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NMR STUDY OF SOME SYDNONES, ISOSYDNONES, AND ISOTHIOSYDNONES*

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Multinuclear ^{1}H, ^{13}C, ^{14}N, ^{15}N, and ^{17}O NMR data are presented for some sydnones, isosydnones and isothiosydnones. The type of valence tautomerism shown in (Fig. 1) is not observed for the compounds studied. At high pH compounds **2** *and* **12** *are found to undergo transformations. The more suitable NMR parameters are reported for establishing the structures of mesoionic compounds containing three heteroatoms in the five-membered conjugated ring. Some* ab initio *GIAO calculations on a model structure of sydnones and related compounds have been performed.*

Key words: Ab initio *calculations, charge distribution, mesoionic structures, multinuclear NMR, protonation site.*

INTRODUCTION

We have previously reported some multinuclear NMR data on sydnones and related compounds [1-3]. These results have been very instructive in determining the structures of the compounds studied. In order to extend this work we turned our attention to sydnones and related compounds **1** to **4** in Table 1, which are used to decrease blood pressure, isosydnones **5** to **9**, and isothiosydnones **10** to **12**.

A major aspect of the present investigation is to study the possibility of the occurrence of valence tautomerism between the mesoionic form **(A)** and the non-cyclic form **(B)** in Fig. 1 of the compounds reported.

An additional aspect of the work is to demonstrate the suitability of ^{14}N, ^{15}N, and ^{17}O NMR measurements for structural studies on sydnones, isosydnones, and isothiosydnones.

RESULTS AND DISCUSSION

The ^{13}C, ^{14}N, ^{15}N, and ^{17}O NMR data obtained for the compounds studied are reported in Tables 1, 2, and 3. In all cases the five-membered rings contain 3 heteroatoms with a carbon atom in position 5 and a second carbon in either position 2 or 4. The ^{13}C signal assignments, reported in Tables 2 and 3, are derived from a composition of the ^{1}H coupled and decoupled ^{13}C spectra. In our previous work on sydnones [1-3] specifically ^{15}N labeled samples were used in order to obtain unambiguous nitrogen NMR assignments. This information forms the basis for the nitrogen signal assignments reported in the present work. Additional support is available from *ab initio* charge density calculations (Tables 4 and 5) which reveal that N-3 in the five-membered ring of model compounds bears a positive charge. The alternative possibility for mesoionic compounds of this type would be for a positive charge to reside on atom 1. However the *ab initio* calculations show that this does not occur for the five-membered mesoionic ring compounds reported in Table 1.

*Dedicated to Professor Dr. Édmund Lukevits on the occasion of his 60th birthday.

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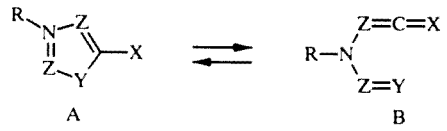


A B

X = NH^-, NR^-, O^-, S^-; Y = O^- or S^-; Z = N^-, CH^-, CR^-

Fig. 1. Valence tautomerism of the mesoionic form **A** and the noncyclic form **B**.

A positively charged nitrogen atom produces a relatively sharp ^{14}N NMR signal since the presence of the charge results in a reduced electric field gradient at the nitrogen atom and thus a smaller relaxation rate from the quadrupolar interaction [4]. Thus the sharpest of the ^{14}N NMR signals found in the spectra of the compounds studied is assigned to N-3. The signal of the nitrogen atom in the morpholine ring of compounds **1** to **4** is assigned by means of the appearance of $^2J(^{15}N\text{-}^1H)$ coupling to the two neighboring methylene groups. The ^{15}N signals of the exocyclic nitrogenous groups of compounds **2**, **3**, **4**, and **12** are found in characteristic spectroscopic positions [5]. The remaining ^{15}N signals correspond to the remaining nitrogen atom in the five-membered ring.

The ^{17}O NMR signals of compounds **5** to **9** are assigned as follows (Table 3). The signal appearing between 250 and 300 ppm is assigned to the five membered ring oxygen atom by comparison of the position of the signals from compounds **5** and **6** with those for the other three compounds which contain an additional oxygen atom in an exocyclic position. This latter oxygen is assigned to the signal appearing at about 170 ppm.

The positions of the ^{13}C and ^{15}N signals observed for compound **1** are typical of the structure shown, and are very different from those found for the mesoionic compounds **(2-12)**, reported here. Thus compound **1** exists in the non-cyclic form shown in Table 1. This is of interest since we wish to investigate the possibility of valence tautomerism as shown in Fig. 1. We find that compounds **1** and **2** are interchangeable, as a function of Ph, but the potential valence tautomerism depicted in Fig. 2 is not observed in the present work.

As indicated in Fig. 2 the transformation of compound **2** to compound **1** commences by the severance of the O1−C5 bond followed by proton transfer from the NH group to C-4. Support for this view is forthcoming from a study of compound **3** which does not contain an exocyclic primary amino group. In this case we are unable to conclude an interchange of structures, of the type shown in Fig. 2, as a function of pH. From which we conclude that it is necessary to have the exocyclic primaries amino group on C-5 for the transformation depicted in Fig. 2 to occur.

In addition the calculated energies (Table 4) of the **C1**, **C3** and **C4** model isomeric structures for compound **1** reveal that the most stable isomer is **C4** and the most nonstable is **C3**.

From the NMR data given in Tables 1, 2, and 3 we conclude that they are consistent with the structures given for compounds **1** to **12**. Thus compounds **2** to **12** are found to exist in the mesoionic structure only. We further observe in the case of compound **12** that at high Ph it becomes unstable. This probably arises from its transformation, similar to that shown in Fig. 2, to a noncyclic form which is unstable (Fig. 3).

Support for this view is forthcoming from reported data [6] for compound **13** which is stable at high Ph. Compound **13** does not contain an exocyclic unsubstituted imino group on C-5, whereas compound **12** does. Thus the situation is similar to that described for compounds **2** and **3**. Thus the anticipated valence tautomerism shown in Fig. 1 is not observed in the present investigation. From the ^{13}C NMR data reported in Table 3 we conclude that the position of the C-5 signal is important in the structural determination of the compounds studied. For sydnone imines and their protonated form the C-5 signal appears between 165 and 175 ppm (Table 2). In addition we have some $^1J(^{13}C4-{}^{13}C5)$ data for these compounds. The value found of about 80 Hz is typical for carbon-carbon double bonds. For isosydnones with exocyclic sulphur on C-5 the signal appears at about 180 ppm (Table 2). For isosydnones with exocyclic oxygen the C-5 signal occurs at around 160 ppm. In the case of isothiosydnones with sulphur in the exocyclic group the signal appears at about 182 ppm, whereas when nitrogen appears in the exocyclic group a value of about 163 ppm is observed.

For isosydnones ^{17}O NMR data for the oxygen atom in the mesoionic ring shows a signal at 290 ppm when sulphur is in the exocyclic group. For isosydnones containing oxygen in the exocyclic group the ring ^{17}O signal appears at about 265 ppm and the exocyclic signal at 170 ppm.

TABLE 1. Nitrogen NMR Data for Some Sydnones, Isosydnones, Isothiosydnones, and Related Compounds

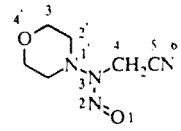
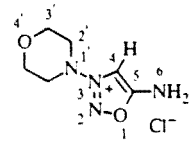
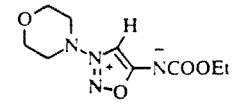
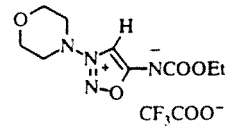
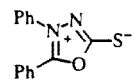
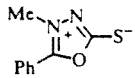
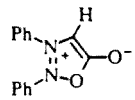
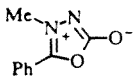
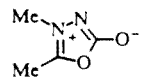
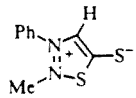
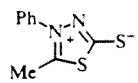
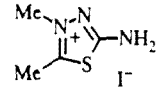
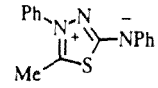
No	Compound	^{15}N NMR chemical shifts in ppm[a] (^{14}N NMR line width in Hz) J_{NH} coupling constants in Hz]				
		N-2	N-3	N-4	N-6	N_{morph}
1[b]		+172,2	-129,1	—	-111,3	-277,2
2[c]		-30,7	-71,9 (746) [2,4][e]	—	-309,6	-258,6
3[b]		-42,9	-73,2 (355) [2,3][e]	—	-219,8	-260,3
4[d]		-22,3	-68,4 (900) [2,8][e]	—	-274,4	-253,8
5[b]		—	-163,9 (750)	-115,6	—	—
6[b]		—	-173,2 (500) [2,4][f]	-116,6 [2,1][g]	—	—
7[b]		—	-173,2 (1660)	-173,8	—	—
8[b]		—	-182,6 (730) [2,1][f]	-175,2 [2,3][g]	—	—
9[b]		—	183,0 (410) [2,3][f]	-182,6 [2,4][g]	—	—
10[b]		—	-137,2 (1000)	-63,6	—	—
11[b]		—	133,4 (900)	-66,5	—	—

TABLE 1. (continued)

No	Compound	^{15}N NMR chemical shifts in ppm[a] (^{14}N NMR line width in Hz) [J_{NH} coupling constants in Hz]				
		N-2	N-3	N-4	N-6	N_{morph}
12[b]		—	-151,9 (1200) [2,4][f]	-107,3 [2,6][g]	-304,1 [90,3][h]	—
13[i]		—[e]	-145,5	-115,5	-184,4	—

[a]Nitrogen chemical shifts are given with respect to external net nitromethane.
[b]Studied in DMSO-d_6.
[c]Studied in CD_3OD.
[d]Studied in CF_3COOH.
[e] $^2J(^{15}N-^1H)$ doublet.
[f] $^2J(^{15}N-^1H)$ quartet.
[g] $^2J(^{15}N-^1H)$ quartet.
[h] $^1J(^{15}N-^1H)$ doublet.
[i]Previously reported data [6].

TABLE 2. Carbon and Proton NMR Data for Some Sydnones and Related Compounds

Compound	^{13}C NMR chemical shifts in ppm (^1H NMR chemical shifts in ppm) [$^1J_{(13C-13C)}$ coupling constants in Hz][a]					
	2'	3'	4	5	6	Other
1[b]	54,1 (3,22)	66,1 (3,79)	32,2 (4,84)	113,7	—	—
2[c]	58,6 (3,35)	70,1 (3,67)	101,7 (7,53)	173,7 [81,8]	(4,34)	—
3[b]	53,5 (3,21)	64,6 (3,59)	98,8 (7,47)	173,6 [76,2]	—	60,1—CH_2, 13,7—CH_3, 160,3 — >C=O (3,73—CH_2, 0,89—CH_3)
4[d]	54,1	65,2	104,0	165,3 [86,0]		64,0—CH_2, 14,3—CH_3, 151,8— >C=O

[a] $^1J(C4-C5)$ coupling constants.
[b]Studied in DMSO-d_6.
[c]Studied in CD_3OD.
[d]Studied in CF_3COOH.

TABLE 3. Carbon, Proton, and Oxygen NMR Data for Some Isosydnones and Isothiosydnones

Compound	^{13}C NMR chemical shifts in ppm[a] (^{1}H NMR chemical shifts in ppm)[a]				^{17}O NMR chemical shifts in ppm (^{17}O NMR line width in Hz)[b]	
	C-2	C-5	R^1	R^2	O-1	O-6
5	158,9	179,4	—	—	288,5 (600)	—
6	158,7	179,5	—	37,8 (3,90)	294,3 (400)	—
7	155,5	159,9	—	—	265,0 (620)	173 (490)
8	152,6	159,0	—	37,6 (3,78)	264,1 (670)	172,9 (380)
9	155,0	159,6	10,4 (2,47)	35,4 (3,51)	270,9 (260)	169,6 (220)
10	166,4	182,9	—	—	—	—
11	168,4	181,9	15,3 (2,79)	—	—	—
12	162,5	164,8	15,4 (2,82)	41,6 (3,87)	—	—
13	162,0[c]	152,5[c]	—	—	—	—

[a]Studied in DMSO-d_6.

[b]Studied in $CDCl_3$.

[c]Previously reported data [6].

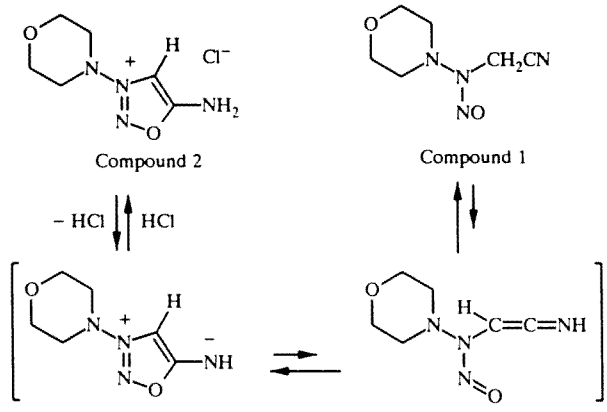


Fig. 2. Potential valence tautomerism of compounds **1** and **2**.

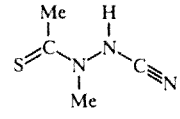
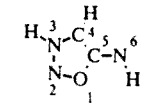
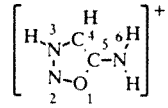
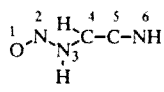
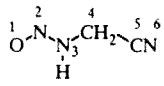


Fig. 3. Hypothetical noncyclic form for compound **12**.

^{14}N and ^{15}N NMR data (Table 1) are also very important for the structure determination of the compounds studied. For sydnone imines the resonance of N-3 appears at about −70 ppm and that for N-2 at about −30 ppm. In the case of isosydnones with sulphur in the exocyclic C-5 group the ^{15}N signals appear at about −170 ppm and −116 ppm for N-3 and N-4 respectively. If the exocyclic group contains oxygen the N-3 and N-4 signals are at about −178 ppm.

TABLE 4. Results of Some *ab initio* GIAO Calculations on a Model Structure for Sydnones and Related Compounds

No	Calculated structures[b]	Calculated chemical shifts in ppma (Calculated net charge)						Electron energy[c] [kJ mol^{-1}]
		O-1	N-2	N-3	C-4	C-5	N-6	
C-1		316,9 (-0,176)	-76,4 (-0,167)	-108,6 (0,318)	88,1 (-0,171)	161,5 (0,433)	-198,1 (-547)	0,000
C-2		370,0 (-0,051)	-27,4 (0,059)	-110,8 (0,307)	87,8 (-0,128)	165,8 (0,429)	-256,8 (-0,199)	—
C-3		814,1 (-0,452)	115,2 (0,248)	-173,1 (-0,028)	39,0 (-0,174)	150,3 (0,314)	-152,8 (-0,280)	90,6
C-4		945,4 (-0,389)	138,5 (0,255)	-166,0 (-0,072)	20,5 (-0,030)	109,3 (0,148)	-112,2 (-0,218)	-111,7

[a]Chemical shifts are reported with respect to net nitromethane for ^{15}N and TMS for ^{13}C using the procedures previously reported [13].

[b]Bond orders are not given.

[c]Relative electron energy.

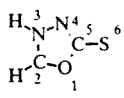
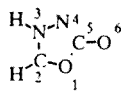
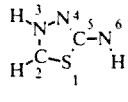
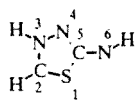
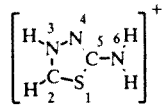
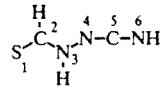
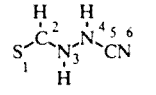
Isothiosydnones with sulphur in the exocyclic group the N-3 signal appears at about −65 ppm and that for N-4 at about −35 ppm. If the exocyclic group contains nitrogen the signals for N-3 and N-4 appear at about −112 ppm and at around −150 ppm respectively.

From ^{15}N results obtained for compounds **2**, **4**, and **12** the site of protonation of the molecules studied is in the exocyclic group. The signal positions for these exocyclic groups are typical of those for the substituents given in Table 1 for compounds **2**, **4**, and **12**.

CONCLUSION

Multinuclear NMR is shown to be well placed to establish the structures of the mesoionic compounds studied containing three heteroatoms in the five-membered ring. No evidence was obtained for the valence tautomerism shown in Fig. 1. Compounds **1** and **12** are found to undergo transformations at high Ph. The ^{14}N NMR line width measurements show that in all cases the formal positive charge of the mesoionic compounds resides on N-3, which is consistent with *ab initio* calculations. However, the calculations explain that the negative charge is distributed between N-6 and N-4 atoms. From measurements on compounds **2**, **4**, and **12** it is shown that protonation occurs on the exocyclic group. In the case of compounds **7**, **8**, and **9** the ^{17}O data are the most suitable for structural determination. For compounds **2**, **3**, and **4** the values of $^{1}J(^{13}C4-^{13}C5)$ and the position of the ^{1}H signal for H-C4, are typical of aromatic compounds. Bond order calculations (Table 6) are similar to previously reported x-ray data for mesoionic compounds [7-9], especially the C5−N6 bond length

TABLE 5. Results of Some *ab initio* GIAO Calculations on a Model Structure for Isosydnones, Isothiosydnones, and Related Compounds

No	Calculated structures[b]	Calculated chemical shifts in ppm[a] (Calculated net charge)						Electron energy[c] [kJ mole^{-1}]
		X-1	C-2	N-3	N-4	C-5	Y-6	
C-5		293,3 (-0,19)	147,8 (0,35)	-165,7 (0,13)	-146,5 (-0,36)	194,4 (0,35)	-44,6 (-0,47)	—
C-6		264,9 (-0,29)	145,9 (0,36)	-172,9 (0,11)	-191,8 (-0,46)	150,3 (0,65)	190,9 (-0,56)	—
C-7		177,5 (0,18)	140,3 (-0,03)	-140,3 (0,24)	-153,1 (-0,46)	162,4 (0,32)	-175,7 (-0,51)	16,7
C-8		165,9 (0,25)	144,9 (-0,03)	-144,4 (0,22)	-157,0 (-0,49)	169,1 (0,33)	-193,8 (-0,57)	0,00
C-9		235,9 (0,41)	162,2 (0,07)	-150,9 (0,21)	-130,7 (-0,31)	169,1 (0,27)	-252,6 (-0,20)	—
C-10		264,9 (-0,31)	207,8 (0,16)	-204,2 (0,01)	-216,5 (-0,27)	152,4 (0,42)	-227,6 (-0,33)	-19,1
C-11		331,3 (-0,26)	214,0 (0,16)	-205,3 (-0,05)	-257,6 (-0,13)	103,9 (0,23)	-142,5 (-0,28)	-54,9

[a]Chemical shifts are reported with respect to net nitromethane for ^{15}N and TMS for ^{13}C using the procedures previously reported [13].

[b]Bond orders are not given.

[c]Relative electron energy.

is in a typical range for a double bond. *Ab initio* molecular orbital calculations are in very good agreement with the NMR results.

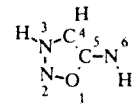
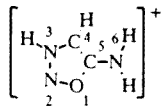
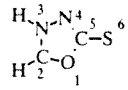
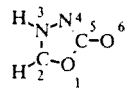
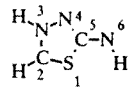
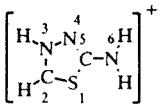
EXPERIMENTAL

Compounds **1** to **4** were received from Polfa Warsaw, the other compounds studied were prepared by published procedures [6, 10, 11]. ^1H NMR was used to characterize the compounds investigated.

The ^1H, ^{13}C, ^{14}N, and ^{15}N NMR measurements were taken on a Bruker AM 500 spectrometer using 0.1-0.5M solutions in DMSO-d_6, CD_3OD, $CDCl_3$, and TFA. Nitromethane was used as an external standard for the nitrogen NMR measurements and TMS for the ^1H and ^{13}C spectra.

For the ^{15}N NMR measurements a pulse angle of 45°, a relaxation delay of 10 sec, an acquisition time of ~2 sec, and about 5000 scans were employed. Measurements using INEPT and inverse gated decoupling were undertaken. For the

TABLE 6. Bond Lengths[a] and Bond Orders Calculated for Sydnone, Isosydnone, and Isothiosydnone

No	Calculated structures	Calculated bond lengths (Calculated bond orders)					
		1—2	1—5	2—3	3—4	4—5	5—6
C-1		1,349 (1,16)	1,370 (1,18)	1,262 (1,61)	1,314 (1,67)	1,433 (1,58)	1,250 (2,00)
C-2		1,308 (1,23)	1,327 (1,29)	1,240 (1,71)	1,355 (1,52)	1,369 (1,82)	1,314 (1,59)
C-5		1,276 (1,47)	1,431 (1,03)	1,276 (1,82)	1,364 (1,27)	1,304 (1,75)	1,651 (1,61)
C-6		1,271 (1,49)	1,497 (0,83)	1,275 (1,82)	1,369 (1,26)	1,317 (1,66)	1,171 (1,86)
C-7		1,706 (1,44)	1,846 (1,13)	1,273 (1,85)	1,334 (1,35)	1,348 (1,56)	1,252 (2,00)
C-9		1,700 (1,47)	1,758 (1,31)	1,274 (1,85)	1,350 (1,31)	1,284 (1,81)	1,324 (1,57)

[a]In angstroms.

^{14}N NMR studies a pulse angle of 90°, a relaxation delay of 0 sec, an acquisition time of 0.2 sec, and between 1000 and 10000 scans were used. For the ^{1}H and ^{13}C data standard instrumental procedures were adopted.

The *ab initio* molecular orbital calculations were performed on a SGI Indigo 2 workstation using the Turbomole program of Biosym Technologies [12]. The tz+2p basis set for each nucleus and CS symmetry was used.

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