^{13}C NMR Spectra of 1,3,4-Thiadiazole/Thiadiazoline Isomeric Pairs

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The ^{13}C NMR spectra of four pairs of 1,3,4-thiadiazole/thiadiazoline isomers have been recorded using broad band and off-resonance proton decoupling techniques and in the coupled mode. Differences in the chemical shifts of the heterocyclic ring and the carbonyl carbons allow identification of the isomer present. Their IR and UV spectra are in agreement with literature reports for azole/azoline analogues.

INTRODUCTION

Reactions of 2-amino-1,3,4-thiadiazoles[1] can lead to the heteroaromatic thiadiazole (e.g. compound **1**) or to the non-aromatic thiadiazoline isomeric species (e.g. **5**) (see Table 1). IR and UV spectroscopy can distinguish between these isomers but ^{1}H NMR is less useful because of the absence of any heteroaromatic ring protons. We have found that the ^{13}C NMR spectra of the four isomeric pairs (**1–4** and **5–8**) show characteristic differences in chemical shifts which can complement the IR and UV information in assigning unknown isomers.

EXPERIMENTAL

^{13}C NMR spectra were obtained on a Bruker WH-90 Fourier transform spectrometer (22.64 MHz; 0.3 mmol solutions; 10 mm tubes; 2000–6000 transients; flip angle = 20°; pulse delay = 1 s) with noise modulated broad band decoupling or with continuous wave off-resonance decoupling displaced 2–3 ppm above TMS. Proton coupled spectra were obtained on a Varian FT-80A spectrometer (20 MHz). The decoupler was switched off during the data acquisition period (1.7 s) and on during the 3 s delay in order to retain the sensitivity advantage due to the nuclear Overhauser effect. Deuterated chloroform (99.8% isotopic purity, Merck Sharp and Dohme) was used for all samples with peaks referred to TMS at $\delta = 0.00$ and $CDCl_3$ at $\delta = 77.2$.

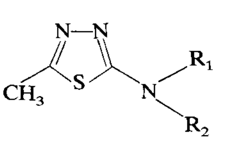
IR and UV spectra were recorded for potassium bromide discs and 'Analar' methanol solutions, respectively, on Perkin Elmer 457 and Pye Unicam SP 800 spectrophotometers. The 1,3,4-thiadiazolines (**5**–**8**) were synthesized[1] by acylation of 2-amino-5-methyl-1,3,4-thiadiazole (**9**) to give the secondary amides, the sodium salts of which were then alkylated in DMF. For **1**, *N*-allyl-2-amino-5-methyl-1,3,4-thiadiazole was treated with benzoyl chloride whereas **2** and **3** were prepared by reductive alkylation of **9** followed by acylation of the resulting benzylamines. For **4**, compound **9** was acylated, the product reduced with lithium aluminium hydride and the secondary amine treated with phenylacetyl chloride.

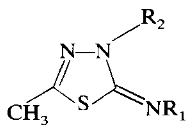
RESULTS AND DISCUSSION

The ^{13}C NMR spectral properties of 1,3,4-thiadiazoles and the isomeric thiadiazolines have received little attention.[2] Bartels-Keith[3] has reported that the 2-SH derivatives of 1,3,4-thiadiazoles and -selenadiazoles exist predominantly as the thione and selenone (C=S or C=Se) tautomers because the chemical shifts of C-2 and C-5 differ greatly from those of the analogous disulphides and diselenides (which can only exist in the thiol heteroaromatic form).

In this paper we present ^{13}C data for four pairs of isomers having identical substituents (Table 1). The ^{13}C chemical shifts are given in Table 2.

Table 1. Compounds studied





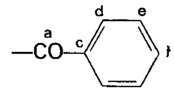
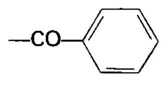
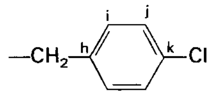
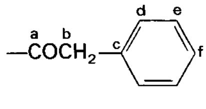
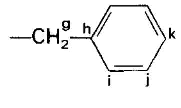
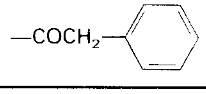
Thiadiazole compounds	R1	R2	Thiadiazoline compounds
1		$-CH_2CH=CH_2$ (g h i)	5
2			6
3			7
4		$-(CH_2)_5CH_3$ (g–k) l	8

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Table 2. ^{13}C Chemical shifts

	Compound number							
Carbon	**1**	**5**	**2**	**6**	**3**	**7**	**4**	**8**
2	162.1	166.0	162.5	166.3	162.5	165.7	162.1	165.5
5	160.1	154.8	160.6	155.1	160.6	154.7	159.8	154.4
5′	15.2	16.3	15.3	16.4	15.2	16.4	15.2	16.4
a	170.4	174.2	170.4	174.2	170.9	180.9	170.1	180.9
b					41.3	47.0	41.3	47.0
c	134.1	136.3	133.9	136.3	133.1	136.7	136.0	136.8
d	128.7	129.5	128.7	129.6	129.2	129.8	129.1	129.8
e	127.2	128.2	127.3	128.3	129.2	128.4	129.1	128.4
f	132.2	132.0	131.3	132.2	127.6	126.5	126.3	126.6
g	52.1	53.0	52.5	53.3	51.0	53.9	48.6	50.7
h	131.1	131.3	135.0	134.1	136.1	135.5	28.4	28.5
i	118.0	119.4	128.9	130.2	126.4	128.4[a]	26.6	26.3
j			128.9	129.1	129.2	128.8[a]	31.6	31.5
k			133.6	132.2	128.0	128.8	22.7	22.7
l							14.2	14.2

[a] Assignments may be reversed.

Table 3. IR and UV data

	IR absorption of C=O stretch (cm^{-1})	UV longest λ max (nm)
Thiadiazoles **1–4**	1660–1675	260 ± 3
Thiadiazolines **5–8**	1610–1620	301 ± 10

The peaks attributed to the carbonyl group and to C-2 and C-5 were clearly seen in a part of the spectrum (δ150–180) well removed from the aromatic ring signals. They were separately identified by recording the spectra of the isomer pair **3** and **7** in the coupled mode (see Experimental). For **7**, two bond proton coupling was clearly revealed by the triplet splitting of the carbonyl carbon [$J(\mathrm{CO}, \mathrm{CH_2}) = 7.2$ Hz] and the quartet splitting on C-5 [$J(\mathrm{C\text{-}5}, \mathrm{CH_3}) = 7.6$ Hz]. The signal for C-2 remained a singlet under these conditions. In the case of **3**, C-5 again appeared as a quartet ($J = 7.3$ Hz), the carbonyl signal showed two bond and three bond couplings to methylene groups (b) and (g) ($J = 7.1$, 4.2 Hz) and C-2 showed a three bond coupling to (g) ($J = 3.9$ Hz).

Other peak assignments were made by reference to model substituted phenyl derivatives and alkyl chains[4,5] and by intercompound correlation (e.g. the common phenyl rings in **1** and **2** or in **3** and **4**).

The most useful signals for distinguishing between each of the isomeric pairs were found to be the carbonyl carbon (difference of 3.8–10.8 ppm) and carbons C-5 (5.3–5.9 ppm), C-2 (3.2–3.9 ppm), the benzylic $\mathrm{COCH_2}$(5.7 ppm) and the 5′-methyl (1.2 ppm). It was notable that the carbonyl carbon (a) of the benzoyl group was much less sensitive to isomer change than was the analogous signal for the $\mathrm{PhCH_2CO}$ group.

IR and UV absorption spectra of compounds **1–8** were in agreement with literature reports for similar isomer pairs. The IR absorptions of the carbonyl groups were clearly distinguished (Table 3).

Werber[6,7] has recorded carbonyl absorption at 1665–1695 cm^{-1} for amido substituted thiadiazoles (similar to **1–4**) and at 1615–1625 cm^{-1} for the isomeric thiadiazolines. In the UV region, the change azole/azoline is accompanied by a bathochromic shift of *c.* 40 nm (Table 3). Tetu[8] has noted a shift of *c.* 40 nm in the thiazole/thiazolines, also to higher wavelength.

Acknowledgements

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REFERENCES

1. D. Evans, W. J. Ross, J. C. Saunders, C. E. Smith, A. Stevens, J. P. Verge, R. Wiley and W. R. N. Williamson, to be published.
2. J. Elguero, C. Marzin, A. R. Katritzky and P. Linda, *The Tautomerism of Heterocycles*, Academic Press, New York (1976).
3. J. R. Bartels-Keith, M. T. Burgess and J. M. Stevenson, *J. Org. Chem.* **42**, 3725 (1977).
4. L. F. Johnson and W. C. Jankowski, *Carbon-13 NMR Spectra*, Wiley Interscience, New York (1972).
5. F. W. Wehrli and T. Wirthlin, *Interpretation of Carbon-13 NMR Spectra*, Heyden, London (1978).
6. G. Werber, F. Buccheri and M. L. Marino, *J. Heterocycl. Chem.* **12**, 581 (1975).
7. G. Werber, F. Buccheri and N. Vivona, *J. Heterocycl. Chem.* **12**, 841 (1975).
8. O. Tetu, M. Selim, M. Selim and P. Rumpf, *Bull. Soc. Chim. Fr.* **1**, 342 (1966).

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