REACTION OF 3-AZIDO-5-PHENYL-1,2,4-OXADIAZOLE WITH DIMETHYLFORMAMIDE, A New Deoxygenative Coupling Reaction

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<u>SUMMARY</u>: When 3-bromo-5-phenyl-1,2,4-oxadiazole (lb) is heated with sodium azide in anhydrous dimethylformamide at 130° , 3-dimethylamino-(<u>lc</u>) and 3-dimethylaminomethyleneamino-5-phenyl-1,2,4-oxadiazole (<u>ld</u>) are formed, the latter by a new deoxygenative coupling of the azide (<u>la</u>), or the nitrene derived from it, with the solvent.

During a synthesis of 3-azido-5-phenyl-1,2,4-oxadiazole (<u>la</u>) from the corresponding bromide (lb) by displacement with sodium azide in hot anhydrous dimethylformamide (DMF)¹, we found that raising the temperature from 90° to 130°, for 3 h, resulted in the formation of two new products. We now report on the structure and mode of formation of these products.



Rapid chromatography (SiO_2) of the product mixture gave (i) 3-dimethylamino-5phenyl-1,2,4-oxadiazole (lc)², m.p. 40-2⁰ (EtOH-H₂O) (39%) identical with a specimen prepared by heating the bromide (<u>1b</u>) with 33% dimethylamine in ethanol for 27 h (83%), and (ii) 3-dimethylaminomethyleneamino-5-phenyl-1,2,4-oxadiazole $(\underline{1d})^2$ m.p. 113-5^o (80 -100^o petroleum ether) (34%) which was identical with the compound prepared by treating 3-ethoxymethyleneamino-5-phenyl-1,2,4-oxadiazole (le)³ with 33% dimethylamine in ethanol at room temperature for two days (91%, after recrystallisation)⁴.



The amine (<u>1c</u>) provides another example of a dimethylamino compound formed by the reaction of an active halide in DMF^5 ; it could arise from dimethylamine produced by thermal decomposition of DMF, or by displacement of bromine by DMF followed by decomposition of the quaternary salt. When the bromide (<u>1b</u>) was heated in DMF alone at 130^o, the amine (<u>1c</u>) was the only product observed (t.l.c.).

The mechanism of formation of the formamide $(\underline{1d})$ is more intriguing. That the azide $(\underline{1a})$ could serve as a direct precursor of $(\underline{1d})$ was shown by control experiments:

(i) heating azide (<u>la</u>) in anhydrous DMF in the presence of sodium bromide⁶ (1 equiv.) at 140° for 30 h gave amidine (<u>ld</u>) (47%); (ii) no detectable amount (t.l.c. or ¹H n.m.r.) of the amidine (<u>ld</u>) was formed when 3-amino-5-phenyl-1,2,4-oxadiazole (<u>lg</u>) was heated in anhydrous DMF at 140° although all of the amine decomposed. This amine might have been formed from the nitrene by hydrogen abstraction.

A mass spectrometric investigation of the gases evolved in the reaction of bromide $(\underline{1b})$ with sodium azide in DMF at $\underline{130}^{O}$ showed the complete absence of nitrous oxide, and the gaseous byproducts are assumed to be nitrogen and oxygen.

Possible mechanisms consistent with these observations are shown in the Scheme. The key oxaziridine intermediate $(\underline{2})$ could be formed from the azide and DMF, by 1,3-cycloaddition or via the open dipolar species, or from the nitrene and DMF. The oxaziridine (2) then rearranges to the nitrone (3) which is thermally deoxygenated to product.

Although an example of intramolecular interaction of an azide with an amide, $(\underline{4})$ to $(\underline{5})$, has been reported⁷, as have similar reductive cyclisations of nitrenes onto ester groups⁸, we believe that the above reaction is the first example of such an intermolecular reaction.



We thank Smith Kline & French, Welwyn Garden City, for generous support. 127

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(Received in UK 26 October 1981)