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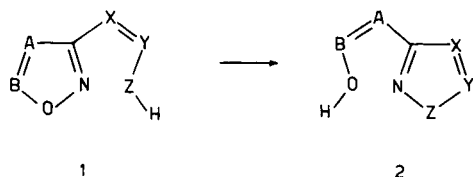
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Photoinduced rearrangements of 1,2,4-oxadiazoles substituted by an XYZ side chain sequence at position 3 of the ring have been recognized. Examples taken out from previous results have been emphasized and some other patterns dealing with a 3-phenoxy and 3-enaminoketone sequence have been investigated. An intermediate species derived from photolysis of the ring O-N bond and characterized by a continuous 6π electron system involving the side chain sequence, was suggested to give ring closure to the rearrangement product.

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Heterocyclic rearrangements of 1,2,4-oxadiazoles containing an XYZ side chain sequence at position 3 of the ring are well documented in literature [1]. According to the Boulton-Katritzky Scheme 1 \rightarrow 2 [2], they have been classified as Azole to Azole interconversions [3], also named and reviewed [1a] as 'mononuclear heterocyclic rearrangements' (*m.h.r.*). Mechanistic studies on these reactions as a typical internal nucleophilic substitution have been also performed [4] and concertedness between the Z-N bond formation and the O-N bond cleavage has been suggested, where electronic effects or base catalysis influence the nucleophilic character of the Z atom.

Scheme 1



Our interest in this class of reactions [1] [4] as well as in photochemical behaviour of five membered heterocycles [5] [6], suggested to us to look at photoinduced rearrangements of 1,2,4-oxadiazoles suitably substituted by an XYZ side chain sequence at position 3 of the ring. Here we will emphasize some examples taken out from our previous studies [6] and report some other patterns that we have now investigated.

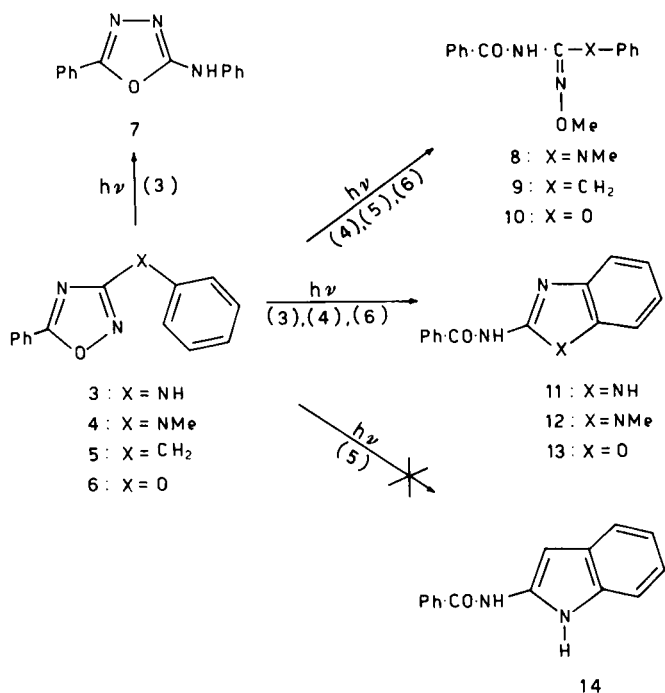
Studying [5] [6] the photochemical behaviour of the 1,2,4-oxadiazole heterocycle in methanol at 254 nm, we pointed out two different photoreactions which depend on the nature and the position of substituents: i) a ring photoisomerization to the 1,3,4-oxadiazole heterocycle by a typical 'ring contraction - ring expansion' pathway [7], which was observed when a tautomerizable group (such as NH_2 , NHR , OH) at the position 3 of the 1,2,4-oxadiazole ring was present; ii) formation of open chain compounds arising from a reaction of the nucleophilic solvent with an intermediate species derived from the photolysis of the O-N bond of the ring [5] [6] [8]. Among the variously substi-

tuted 1,2,4-oxadiazoles, we have investigated [6] the 3-*N*-phenylamino-5-phenyl- (**3**), 3-(*N*-methyl-*N*-phenyl)amino-5-phenyl- (**4**), and 3-benzyl-5-phenyl-1,2,4-oxadiazole (**5**) (Scheme 2). These systems are characterized by a side chain sequence $\text{XYZ} = \text{NCC}$ and CCC , where two carbon atoms are part of a phenyl ring. However, compounds **3** and **4** contain a continuous 6π electron system involving the heterocycle and the side chain, whereas compound **5** does not. This different electron structure caused a different photochemical result [6]. In fact, irradiation of compounds **3** and **4** gave photorearrangement products **11** and **12**, together with the photoisomer 1,3,4-oxadiazole **7** and the open chain compound **8**, respectively. In contrast, irradiation of **5** did not give the indole **14**, as one could have expected by a rearrangement reaction involving the CCC side chain of the benzyl group, but it gave the open chain compound **9**. The observed photorearrangement of compounds **3** and **4** into the benzimidazole system is significant, since it was reported [1a] [9] that a typical *m.h.r.* of compound **3** failed.

In connection with these results, we have now looked at the photorearrangement of the 3-phenoxy derivative **6** ($\text{XYZ} = \text{OCC}$, where carbon atoms are part of a phenyl ring), (Scheme 2). As forecast on the basis of the previous discussion, irradiation of compound **6** in methanol at 254 nm gave a mixture of the benzoxazole **13** and the open chain compound **10**. Clearly, as expected on the basis of our previous claims [6] on ring photoisomerizable 1,2,4-oxadiazoles, formation of the corresponding photoisomer 2-phenyl-5-phenoxy-1,3,4-oxadiazole was not observed. In view of the fact that the nucleophilic solvent may interact with a photolytic intermediate to give open chain products, we have also irradiated compounds **4** and **6** in anhydrous acetonitrile. As expected, the photoreaction in this solvent gave the benzimidazole **12** and the benzoxazole **13**, respectively, as only significant photoproducts.

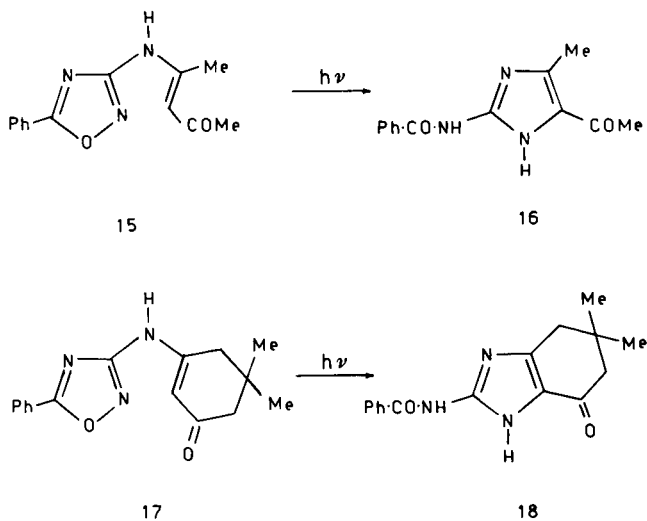
We have next enlarged this photochemical approach to the 1,2,4-oxadiazoles **15** and **17**, where the NCC side chain is part of an enaminoketone moiety (Scheme 3). The base induced *m.h.r.* of **15** into the imidazole **16** is a well estab-

Scheme 2



lished reaction [10] and proceeds through a nucleophilic attack of the side chain carbanion to the nitrogen atom of the ring [10] [11]. Now, we have observed that irradiation at 254 nm in methanol of enaminketones **15** and **17** induced their rearrangement into imidazoles **16** and **18**, respectively, which were isolated as the only significant photoproducts. The ring photoisomerization process as well as formation of methanol addition products was not evidenced.

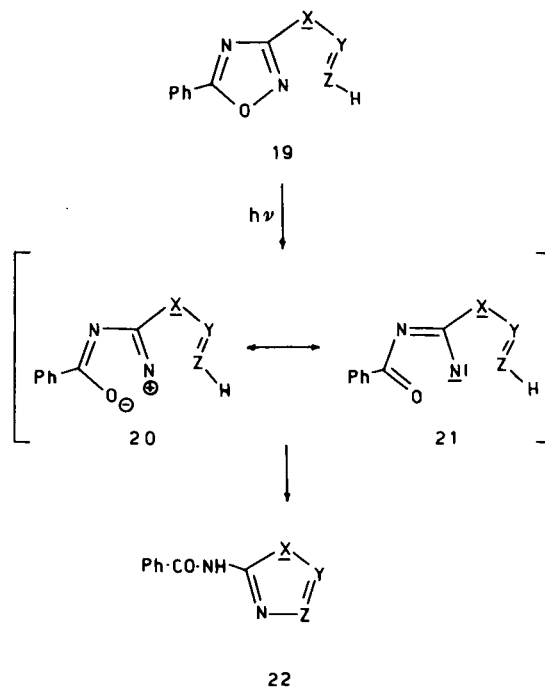
Scheme 3



All of the results so far collected suggest to us to point out some generalization for photoinduced rearrangements of 1,2,4-oxadiazoles substituted by and XYZ sequence at

position 3 of the ring [12]. Unlike thermal or base catalyzed processes, for which a concertedness between the Z-N bond formation and the ring O-N bond cleavage has been suggested, to explain photoinduced rearrangements of the type observed one can reasonably propose an initial photolysis of the weakest O-N bond of the 1,2,4-oxadiazole ring to form an open chain intermediate species, zwitterion type **20** or nitrene type **21** (Scheme 4). This intermediate species, by which formation of different photoproducts may be explained [6], leads to the rearrangement product **22** when ring closure is assisted by an aromatic transition state involving the XYZ sequence.

Scheme 4



EXPERIMENTAL

Melting points were determined on a Kofler hot-stage apparatus. The ir spectra (Nujol) were determined with a Perkin-Elmer 257 instrument, 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. Flash chromatography [13] was performed on Merk silica gel (0.040-0.063 mm). Light petroleum refers to that fraction boiling in the range 40-60°. Methanol [14] and acetonitrile [14] were purified as reported in literature.

3-Phenoxy-5-phenyl-1,2,4-oxadiazole (**6**) was prepared by reacting 3-chloro-5-phenyl-1,2,4-oxadiazole [15] with sodium phenate in refluxing dioxane (6 hours). After removing the solvent under reduced pressure, the residue was taken up with water and filtered. The crude material was chromatographed by using a mixture of light petroleum-ethyl acetate (30/1) as eluent affording compound **6** (80%), mp 60-61° (from light petroleum); nmr (deuteriochloroform): δ 7.2-8.2 (m, aromatic, 10 H); ms: m/z (abundance) 238 (4, M⁺), 105 (33), 77 (100).

Anal. Calcd. for C₁₄H₁₀N₂O₂: C, 70.59; H, 4.20; N, 11.76. Found: C, 70.50; H, 4.10; N, 11.60.

The enaminketone **15** [10] was prepared as reported in the literature. By the same procedure, the reaction between 3-amino-5-phenyl-1,2,4-oxadiazole and dimedone gave the enamino ketone **17** (80%), mp 260° (ethanol); ir: 3260, 3190 cm⁻¹ (NH), 1610 cm⁻¹ (CO); nmr (pyridine-d₅): δ 2.3 (s, 2 x CH₃, 6 H), 2.6 (s, 2 x CH₂, 4H), 5.8 (s, CH, 1 H), 6.2-7.1 (m, aromatic, 5 H), 10.3 (s, NH, 1 H).

Anal. Calcd. for C₁₆H₁₇N₃O₂: C, 67.82; H, 6.05; N, 14.83. Found: C, 67.60; H, 5.90; N, 14.70.

Photochemical Reactions.

General Procedure.

A solution of the sample [500 mg (100 mg compound **17**)] in freshly prepared anhydrous methanol or acetonitrile (100 ml), in a quartz tube, was degassed by nitrogen bubbling (20 minutes), and then irradiated at 254 nm in an immersion well apparatus with a low-pressure mercury lamp (Helios Italquartz, 17 W). Irradiation times were chosen in order to avoid formation of secondary photoproducts. The solvent was removed under reduced pressure and the residue chromatographed by using a mixture of light petroleum-ethyl acetate at varying ratios as eluent. Minor components were discarded.

Irradiation of Compound **6** in Methanol.

Irradiation for 2 hours gave unchanged starting material (55%), compound **10** (25%) and compound **13** (15%), mp 186-190°, lit [16], mp 186-190°, compared with an authentic sample [16].

Compound **10** had mp 40° (from light petroleum); ir: 3300 (NH), 1670 cm⁻¹ (C=O); nmr (deuteriochloroform): δ 3.8 (s, CH₃, 3 H), 7.1-8.0 (m, aromatic, 10 H), 8.5 (br s, NH, 1 H); ms: m/z (abundance) 270 (17, M⁺), 134 (43), 106 (93), 105 (97), 94 (95), 93 (54), 77 (100).

Anal. Calcd. for C₁₅H₁₄N₂O₃: C, 66.66; H, 5.19; N, 10.37. Found: C, 66.80; H, 5.10; N, 10.20.

Irradiation of Compounds **4** and **6** in Acetonitrile.

Irradiation of compound **4** (2 hours) gave unchanged starting material (85%) and then compound **12** (10%), mp 157-158°, lit [6], mp 157-158°.

Irradiation of compound **6** (2 hours) gave unchanged starting material (80%) and then compound **13** (7%).

Irradiation of Compound **15** in Methanol.

Irradiation for 8 hours gave unchanged starting material (80%) and then compound **16** (10%), mp 221°, lit [10], mp 221°, compared with an available sample obtained by a base induced rearrangement of **15**.

Irradiation of Compound **17** in Methanol.

Irradiation for 10 hours gave unchanged starting material (70%) and then **18** (20%), mp 220° (from ethanol); ir: 3240, 3260 (NH), 1640, 1685 (CO) cm⁻¹; nmr (DMSO-d₆): δ 1.1 (s, 2 x CH₃, 6 H), 2.3 (s, CH₂, 2 H), 2.7 (s, CH₂, 2 H), 7.4-8.1 (m, aromatic, 5 H), 12.0 (s, 2 x NH, 2 H).

Anal. Calcd. for C₁₆H₁₇N₃O₂: C, 67.82; H, 6.05; N, 14.83. Found: C, 67.90; H, 6.10; N, 14.90.

Acknowledgements.

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