HETEROCYCLIC PHOTOREARRANGEMENTS - PHOTOCHEMICAL BEHAVIOUR OF SOME 3-ACETYLAMINO-5-ARYL-1,2,4-OXADIAZOLES. A PHOTOINDUCED *ISO*-HETEROCYCLIC REARRANGEMENT

Silvestre Buscemi, Gabriella Macaluso, and Nicolò Vivona*
Dipartimento di Chimica Organica, Università di Palermo,
Via Archirafi 20, 90123 Palermo, Italy

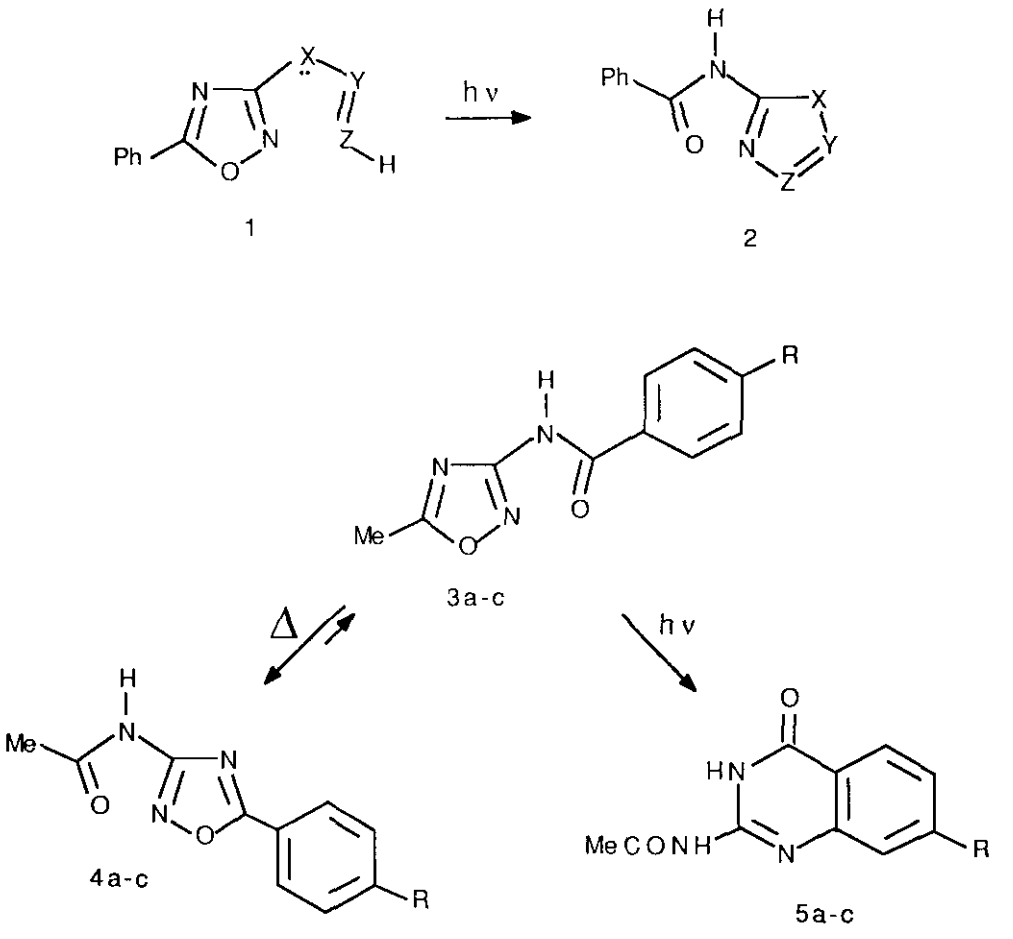
Abstract -The photochemical behaviour of some 3-acetylamino-5-aryl-1,2,4-oxadiazoles in methanol at 254 nm has been investigated. A photoinduced rearrangement to the corresponding 2-acetylaminoquinazolin-4-one derivatives has been pointed out and explained as proceeding through a preliminary *iso*-heterocyclic photoinduced rearrangement to the corresponding 3-aroylamino-5-methyl-1,2,4-oxadiazoles, followed by a subsequent photoreaction of the latter. Some mechanistic considerations are reported.

Studying[1,2] the photochemical behaviour of five membered rings and in connection with our interest[3] in heterocyclic rearrangements, we have recently[4] focused our attention to the photoinduced rearrangements of 1,2,4-oxadiazoles containing suitable side chains at the position 3 of the ring. In this context, we have reported[4] photorearrangements of 1,2,4-oxadiazoles of type **1** into benzimidazoles, benzoxazoles, and imidazoles. We have also extended[5] this photochemical approach to the 3-acylamino-1,2,4-oxadiazoles, for which a thermally induced rearrangement of iso-heterocyclic type had been reported[6,7]. Preliminary results[5] concerning with the photochemical behaviour of 3-aroylamino-5-methyl-1,2,4-oxadiazoles **3** has revealed the difference between thermally and photoinduced rearrangement of these systems. The thermally induced rearrangement of **3a-c** gave the corresponding 3-acetylamino-5-aryl-1,2,4-oxadiazoles **4a-c,** by involving the NCO side chain sequence of the aroylamino group, as a reversible *iso*-heterocyclic reaction significantly shifted towards the 5-aryl-substuituted oxadiazoles[5,6]. However, the irradiation

of **3a-c** did not give the *iso*-heterocyclic rearrangement but gave a ring closure involving carbon atoms of the side chain aryl ring, leading to acetylaminoquinazolin-4-ones **5a-c**[5].

Aiming to have more insight into the photochemistry of 3-acylamino-1,2,4-oxadiazoles, particularly into a photochemical approach to the *iso*-heterocyclic process, we have now extended our investigation to 3-acetylamino-5-aryl-1,2,4-oxadiazoles **4** which are to the corresponding *iso*-heterocyclic components of the 3-aroylamino-5-methyl-1,2,4-oxadiazoles **3**.

Scheme 1



a; R = H b; R = Me c; R = MeO

RESULTS AND DISCUSSION

Likewise irradiation of 3-aroylamino-oxadiazoles **3**, irradiations of 3-acetylamino-oxadiazoles **4** have been carried out in anhydrous methanol at 254 nm by using low pressure Hg lamps (17 W) in an immersion apparatus, at running water temperature. After 18 h of irradiation, compounds **4a,b** gave the corresponding 2-acetylaminoquinazolinones **5a** (90%) and **5b** (80%), respectively. On the other hand, compound **4c** showed a slower photoconversion into the corresponding acetylaminoquinazolinone **5c**. In fact, after 50 h of irradiation, a chromatographic purification of the photoreaction mixture gave compound **5c** (50%), together with some amounts (30%) of p-methoxybenzoic acid. However, we have observed that irradiation of compound **4c** for 10 h allowed us to isolate high yields (70%) of the 3-aroylamino derivative **3c**, *i.e.*, the *iso*-heterocyclic component together with a small amount (10%) of the acetylaminoquinazolinone **5c**. This result means that formation of the rearrangement product **5c** from 3-acetylaminooxadiazole **4c** is a slow process, but the photoreaction of compound **4c** is not; moreover, formation of the quinazolinone species **5c** from **4c** has to be interpreted as proceeding with a preliminary *iso*-heterocyclic rearrangement of **4c** into the corresponding 3-aroylaminooxadiazole **3c**. A confirmation of this statement has been provided by following the photoreaction of compounds **4a,b** as a function of irradiation time. Figure 1 reports the composition (%) of the photoreaction mixture analysed by means of hplc. For comparison we report in Figure 2 the composition (%) of the photoreaction mixture of the irradiation of 3-benzoylamino derivative **3a**.

All these results allow us to point out some conclusive comments: as previously reported[5], the irradiation of the 3-aroylamino derivatives **3a-c** gave only the rearrangement to the quinazolin-4-one system. A photoinduced *iso*-heterocyclic rearrangement to 3-acetylaminooxadiazoles was not observed (see Figure 2). The presence of trace amounts of compound **4a** may be explained as result of a thermal process. On the other hand, irradiation of 3-acetylamino-5-aryl-1,2,4-oxadiazoles **4a-c** gave at first the corresponding 3-aroylamino compounds **3a-c**, whose concentration increases until values of 25% (for **4a**; see Figure 1A), 40% (for **4b**; see Figure 1B), and 70% (for **4c**).

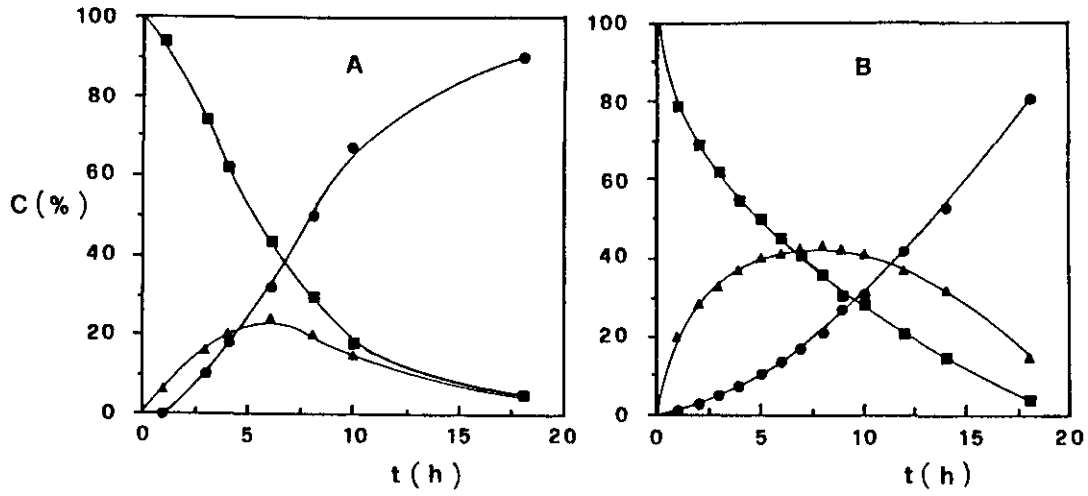


Figure 1 - Composition (%) of the photoreaction mixture as a function of irradiation time. A, irradiation of **4a**; B, irradiation of 4b. (■ = **4a,b**; ▲ = **3a,b**; ● = **5a,b**)

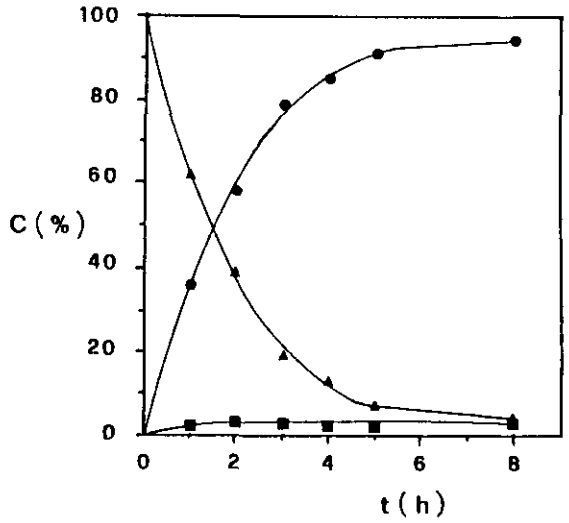
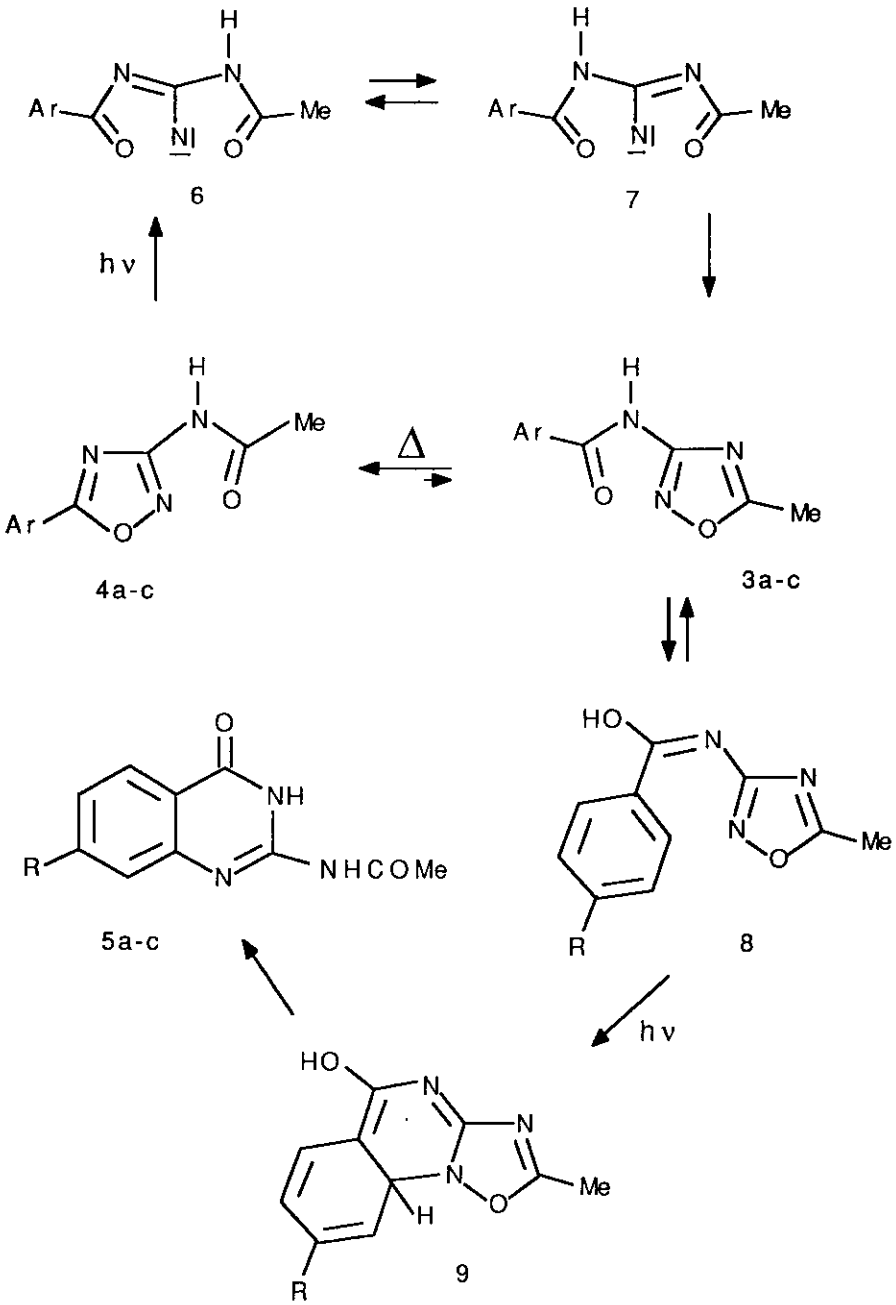


Figure 2 - Composition (%) of the photoreaction mixture of the irradiation of compound **3a** as a function of irradiation time. (▲= **3a**; ■ = **4a**; ● = **5a**)

Therefore, formation of the quinazolin-4-one system, which was observed both from 3-aroylamino-5-methyl-1,2,4-oxadiazoles and from 3-acetylamino-5-aryl-1,2,4-oxadiazoles, has to be interpreted as proceeding through the 3-aroylamino component. Moreover, as to the *iso*-heterocyclic process, we observed that the irradiation caused the rearrangement of the 3-acetylamino-5-aryl system **4** to 3-aroylamino-5-methyl component **3**, *i.e.*, in the opposite direction if compared with the thermally induced rearrangement.

The whole of these results may be rationalised in terms of the Scheme 2. The photoinduced *iso*-heterocyclic rearrangement may be explained as involving open chain nitrene intermediates of type **6** (which arises from the oxadiazole ring opening by the O-N bond

Scheme 2



cleavage in compounds **4**), and **7** (which collapses to the oxadiazole heterocycle of the type **3** by ring closure involving an O-N bond formation). On the other hand, formation of the quinazolin-4-one system **5** from 3-aroylamino-5-methyl-1,2,4-oxadiazoles **3** may be interpreted as proceeding through an initial 6π heteroelectrocyclic ring closure into **9**, followed by a subsequent ring opening of the 1,2,4-oxadiazole moiety. Open chain species of the type **6** or **7** arising from photolysis of the oxadiazole ring should not be involved in this rearrangement. The different photochemical reactivity of the 3-acetylamino-5-aryl- and 3-aroylamino-5-methyl-1,2,4-oxadiazole systems may be explained on the basis of different chromofores and/or different excited states which could be involved in the two oxadiazole series. Results on this aspect of photochemistry of 3-acylamino-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, ^{1}H nmr spectra (60 MHz) with a Varian EM 360 spectrometer (tetramethylsilane as internal standard). 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/min, monitoring the optical density at 230 nm (for compounds **3a** and **4a**), or at 254 nm (for compounds **3b,c** and **4b,c**). Flash chromatography[8] was performed on Merck silica gel (0.040-0.063 mm). Light petroleum refers to that fraction boiling in the range 40-60°C. Methanol was purified as reported[9] and was used freshly prepared. As for compounds **3**, **4**, and **5**, see the previous paper in this Journal[5]. Compound **4a** had λ_{max} 244 nm (ε_{max} 15,800, ε_{254} 14,600); compound **4b** had λ_{max} 262 nm (ε_{max} 18,400, ε_{254} 17,000); compound **4c** had λ_{max} 280 nm (ε_{max} 25,200, ε_{254} 10,600).

Photochemical Reactions - General Procedure.

A solution of the oxadiazole (200 mg) in a freshly prepared anhydrous methanol (100 ml), in a quartz tube, was degassed by nitrogen bubbling (20 min), and then irradiated at 254 nm in an immersion well apparatus, equipped with a running water system, 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. Minor components were discarded. Quantitative hplc analyses for drawing figures 1 and 2 were performed by irradiation of compounds **4a,b** and **3a** respectively, in similar experimental conditions and correction factors were determined by using pure samples of the corresponding compounds **3**, **4**, and **5**.

Irradiation of Compound **4a**.

Irradiation for 18 h gave compound **5a** (90%), mp 277-280°C (from ethanol) (lit[5,10] mp 277-280°C).

Irradiation of Compound **4b**.

Irradiation for 18 h gave compound **5b** (80%), mp 278-284°C (from ethanol) (lit[5] mp 278-284°C).

Irradiation of Compound **4c**.

Irradiation for 50 h gave p-methoxybenzoic acid (30 %), and compound **5c** (50%), mp 282-286°C (from ethanol) (lit[5] mp 282-286°C). Irradiation for 10 h gave the aroylamino derivative **3c** (70%), and compound **5c** (10%).

ACKNOWLEDGEMENTS

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

REFERENCES

1) S. Buscemi, M. G. Cicero, N. Vivona, and T. Caronna, *J. Chem. Soc., Perkin Trans. 1*, 1988, 1313.

2) S. Buscemi, M. G. Cicero, N. Vivona, and T. Caronna, *J. Heterocycl. Chem.*, 1988, **25**, 931.

3) M. Ruccia, N. Vivona, and D. Spinelli, *Adv. Heterocycl. Chem.*, 1981, **29**, 141; N. Vivona, S. Buscemi, V. Frenna, and M. Ruccia, *J. Chem. Soc., Perkin Trans. 1*, 1986, 17, and references cited therein.

4) S. Buscemi and N. Vivona, *J. Heterocycl. Chem.*, 1988, **25**, 1551.

5) S. Buscemi and N. Vivona, *Heterocycles*, 1989, **29**, 737.

6) N. Vivona, G. Cusmano, M. Ruccia, and D. Spinelli, *J. Heterocycl. Chem.*, 1975, **12**, 985.

7) N. Vivona, M. Ruccia, G. Cusmano, M. L. Marino, and D. Spinelli, *J. Heterocycl. Chem.*, 1975, **12**, 1327.

8) W.C. Still, M. Kahn, and A. Mitre, *J. Org. Chem.*, 1978, **43**, 2923.

9) A. Weissberger, 'Technique of Organic Chemistry,' vol. 7, 2nd. ed., Interscience, New York, 1963.

10) R. J. Grout and M. W. Partridge, *J. Chem. Soc. (C)*, 1960, 3540.

Received, 10th March, 1989