

Photoinduced Rearrangement of 3-Styryl-1,2,4-oxadiazoles
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 Received September 27, 1989

The photochemical behaviour of 3-styryl-5-phenyl-(5-methyl)-1,2,4-oxadiazoles in methanol at 254 nm has been investigated. A photoinduced rearrangement to the quinoline system has been pointed out and explained as proceeding through an initial photolysis of the ring O-N bond, followed by a six membered ring closure reaction involving the styryl moiety.

J. Heterocyclic Chem., **27**, 861 (1990).

In connection with researches on the photochemistry of five membered heterocycles [1] [2] recently attention was paid to the photoinduced rearrangements of 1,2,4-oxadiazoles containing a suitable XYZ side chain at the position 3 of the ring [3]. In this context, the photorearrangements of suitably substituted 1,2,4-oxadiazoles into benzimidazoles, benzoxazoles and imidazoles have been reported. These reactions were explained as proceeding through a general pathway which implies an initial photolysis of the ring O-N bond, followed by a five membered ring closure reaction involving the three atoms side chain sequence. For the 3-acetyl-amino-5-aryl-1,2,4-oxadiazoles (were XYZ = NCO) a photorearrangement of the *iso*-heterocyclic type [4] (starting and final ring being equal) has been evidenced [5]. Moreover, the 3-arylamino-5-methyl-1,2,4-oxadiazoles gave a photorearrangement leading to a six membered ring closure involving the aryl ring of the aryloamino group in a four atoms side chain sequence [6].

Continuing the studies on this aspect of the photochemistry of five membered heterocycles, and aiming to have

more insight into the photoinduced rearrangements of 1,2,4-oxadiazoles, we became interested in how changes in the nature of the side chain sequence influence the photorearrangements. On the other hand, our opinion is that it should be of interest to investigate these photoreactions as a tool for synthesis of heterocyclic compounds. In this communication we report the results concerning with the photochemical behaviour of 3-styryl-5-phenyl- (**1**) and 3-styryl-5-methyl-1,2,4-oxadiazole (**2**). For these derivatives one can recognise a photorearrangement leading to the quinoline system, through a six membered ring closure reaction involving the phenyl ring of the styryl moiety.

Oxadiazoles **1** and **2** were prepared by adopting the procedure reported [7], and the nmr spectra confirmed the expected *E* geometry around the carbon-carbon double bond

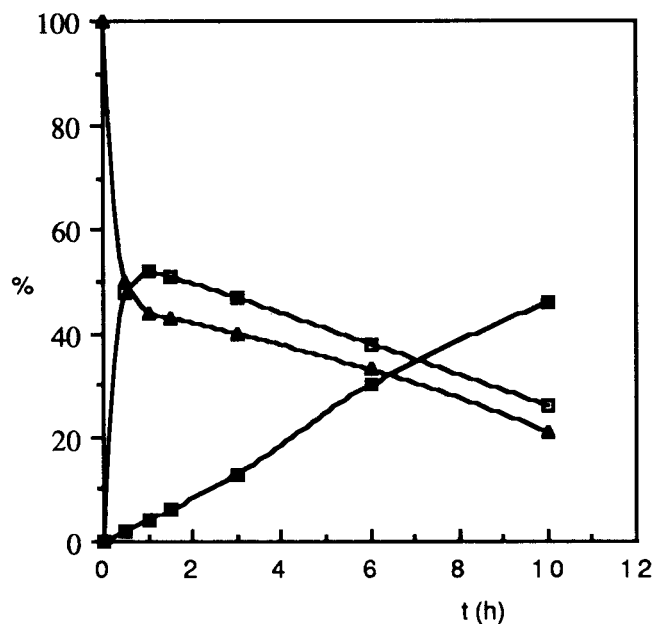
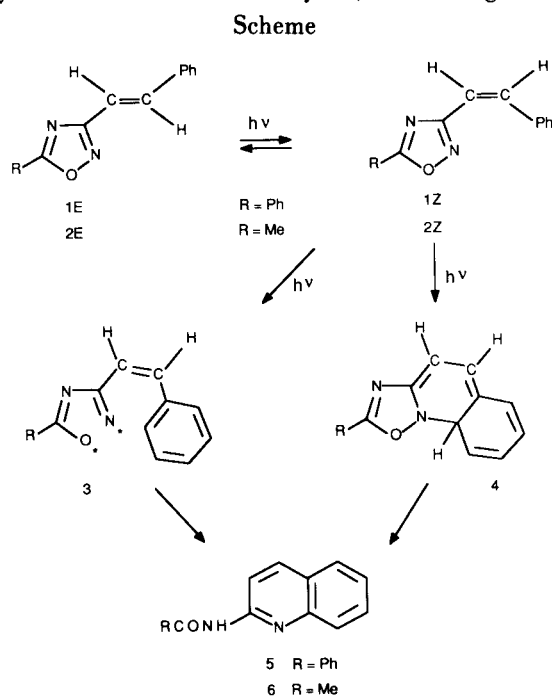


Figure: Irradiation of compound **1E** in the Rayonet apparatus. Composition (%) of the photoreaction mixture as a function of irradiation time. (▲ = **1E**; □ = **1Z**; ● = **5**)

of the styryl group. As regards the photochemical investigation, likewise previous experimental conditions, irradiations have been carried out in anhydrous methanol at 254 nm, by using low pressure Hg lamps (17 W) in an immersion apparatus, and photoreactions were monitored by hplc analyses. Under these conditions, after 10 hours of irradiation the 3-styryl-5-phenyl-1,2,4-oxadiazole (**1E**) gave a photoreaction mixture from which we were able to isolate the starting oxadiazole **1E** (40%), the *Z*-isomer **1Z** (40%), and the 2-benzoylaminoquinoline (**5**) [8] (10%).

In order to have some information on the course of the reaction, we decided to follow the composition of the photoreaction mixture as a function of the irradiation time. With this aim, we performed the irradiation in a Rayonet apparatus equipped with 254 nm lamps and the results are reported in the Figure [9]. Clearly, one can recognise that the irradiation causes two photochemical processes: *i*) a fast $E \rightleftharpoons Z$ isomerization between the two geometries around the carbon-carbon double bond of the styryl group; and, *ii*) a slow formation of the rearrangement product. Similar results were obtained in the irradiation of **1Z**. However, a different result was observed in the irradiation of 3-styryl-5-methyl-1,2,4-oxadiazole (**2E**). In fact, irradiation of compound **2E** for 10 hours mainly gave the $2E \rightleftharpoons 2Z$ isomerization process, while only trace amounts of the corresponding 2-acetylaminoquinoline (**6**) [8] were present. On the basis of these observations, one can suggest that two chromophores are involved in the excitation of the styryloxadiazoles. Regardless of the expected $E \rightleftharpoons Z$ isomerization process for which the styryl chromophore is operative, the rearrangement reaction should involve the oxadiazole chromophore and could be explained as in the general scheme: *i.e.*, the photolytic intermediate **3**, arising from the ring O-N bond cleavage, collapses to the quinoline system through a six membered ring closure involving the styryl group in a suitable configuration. Therefore, the alternative pathway which implies an initial heteroelectrocyclic reaction of the *Z*-styryloxadiazoles into an intermediate of the type **4**, followed by a subsequent ring opening of this latter to the rearrangement product, could be excluded. Results on this aspect of photorearrangements of 1,2,4-oxadiazoles will be reported.

EXPERIMENTAL

Melting points were determined with a Kofler hot-stage apparatus; ir spectra (nujol mulls) were determined with a Perkin-Elmer 257 instrument, uv spectra (in methanol) with a Varian Superscan 3 spectrophotometer, ¹H nmr spectra (60 MHz) with a Varian EM 360 spectrometer (tetramethylsilane as internal standard) and mass spectra with a JEOL JMS 01-SG-2 instrument (75 eV). Hplc analyses were performed with a Perkin-Elmer Series 10 instrument, by using a C-18 SIL-X-10 Perkin-Elmer column (25 cm x 4.6 mm diameter) eluting with water/acetonitrile (7:3 v/v) at flow rate of 2.0 ml/minute, monitoring the optical density at 254

nm. Flash chromatography [10] was performed on Merck silica gel (0.040-0.063 mm). Light petroleum refers to that fraction boiling in the range 40-60°. Methanol was purified as reported [11] and was used freshly prepared. Oxadiazoles **1** and **2** were prepared as reported [7].

Compound **1E** had mp 102° (from light petroleum), lit [6], mp 102°; uv: λ max 276 nm (ϵ max 40,300, ϵ 254 20,800); ¹H-nmr (deuteriochloroform): δ 6.80, 7.55 (two doublets of an AB system overlapped with aromatic protons, E -CH=CH-, J = 18 Hz, 2H), 7.1-8.1 (m, aromatic, 10H).

Compound **2E** had mp 78° (from light petroleum), lit [6], mp 78°; uv: λ max 276 nm (ϵ max 27,000, ϵ 254 8,700); ¹H-nmr (carbon tetrachloride): δ 2.60 (s, CH₃, 3H), 7.20, 7.60 (two doublets of an AB system overlapped with aromatic protons, E -CH=CH-, J = 18 Hz, 2H), 7.3-7.8 (m, aromatic, 5H).

Photochemical Reactions.

General Procedure.

A solution of the oxadiazole (500 mg) in anhydrous methanol (100 ml), in a quartz tube, was degassed by nitrogen bubbling (20 minutes), and then irradiated at 254 nm in an immersion well apparatus by a low-pressure mercury lamp (Helios Italquartz, 17 W). The solvent was removed under reduced pressure and the residue was subjected to chromatography by using mixtures of light petroleum-ethyl acetate in varying ratios as eluent. Quantitative hplc analyses for drawing the figure, were performed by irradiation of compound **1E** (20 mg) in anhydrous methanol (10 ml) in a RPR-100 Rayonet apparatus and correction factors were determined by using pure samples of compounds **1E**, **1Z**, and **5**.

Irradiation of Compound **1E**.

Irradiation for 10 hours gave starting material (40%), the isomer **1Z** (40%) and 2-benzoylaminoquinoline **5** (10%).

Compound **1Z** (oil) had ¹H-nmr (carbon tetrachloride): δ 6.45, 6.95 (two doublets of an AB system, Z -CH=CH-, J = 12 Hz, 2H), 7.1-8.2 (m, aromatic, 10H).

Anal. Calcd. for C₁₆H₁₂N₂O: C, 77.42; H, 4.84; N, 11.29. Found: C, 77.35; H, 4.92; N, 11.30.

Compound **5** had mp 124° (from light petroleum), lit [8] mp 129-130°; ir: 3220 cm⁻¹ (NH), 1680 cm⁻¹ (CO); ¹H-nmr (DMSO-d₆): δ 7.3-8.4 (m, aromatic, 11H), 11.20 (s, NH, 1H); ms: m/z 248 (M⁺). A pure sample of **5** was prepared by benzylation of the 2-aminoquinoline [12].

Irradiation of Compound **2E**.

Irradiation for 10 hours gave starting material (45%) and the isomer **2Z** (45%). Hplc analyses of the photoreaction mixture revealed the presence of trace amounts of compound **3**. A pure sample of **3** was prepared by acetylation of the 2-aminoquinoline [12].

Compound **2Z** (oil) had ¹H-nmr (carbon tetrachloride): δ 2.50 (s, CH₃, 3H), 6.35, 6.90 (two doublets of an AB system, Z -CH=CH-, J = 12 Hz, 2H), 7.2-7.7 (m, aromatic, 5H); ms: m/z 186 (M⁺).

Anal. Calcd. for C₁₁H₁₀N₂O: C, 70.97; H, 5.38; N, 15.05. Found: C, 70.95; H, 5.25; N, 15.10.

Acknowledgements.

We thank CNR (Rome) and Ministero P. I. (Rome) for financial support.

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