1:7 v/v; d – in ether 1:3 v/v; e – neat; f – in chloroform 1:7 v/v; g – in methanol 1:3 v/v; h – in methanol 1:7 v/v

shifts very close to value (4.2 ppm downfield from TMS) observed for the oxypyridylbetaine.[8]

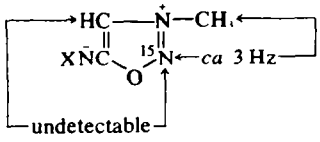
Thus, the NMR data show that the molecular structure in solution is as indicated above for the sydnones, their hydrochlorides, the N(6)-acetylsydnonimines, their hydrochlorides and the sydnonimine hydrochlorides.

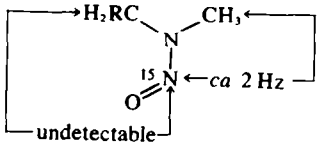
The proton spectra of the ^{15}N labelled compounds (in the position 2, 3 or 6) of 3-methyl-6-acetyl-sydnonimines, their hydrochlorides and 3-methyl-sydnonimine hydrochlorides indicate the following stereochemical correlations for the ^{15}N—^{1}H couplings (Table 2).

(i) The site of protonation in the latter case is identified by means of $^1J(^{15}N—^1H)$ spin–spin coupling. The hydrochloride of 3-methyl-6-^{15}N-sydnonimine does not show any measureable coupling in a CD_3OD solution, but in CF_3COOH a two-proton doublet was observed, spaced at $^1J(^{15}N—^1H) = 96.8$ Hz. Thus, the cation contains an exocyclic NH_2 group and this corresponds to protonation at N-6 of the sydnonimine ring.

(ii) The $^2J(^{15}N—^1H)$ coupling constants for sydnonimine derivatives between the betaine-type ^{15}N and CH_3 protons lie in the region 2.1 – 2.5 Hz and the couplings with the aromatic proton is between 4.2 and 5.5 Hz. These coupling constants show that the two-bond coupling is stronger across a tricoordinate carbon atom as compared with that across the saturated C atom of the Me group.

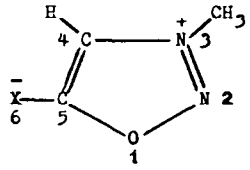
(iii) The $^3J(^{15}N—^1H)$ coupling constants for sydnonimine derivatives between the azine-type N atom and the Me protons has values between 2.6 and 3.1 Hz. The $^3J(^{15}N—^1H)$ interaction with the aromatic proton is undetectable. It is interesting to note that formally the same effects of geometry are found in some N-nitrosoamine derivatives.[10]





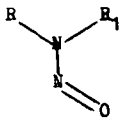
(iv) The $^3J(^{15}N—^1H)$ coupling constants for N-(6)-acetylsydnonimine derivatives between the amide-type N atom and the acetyl protons lie in the range 1.4 – 1.9 Hz, but the coupling to the aromatic proton is undetectable.

Table 2. ^{15}N–^{1}H Spin–spin coupling constants in ^{15}N labelled sydnonimine structures



^{15}N label sites	Compound (X =)	Solvent	$J(^{15}N-^{1}H)$ in Hz (± 0.1)	
^{15}N-3			^{2}J(N–CH_3)	^{2}J(N–H–aromatic)
	$NCOCH_3$	$CDCl_3$	2.1	5.5
	$NCOCH_3$ + HCl	CD_3OD	2.4	4.6
		CF_3COOH	2.3	4.8
	NH + HCl	CD_3OD	2.3	4.2
		CF_3COOH	2.5	4.3
^{15}N-2			^{3}J(N–CH_3)	^{3}J(N–H–aromatic)
	$NCOCH_3$	$CDCl_3$	2.6	ca. 0
	$NCOCH_3$ + HCl	CD_3OD	3.1	ca. 0
		CF_3COOH	3.0	ca. 0
	NH + HCl	CD_3OD	2.9	ca. 0
		CF_3COOH	2.9	ca. 0
^{15}N-6			^{3}J(N–H–Ac)	
	$NCOCH_3$	$CDCl_3$	1.9	ca. 0
	$NCOCH_3$ + HCl	CD_3OD	1.4	ca. 0
		CF_3COOH	1.6	ca. 0
			^{1}J(N–H)	
	NH + HCl	CD_3OD	undetectable	ca. 0
		CF_3COOH	96.8 ± 0.2	ca. 0

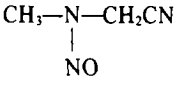
Table 3. Nitrogen chemical shifts of some nitrosoamines



Compound R	Compound R_1	Nitrogen chemical shift[a] in ppm (in acetone 1:3 V/V) –N=O	–N–	–CN	Signal half-height width in Hz –N=O	–N–	–CN
Me	Me	−157 ± 1	+149 ± 1	–	143 ± 15	72 ± 5	–
Et	Et	−161 ± 2	+123 ± 2	–	240 ± 20	104 ± 10	–
Me	CH_2CN	−165 ± 3	+151 ± 3	+125 ± 3	400 ± 40	270 ± 30	300 ± 30
Et	CH_2CN	−166 ± 3	broad overlapping signals centered at about +135		450 ± 50	–	–

a – all shifts are referred to external neat nitromethane; positive values correspond to upfield shifts

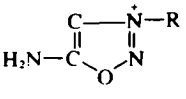
However, neutralization of the sydnonimine hydrochloride solutions with $NaHCO_3$ proceeds slowly (several hr) and gives not sydnonimines, but isomeric N-methyl-N-cyanomethyl-nitrosoamine, as is shown in this work. An unambiguous evaluation of the structure is provided by the ^{14}N NMR spectrum which contains three signals at −165 ppm, +125 ppm and +151 ppm (Table 3). Since there is a considerable signal overlap in the spectrum, the shifts were determined with the aid of ^{15}N labelled compounds where the ^{15}N was introduced as $KC^{15}N$ and $CH_3{}^{15}NH_2 \cdot HCl$, respectively. The nitrogen shifts show that the structure is



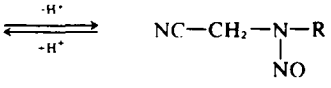
since the N-nitroso group appears at about −160 ppm and the amino group at about +140 ppm in the nitrogen NMR spectra (data for dimethyl- and diethyl-nitrosamine; Table 3) and the shifts are very characteristic of this structure, whilst the signal at +125 ppm is within the range typical of cyano groups.[7]

The proton resonance spectra of the product are quite consistent with the structure given above.[10]

The N-methyl-N-cyanomethyl-nitrosoamine may be readily converted to the sydnonimine hydrochloride upon acidification. Thus there is no indication of the existence of free sydnonimines apart from the possibility of their being instable intermediates, and the complete description of the process may be summarized as follows:



cation derived formally from sydnonimine by N-6 protonation



N-alkyl-N-cyanomethyl-nitrosoamine

The characteristics of nitrogen chemical shifts of the sydnone and sydnonimine structures may be deduced from the following considerations:

(i) N-2 appears at +20 − +40 ppm irrespective of the nature of R.

(ii) N-3 appears at +78 − +108 ppm and exhibits the β-effect upon increasing the size of the alkyl substituent at the C atom bonded directly to N-3.

(iii) The exocyclic N-6 in acetyl-sydnonimines appears at +200 − +230 ppm, close but somewhat below the shift range characteristic of amides.[7]

(iv) The exocyclic N-6 in sydnonimine hydrochlorides appears at +350 − +370 ppm, within the range characteristic of amines.[7]

EXPERIMENTAL

The compounds examined in this work were prepared according to published procedures: 1[11], 2[12], 3[13], 4[14], 5[15], 6[14], 7[14], 8[13], 9[16], 10[15], 11[17], 12[18], 13[18], 14[19], 15[20], 16[21], 17[22], 18[23], 19-according to[23], m.p. 110–112°, 20-according to[23], m.p. 105–107°, 21-according to[23], m.p. 113–114°, 22[23], 23[23], 24-from alcoholic HCl, m.p. 136–142°, 25-from alcoholic HCl, m.p. 146–152°, 26-from alcoholic HCl, m.p. 130–133°, 27[24], 28[14], 29[14], 30[25], 31[24], 32[24], 33-according to[24], m.p. 134–135° and 34-according to[24], m.p. 125–126°.

The identity of all substances was checked by means of their proton NMR spectra.

The ^{14}N NMR spectra were measured at 4.3346 MHz (14.09 kG) and modulated with an audio-frequency of 2002 Hz. The spectrometer used was a Varian HA-60IL model operating at temperature 30° in the field-sweep HR mode with 15 mm o.d. sample tubes without spinning. Nitromethane was employed as an external reference compound and the shifts are expressed on the screening-constant scale, i.e. high-field shifts are taken as positive.

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