

The Thermally Degenerate Mononuclear Rearrangement of  
3-Acetylamino-5-methyl-1,2,4-oxadiazole (1)

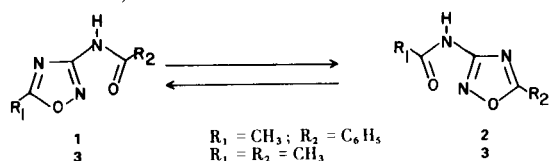
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Sir:

In connection with mononuclear heterocyclic rearrangements generalized by Katritzky and Coworkers (2) and with our previous researches in this field (3), we pointed out recently (4) for the first time the possibility of a reversible *iso*-heterocyclic mononuclear rearrangement in some 5-substituted-3-acylamino-1,2,4-oxadiazoles ( $1 \rightleftharpoons 2$ ). The example reported (4) represents an equilibrium significantly shifted towards **2** ( $K_{\text{eq}} = 5 \div 10$ , as a function of the solvent).



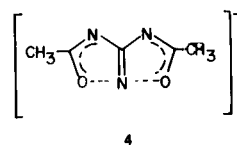
Now we have looked at the 3-acetylamino-5-methyl-1,2,4-oxadiazole (**3**) (5) with the aim of providing evidence on the possible degenerate rearrangement, if this were rapid enough to be observed by dynamic nmr. If this were the case, we should have the first example of a degenerate heterocyclic rearrangement in the mononuclear series (6). The  $^1\text{H}$  nmr spectrum (7) of **3** in DMSO shows two sharp singlets at 2.52 and 2.08  $\delta$  for the nuclear and acetamide methyls, respectively and a broad singlet at 10.82  $\delta$  for NH.

On heating a solution of **3** in DMSO up to 190° the two methyl signals do not coalesce, indicating, for the reversible process, a  $\Delta G^\ddagger$  which can be evaluated to be higher than 25 kcal mole $^{-1}$ . Considering however, that the rearrangement  $1 \rightleftharpoons 2$  was largely base-catalyzed (4), we have investigated the behaviour of **3** in the presence of a base. The  $^1\text{H}$  nmr spectrum of the potassium salt of **3** (prepared *in situ* by adding a solution of *t*-ButOK in DMSO to a solution of **3** in the same solvent in stoichiometric amount) shows the two singlets for methyl proton resonances at 2.45 and 1.97  $\delta$ . On heating at 112° these signals coalesced into a singlet; the original spectrum can be reproduced on cooling.

From the coalescence temperature and the frequency

separation of the methyl singlets, a value of free energy of activation,  $\Delta G^\ddagger$ , of 19.6 $\pm$ 0.4 kcal mole $^{-1}$  was calculated (8).

The reaction probably proceeds through the formation of the anion **4**, which can represent a transition state or a metastable intermediate. In the anion **4**, owing to the degenerate rearrangement, the new and the old nitrogen-oxygen bonds should be formed and broken to the same extent, with the central nitrogen atom presumably interacting through a *p*-type orbital.



REFERENCES AND NOTES

- (1) Presented at a meeting of the "Società Chimica Italiana", Messina, Italy, 28th November, 1974 (M. Ruccia, N. Vivona, G. Cusmano, M. L. Marino and D. Spinelli).
- (2) A. J. Boulton, A. R. Katritzky and A. M. Hamid, *J. Chem. Soc. (C)*, 2005 (1967).
- (3) M. Ruccia and D. Spinelli, *Gazz. Chim. Ital.*, **89**, 1654 (1959); M. Ruccia and N. Vivona, *Ann. Chim. (Rome)*, **57**, 680 (1967); *Chem. Commun.*, 866 (1970); M. Ruccia, N. Vivona and G. Cusmano, *J. Heterocyclic Chem.*, **8**, 137 (1971); *Tetrahedron Letters*, 4959 (1972); *Tetrahedron*, **30**, 3859 (1974); *J. Chem. Soc., Chem. Commun.*, 358 (1974).
- (4) N. Vivona, G. Cusmano, M. Ruccia and D. Spinelli, *J. Heterocyclic Chem.*, in press.
- (5) Obtained by acetylation of 3-amino-5-methyl-1,2,4-oxadiazole [m.p. 163°, from benzene. *Anal. Calcd.* for  $\text{C}_5\text{H}_7\text{N}_3\text{O}_2$ : C, 42.55; H, 5.00; N, 29.78. Found: C, 42.60; H, 4.95; N, 29.80].
- (6) A degenerate rearrangement in the benzo-fused series has been reported [K. P. Parry and C. W. Rees, *Chem. Commun.*, 833 (1971)] to occur on heating 7-acetyl-3-methylantranil, was observed by dynamic nmr. In this case, however, the intermediate (or transition state) is stabilized by the full benzenoid resonance energy, which is lacking in both starting material and product.

Moreover, it is well known that in the benzo-fused cases the free energy of activation for the rearrangement process is largely lower than in the simple systems [e.g., see the difference in  $\Delta G^\ddagger$  for benzofuroxane and furoxane isomerization in: F. B. Mallory, S. L. Manatt and C. S. Wood, *J. Am. Chem. Soc.*, **87**, 5433 (1965); F. B. Mallory and A. Cammarata, *ibid.*, **88**, 61 (1966)].

(7)  $^1\text{H}$  nmr spectra (60 MHz) were recorded on a Jeol C-60H spectrometer (TMS as internal standard) equipped with variable temperature probe. Accuracy of  $T_c$  as  $\pm 1^\circ$ .

(8) H. Kessler, *Angew. Chem. Int. Ed. Engl.*, **9**, 219 (1970); D. Kost, E. H. Carlson and M. Raban, *Chem. Commun.*, 656 (1971).