

## Stereoselective S-Oxidation of 5-Substituted 4-Acetyl- $\Delta^2$ -1,3,4-thiadiazolines: X-Ray Crystal Structure of 4-Acetyl-2-acetylamino-5-methyl-5-phenyl- $\Delta^2$ -1,3,4-thiadiazoline 1-Oxide

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N.m.r. spectroscopy and X-ray crystallography show that oxidation of 5-substituted 4-acetyl-2-acetylamino- $\Delta^2$ -1,3,4-thiadiazolines with *m*-chloroperbenzoic acid gives the corresponding  $\Delta^2$ -1,3,4-thiadiazoline 1-oxides; the novel reactions of the product (**2a**) are also described.

It is well known that the oxidation of sulphides with potassium permanganate generally gives sulphones instead of sulphoxides, since sulphoxides are more reactive than sulphides toward transition metal oxidants.<sup>1</sup> However, we have now found that the oxidation of 4-acetyl-2-acetylamino-5-phenyl- $\Delta^2$ -1,3,4-thiadiazoline (**1a**)<sup>2</sup> with potassium permanganate (1 mol. equiv.) gives the sulphoxide (**2a**; 8.6%), m.p. 148–149 °C (decomp.) {i.r. (KBr disc),  $\nu_{\max}$  1024  $\text{cm}^{-1}$ (SO); <sup>1</sup>H n.m.r. ( $\text{CDCl}_3$ )  $\delta$  6.61 (C5-H); <sup>13</sup>C n.m.r. [ $(\text{CD}_3)_2\text{SO}$ ]

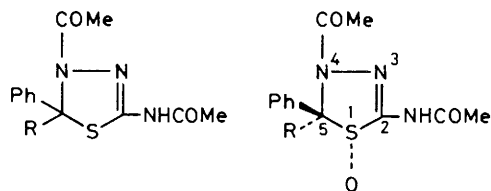
$\delta$  81.32 p.p.m. (C-5)} together with the expected 1,3,4-thiadiazole derivative (**3**; 68%).<sup>2</sup>

Very few examples of the synthesis of  $\Delta^2$ -1,3,4-thiadiazoline 1-oxides have been reported hitherto. Epimeric mixtures of 2,4-diphenyl-5,5-disubstituted  $\Delta^2$ -1,3,4-thiadiazoline 1-oxides have been obtained from the cycloaddition of aromatic sulphines with nitrilimines, or by peroxy acid oxidation of the corresponding  $\Delta^2$ -1,3,4-thiadiazolines.<sup>3</sup> We now report the stereoselective S-oxidation of  $\Delta^2$ -1,3,4-thiadiazolines with *m*-chloroperbenzoic acid. The oxidation of (**1a**) and 5-methyl compound (**1b**) with *m*-chloroperbenzoic acid in chloroform at room temperature gave single isomers (with sulphoxide *trans* to phenyl) of 5-substituted 4-acetyl-2-acetylamino- $\Delta^2$ -1,3,4-thiadiazoline 1-oxides (**2a**; 75%) and (**2b**; 78%), m.p. 172.5–174.5 °C (decomp.) {i.r. (KBr disc),  $\nu_{\max}$  1046  $\text{cm}^{-1}$ (SO); <sup>1</sup>H n.m.r. ( $\text{CDCl}_3$ )  $\delta$  2.11 (C5-CH<sub>3</sub>); <sup>13</sup>C n.m.r. [ $(\text{CD}_3)_2\text{SO}$ ]  $\delta$  87.35 p.p.m. (C-5)}, respectively.

The stereochemistry of the sulphinyl groups of (**2a**) was established by benzene-induced chemical-shift studies.<sup>4</sup> The oxygen atom of the sulphinyl group was assigned the orientation *trans* to the phenyl group, on the basis that a small downfield shift of the C5-H proton signal was detected on changing the solvent from  $\text{CDCl}_3$  to  $\text{C}_6\text{D}_6$ - $\text{CDCl}_3$  (1:1 v/v) [ $\Delta\delta = \delta(\text{CDCl}_3) - \delta(\text{C}_6\text{D}_6\text{-CDCl}_3) = 0.05$ ].

The detailed structure of (**2b**) in which the oxygen atom is *trans* to the 5-phenyl group was established by single-crystal X-ray analysis. Data were collected on a Syntex R3 diffractometer system by the  $\omega$  scanning technique using a variable-scan speed and graphite-monochromated Mo- $K_\alpha$  radiation.

Crystal data:  $\text{C}_{13}\text{H}_{15}\text{N}_3\text{O}_3\text{S}$ ,  $M = 293.34$ , monoclinic,

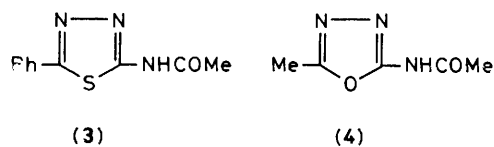


(**1a**) R = H

(**1b**) R = Me

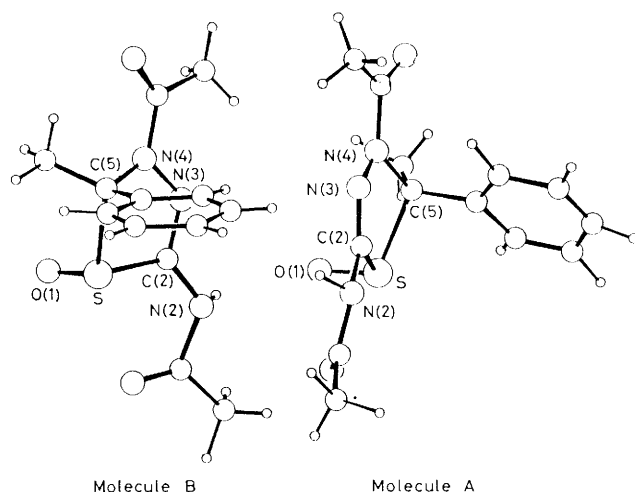
(**2a**) R = H

(**2b**) R = Me



(**3**)

(**4**)



**Figure 1.** Molecular structure of compound (**2b**). The structure includes the following hydrogen bonds: N(2)A—H...O(1)B, ( $1 + x, y, z$ ), 2.842(10) Å and N(2)B—H...O(1)A, ( $x, y, z$ ), 2.777(10) Å.

space group  $P2_1$ ,  $a = 8.754(7)$ ,  $b = 16.818(18)$ ,  $c = 10.465(7)$  Å,  $\beta = 105.50(6)^\circ$ ,  $D_c = 1.31$  g cm $^{-3}$ ,  $\mu = 2.3$  cm $^{-1}$ , and  $Z = 4$ . The structure was solved by the heavy-atom method and refined by block-diagonal least-squares calculations. The final  $R$  value is 0.057 for 1153 reflections

[ $I \geq 1.96\sigma(I)$ ].† The molecular structure of (**2b**) is illustrated in Figure 1.

An attempt to obtain the isomer with sulphoxide *cis* to phenyl, by oxidation of (**1a**) with *t*-butyl hypochlorite<sup>5</sup> in methanol, was unsuccessful and compound (**3**) and 2-acetyl-amino-5-methyl-1,3,4-oxadiazole (**4**) were obtained. Treatment of (**2a**) with triethylamine at room temperature gave (**3**; 90%). The reaction of (**2a**) with excess of dimethyl sulphoxide at 100 °C gave (**4**; 74%), benzaldehyde, *trans*-stilbene, and sulphur.

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### References

- 1 H. B. Henbest and S. A. Khan, *Chem. Commun.*, 1968, 1036; D. Arndt, 'Methoden der Organischen Chemie (Houben-Weyl)', Bd.4/1b: Oxidation II, Georg Thiem Verlag, Stuttgart, 1975, p. 647.
- 2 S. Kubota, Y. Ueda, K. Fujikane, K. Toyooka, and M. Shibuya, *J. Org. Chem.*, 1980, **45**, 1473.
- 3 B. F. Bonini, G. Maccagni, G. Mazzanti, L. Thijs, G. E. Veenstra, and B. Zwanenburg, *J. Chem. Soc., Perkin Trans. 1*, 1978, 1218.
- 4 C. H. Chen, G. A. Reynolds, and B. C. Cossar, *J. Org. Chem.*, 1981, **46**, 2752.
- 5 M. Kishi and T. Komeno, *Tetrahedron Lett.*, 1971, 2641.

† The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.