Is the Nitro Group attracted towards Sulphur?

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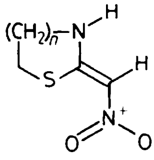
Evidence is presented for a significant, orientation sensitive, attractive intramolecular interaction between sulphur and a nitro group.

There is considerable interest,[1–6] and some controversy,[5,6] in the current literature regarding noncovalent interactions involving the sulphur atom. The interest stems from their potential role in determining the structures of biomolecules containing sulphur[7] and from their possible use in designing crystals with specific material properties.[8] Since the bulk of the experimental evidence for these interactions is structural rather than energetic, the interpretations have been contested.[5] We now provide spectral evidence for an intramolecular attractive interaction between sulphur and a nitro group. The interaction is highly orientation dependent and its magnitude is of the order of a typical N–H · · O hydrogen bond.

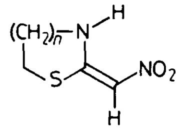
A stereochemical study of the nitroenamine, (**1**), using ^{1}H, ^{13}C, and ^{15}N NMR, revealed several intriguing features.[9] This compound exists in the intramolecular hydrogen bonded E-configuration in $CDCl_3$, but on addition of $[^{2}H_{6}]$DMSO, progressively changes to the Z form; in pure $[^{2}H_{6}]$DMSO, the Z:E ratio is 4 : 1. Interestingly, the preference for a geometry in which the nitro group is *trans* to the ring NH in polar solvents was not observed when the sulphur in (**1**) was replaced by CH_2 or NCH_3. Further, X-ray structure determination proved that (**1**) exists in the Z-configuration in the solid state also.[9] Significantly, there is intermolecular NH · · O hydrogen bonding as well as an intramolecular short contact between the sulphur atom and one of the oxygen atoms of the nitro group of only 2.68 Å, well below the sum of their van der Waals radii. Thus, under conditions when it is not required to form an intramolecular hydrogen bond, the nitro group seems to have an attractive interaction with sulphur.

To understand the phenomenon, we have now studied the NMR spectra of the 6-membered homologue, (**2**),[10] and the acyclic analogue, (**3**). Remarkably, ^{1}H as well as ^{13}C NMR spectral patterns remain unchanged on going from $CDCl_3$ to $[^{2}H_{6}]$DMSO for both (**2**) and (**3**) (Table 1). The presence of a single set of signals proves that these two compounds continue to exist in the E-configuration even in $[^{2}H_{6}]$DMSO, in stark contrast to the 5-membered analogue, (**1**). Since the rotational barriers about the formal C=C bond in these related systems are not likely to be significantly different,[11] the inability to detect the Z isomers of (**2**) and (**3**) indicates that these are energetically inaccessible.[12] One is forced to conclude that a proper alignment is essential for an attractive interaction between sulphur and the nitro group. Such an alignment apparently exists in (**1**), but not in (**2**) or (**3**).

Additional studies on the carbonyl compound, (**4**)† establish the generality of the interaction. While (**4**) exists exclusively in the E form in $CDCl_3$, the Z form becomes populated in $[^{2}H_{6}]$DMSO, the Z:E ratio being approximately 1 : 2. The carbonyl oxygen also seems to have attractive interaction with sulphur, but the magnitude is less than that involving the nitro group. This is confirmed by the 4 : 1 preference observed even in a nonpolar solvent like $CDCl_3$ for the Z conformer of the nitroacetic acid ester derivative, (**5**).[13]

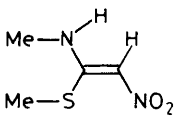


(Z)

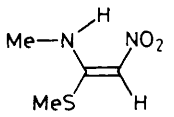


(E)

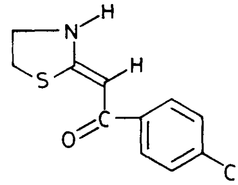
(**1**) n = 1
(**2**) n = 2



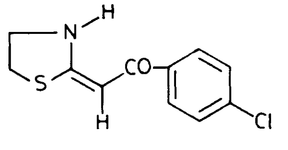
(**3**)(Z)



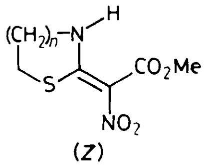
(**3**)(E)



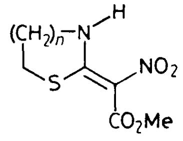
(**4**)(Z)



(**4**)(E)

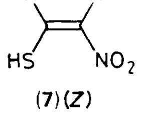


(Z)

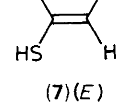


(E)

(**5**) n = 1
(**6**) n = 2



(**7**)(Z)



(**7**)(E)

Correspondingly, the IR spectrum in $CHCl_3$ reveals two carbonyl peaks at 1650 cm^{-1} (strong, intramolecularly H-bonded) and 1730 cm^{-1} (weak). In $[^{2}H_{6}]$DMSO solution, the ^{1}H NMR spectrum indicates the presence of only the Z-isomer (Table 1). In this geometry an ideal combination of sulphur–nitro group interaction and carbonyl–NH hydrogen bonding exists. Interestingly, only one species is seen in both ^{1}H and ^{13}C NMR spectra of the 6-membered homologue, (**6**)[10] in $CDCl_3$ as well as in $[^{2}H_{6}]$DMSO. By analogy with (**2**), we suspect that the molecule is in the E form, and has no tendency to switch over to the Z isomer even in polar solvents.

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Table 1. ^{1}H NMR data for compounds (**1—6**).

		Chemical shift values (δ)		
Compound	Solvent	SCH_3/SCH_2	=CH	NH
(**1**)	$CDCl_3$	3.39 (*E*)	6.75 (*E*)	9.80 (*E*)
	$[^2H_6]$DMSO	3.28	6.75 (*E*)	9.70 (*E*)
			7.07 (*Z*)	8.92 (*Z*)
(**2**)	$CDCl_3$	3.13 (*E*)	6.61 (*E*)	11.02 (*E*)
	$[^2H_6]$DMSO	3.12 (*E*)	6.61 (*E*)	10.59 (*E*)
(**3**)	$CDCl_3$	2.40 (*E*)	6.55 (*E*)	10.37 (*E*)
	$[^2H_6]$DMSO	2.38 (*E*)	6.50 (*E*)	10.13 (*E*)
(**4**)	$CDCl_3$	3.25 (*E*)	5.9 (*E*)	10.50 (*E*)
	$[^2H_6]$DMSO	3.25 (*E*)	5.9 (*E*)	10.25 (*E*)
		3.1 (*Z*)	6.2 (*Z*)	8.37 (*Z*)
(**5**)	$CDCl_3$	3.31 (*E*)	—	10.22 (*E*)
	$[^2H_6]$DMSO	3.25 (*Z*)	—	9.96 (*Z*)
		3.25 (*Z*)	—	9.91 (*Z*)
(**6**)	$CDCl_3$	3.06 (*E*)	—	11.2 (*E*)
	$[^2H_6]$DMSO	3.11 (*E*)	—	10.8 (*E*)

The magnitude of the interaction involving sulphur was sought by means of theoretical calculations.[4] However, as in the earlier study on S · · N interactions,[5] MNDO calculations[14] fail to reveal any nonbonded attraction involving sulphur in (**1**) and (**3**), as well as in the simpler model (**7**). In all these systems, the *E* − *Z* energy differences are small (7.5, 3.8, and 9.2 kJ mol^{-1}, respectively), consistently favouring the *E* isomer. The experimentally observed short S · · O contact in (**1**) is also not reproduced; the calculated S · · O distances are greater than 3 Å in all the cases.

The experimental results suggesting a relatively strong, direction dependent interaction between the nitro group and sulphur, as well as the failure of MNDO to reproduce the geometric and energetic effect, can be understood on the basis of the possible electronic origin of the interaction. It is known from a detailed analysis of numerous crystal structures[1] that the sulphide group can interact with an electrophile as well as a nucleophile with characteristic directionality owing to the presence of a high energy p type HOMO and low lying σ* orbitals. In particular, the oxygen atom of a nitro or carbonyl group can make a favourable nucleophilic approach if the lone pair is directed along the back side of an S–C bond.[1,15] The geometric requirement is apparently met particularly well when the sulphur is enclosed in a 5-membered ring, as in (**1**), (**4**), and (**5**). Since an adequate description of the electronic interaction involving the S–C σ* orbital would need the inclusion of d functions on sulphur, the MNDO method fails to reproduce the effect. For the same reason, the earlier rejection of attractive S · · N interactions on the basis of MNDO, AMI, and split-valence basis *ab initio* calculations[5] calls for a re-evaluation.

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