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HETEROCYCLIC PHOTOREARRANGEMENTS - PHOTOINDUCED REARRANGEMENTS OF SOME 3-AROYLAMINO-5-METHYL-1,2,4-OXADIAZOLES[1]

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Abstract - The photochemical behaviour of some 3-aroylamino-5-methyl-1,2,4-oxadiazoles in methanol at 254 nm has been studied. On irradiation, the oxadiazoles underwent a photorearrangement reaction to the corresponding 2-acetylaminoquinazolin-4-one derivatives.

Heterocyclic rearrangements of suitably substituted azoles have attracted a great amount of attention of organic chemists because of their interest in synthesis as well as in mechanistic investigations[2]. In this context, the azole to azole interconversions of the general type **1** ⟶ **2**[3] have been widely investigated[4].

Following our interest in this field, and in connection with our studies[5,6] on photochemical behaviour of 1,2,4-oxadiazole heterocycles, we have recently reported[7] some examples of photoinduced rearrangements of suitably substituted 1,2,4-oxadiazoles. In fact, we have achieved photorearrangements of 1,2,4-oxadiazoles containing side chains such as 3-N-phenylamino **3** (XYZ = NCC), 3-phenoxy **3** (XYZ = OCC), and 3-enaminoketone **3** (XYZ = NCC), into benzimidazoles, benzoxazoles, and imidazoles, respectively. An intermediate species arising from photolysis of the ring O-N bond, was suggested to give the rearrangement product **4** by a 6π ring closure involving the XYZ side chain[7].

Aiming at a photochemical approach to this class of heterocyclic rearrangements, and in the context of our interest in photochemistry of five membered heterocycles, we have now planned to investigate the photochemical behaviour of 3-acylamino-1,2,4-oxadiazoles. In this paper we report some preliminary results dealing with the irradiation of the 3-aroylamino-5-methyl-1,2,4-oxadiazoles **6a-c**.

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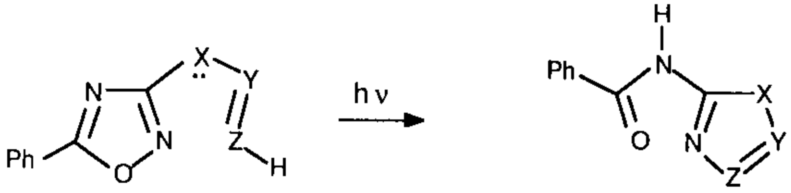

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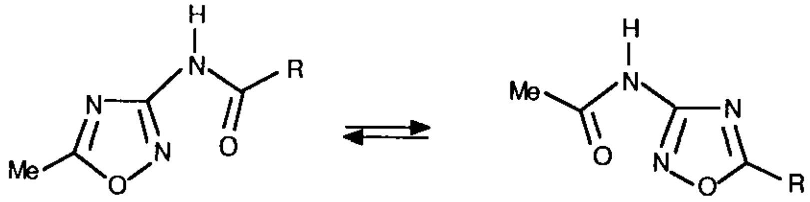


5

R = Me

5

6a-c

7a-c

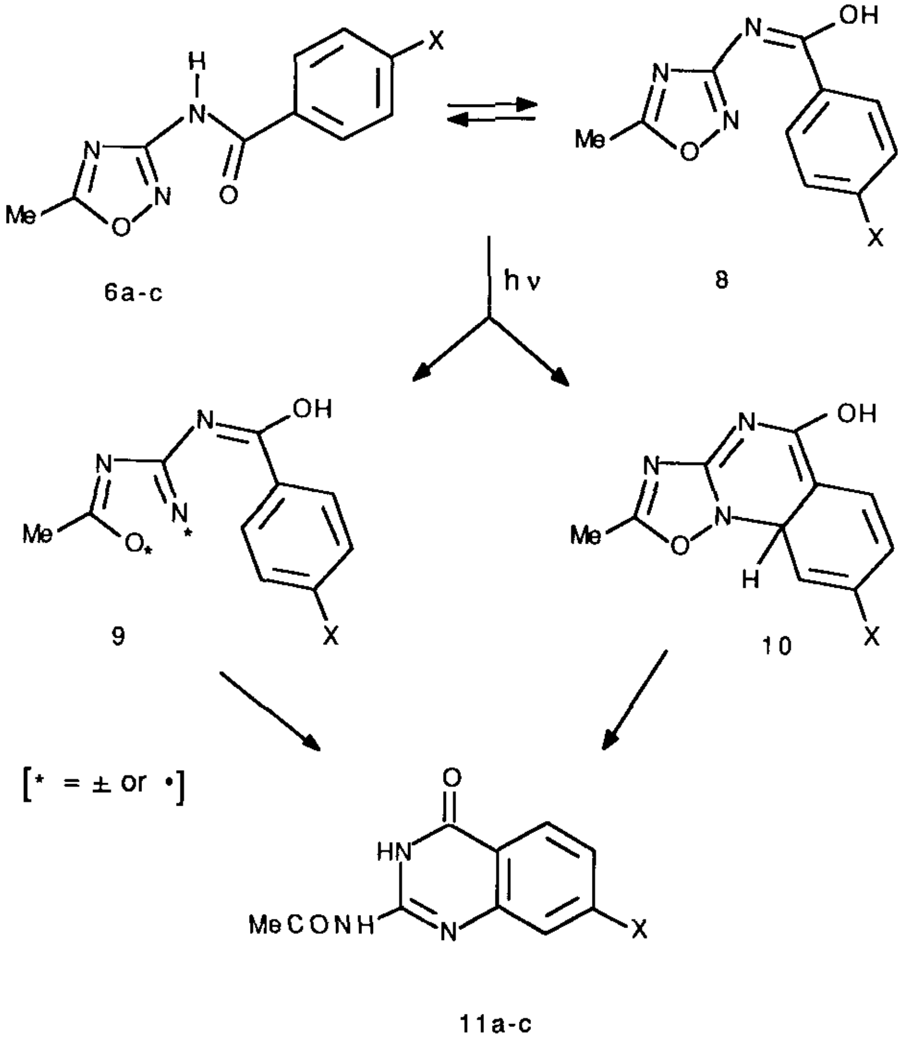
6,7	R
a	Ph
b	p-MeC_6H_4
c	p-MeOC_6H_4

It is known[8,9] that 3-acylamino-1,2,4-oxadiazoles (**1**; ABD = XYZ = NCO) have furnished interesting examples of thermally induced rearrangements of *iso*-heterocyclic type as a reversible reaction. In fact, a degenerate process involving a symmetric species as a transition state has been pointed out[9] by means of nmr spectroscopy on the anion of 3-acetylamino-5-methyl-1,2,4-oxadiazole **5**, which showed two methyl signals coalescing at 112°C in DMSO. Moreover, 3-benzoylamino-5-methyl-1,2,4-oxadiazole **6a** on melting gave 3-acetylamino-5-phenyl-1,2,4-oxadiazole **7a** as an equilibrium mixture, where the 5-phenyl substituted oxadiazole **7a** was the significantly favoured component[8]. In the photochemistry of the 3-aroylamino-5-methyl-1,2,4-oxadiazoles **6a-c** one should expect the *iso*-heterocyclic process too, leading to the corresponding 3-acetylamino-5-aryl-1,2,4-oxadiazoles **7a-c**. However, taking into account the photochemical behaviour of the 1,2,4-oxadiazole ring, a different heterocyclic closure, involving the aryl ring of the aroylamino moiety, could also be operative.

RESULTS

The irradiations of oxadiazoles **6a-c** have been carried out in anhydrous methanol at 254 nm by using low pressure Hg lamps (17 W) in an immersion apparatus, where the samples were cooled with running water in order to avoid a possible thermal process. After 9 h of irradiation, compounds **6a,b** gave high yields (80-90%) of the corresponding 2-acetylamino-quinazolinones **11a,b**, whose structure was assigned on the basis of analytical, spectroscopic and chemical evidences (see experimental). HPLC analysis of the photoreaction mixture revealed only few amounts of the corresponding *iso*-heterocyclic compounds **7a,b**, whose formation may be explained as a result of a thermal process. On the other hand, the ring photoisomerization[5,6] to the corresponding 1,3,4-oxadiazole system was not observed. Compound **6c** exhibited a much slower photoreaction[10]. In fact, after 40 h of irradiation, a chromatographic purification of the reaction mixture gave the rearrangement product **11c** in 50% yield, together with some amounts of unreacted starting material (20%).

These results, which claim the synthetic value of the observed photoreaction, point out the difference between thermal and photoinduced rearrangement of 3-aroylamino-5-methyl-1,2,4-oxadiazoles **6a-c**. In fact, as already observed[8] for **6a**, compounds **6a-c**, on melting as well as on refluxing methanol, gave only the product of *iso*-heterocyclic process , leading to the corresponding 3-acetylamino derivatives **7a-c**, as a result of a reversible



reaction significantly shifted towards the 5-aryl substituted oxadiazoles **7a-c**[11]. Unlike this thermal process, which involves the NCO sequence of the aroylamino group, in the case of the photoinduced rearrangement a different side chain sequence of the aroylamino moiety has to be considered. Therefore, for the observed photorearrangement, one could reasonably suggest a 6π heteroelectrocyclic ring closure involving a photolytic intermediate **9**, arising from the cleavage of the ring O-N bond, and the aryl system of the aroylamino moiety. However, an alternative pathway could be envisaged in an initial 6π heteroelectrocyclic ring closure into **10**, followed by a subsequent ring opening to the rearrangement products **11** through a cleavage of the O-N bond present in the oxadiazole moiety of **10** (see scheme).

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 instrument, by using a C-18 SIL-X-10 Perkin-Elmer column. Flash chromatography[12] 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[13] and was used freshly prepared.

Compounds **6a-c** were prepared by reacting 3-amino-5-methyl-1,2,4-oxadiazole with the appropriate aroyl chloride in anhydrous benzene containing equimolar amounts of pyridine at room temperature, following the procedure previously used for **6a**[8].

Compound **6a** had mp 144°C (from benzene)(lit.[8] mp 144°C); uv nm: λ_{max} 233 (ε_{max} 14,800, ε_{254} 7,400).

Compound **6b** had mp 137°C (from benzene); ir: 3240,3180 and 3100 cm^{-1} (NH), 1680 cm^{-1} (CO); uv nm: λ_{max} 245 (ε_{max} 17,700, ε_{254} 14,500); ^{1}H nmr (DMSO)

∂: 2.35 and 2.55 (2s,6H,2CH_3), 7.2-8.0 (m,4H,aromatic), 11.35 (s,1H,NH). Anal. Calcd for $C_{11}H_{11}N_3O_2$: C, 60.83; H, 5.07; N, 19.35. Found C, 60.70, H, 5.10, N, 19.20.

Compound **6c** had mp 145-148°C (from benzene); ir: 3295, 3280, and 3210 cm^{-1} (NH), 1670 cm^{-1} (CO); uv nm: λ_{max} 264 (ε_{max} 20,300, ε_{254} 17,400); ^1H nmr (DMSO) ∂: 2.55 and 3.85 (2s,6H,2CH_3), 6.9-8.1 (m,4H,aromatic), 11.00 (s,1H,NH). Anal. Calcd for $C_{11}H_{11}N_3O_3$: C, 56.65; H, 4.72; N, 18.03. Found C, 56.50, H, 4.80, N, 18.10.

Compounds **7a-c** were prepared by acetylation of the appropriate 3-amino-5-aryl-1,2,4-oxadiazole, as for **7a**[8].

Compound **7a** had mp 164°C (from benzene)(lit.[8] mp 164°C).

Compound **7b** had mp 193°C (from benzene); ir: 3240,3180, and 3100 cm^{-1} (NH), 1675 cm^{-1} (CO); ^1H nmr (DMSO) ∂: 2.10 and 2.40 (2s,6H,2CH_3), 7.2-8.0 (m,4H,aromatic), 11.20 (s,1H,NH). Anal. Calcd for $C_{11}H_{11}N_3O_2$: C, 60.83; H, 5.07; N, 19.35. Found C, 60.75, H, 5.00, N, 19.30.

Compound **7c** had mp 168°C (from benzene); ir: 3230,3210, and 3180 cm^{-1} (NH), 1690 cm^{-1} (CO); ^1H nmr (DMSO) ∂: 2.10 and 3.85 (2s,6H,2CH_3), 7.0-8.1 (m,4H, aromatic), 11.20 (s,1H,NH). Anal. Calcd for $C_{11}H_{11}N_3O_3$: C, 56.65; H, 4.72; N, 18.03. Found C, 56.70, H, 4.60, N, 18.00.

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). HPLC analysis performed by using authentic samples revealed the presence of few amounts of compounds **7a-c**. 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.

Irradiation of Compound **6a**.

Irradiation for 9 h gave compound **11a** (90%), mp 277-280°C (from ethanol); ir: 3220 and 3180 cm^{-1} (NH), 1660 cm^{-1} (C=O); ^1H nmr (DMSO) ∂: 2.15 (s,3H,CH_3), 7.2-8.2 (m,4H,aromatic), 11.80 (br s,2H,2NH) Anal. Calcd for $C_{10}H_9N_3O$: C, 64.17; H, 4.81; N, 22.46. Found C, 64.10, H, 4.70, N, 22.30. A sample of **11a** was also prepared by acetylation of the 2-amino-3,4-dihydroquinazolin-4-one[14].

Irradiation of Compound **6b**.

Irradiation for 9 h gave compound **11b** (80%), mp 278-284°C (from ethanol); ir: 3210, 3180, 3140 and 3120 cm^{-1} (NH), 1660 and 1630 cm^{-1} (C=O); ^1H nmr (DMSO) ∂: 2.30 and 2.55 (2s,6H,2CH_3), 7.2-8.2 (m,3H,aromatic), 11.80 (br s,2H,2NH). Anal. Calcd for $C_{11}H_{11}N_3O_2$: C, 60.83; H, 5.07; N, 19.35. Found C, 60.85, H, 5.00, N, 19.20.

Irradiation of Compound **6c**.

Irradiation for 40 h gave unreacted starting material (20%), p-methoxybenzoic acid (25 %), and compound **11c** (50%), mp 282-286°C (from ethanol); ir: 3210, 3180, 3140 and 3100 cm^{-1} (NH), 1640 and 1620 cm^{-1} (C=O); ^1H nmr (DMSO) ∂: 2.20 and 3.85 (2s,6H,2CH_3), 6.9-8.2 (m,3H,aromatic), 11.80 (br s,2H,2NH). Anal. Calcd for $C_{11}H_{11}N_3O_3$: C, 56.65; H, 4.72; N, 18.03. Found C, 56.60, H, 4.70, N, 18.10.

ACKNOWLEDGEMENTS

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REFERENCES AND NOTES

1) Part of a poster communication presented at the XIIIth European Colloquium on Heterocyclic Chemistry, Fribourg, 26-28 September, 1988.
2) See, *e.g.*, H.C van der Plas, 'Ring Transformations of Heterocycles,' vol. 1, Academic Press, New York, 1973; 'Aromatic and Heteroaromatic Chemistry,' Specialist Periodical Reports, vols. 1-7, Chemical Society, London; A. Padwa, 'Rearrangements in Ground and Excited States',

vol. 3, ed by P de Mayo, Academic Press, Inc., New York, 1980, p. 501; G. L'Abbé, *J. Heterocycl. Chem.*, 1984, **21**, 627.

3) A.J. Boulton, A. R. Katritzky, and A. M. Hamid, *J. Chem. Soc. C*, 1967, 2005 ; A.J. Boulton, 'Lectures in Heterocyclic Chemistry', 1974, 4th International Congress of Heterocyclic Chemistry, Salt Lake City, Utah, U.S.A., July 1973; A. S. Afridi, A.R. Katritzky, and C.A. Ramsden, *J. Chem. Soc., Perkin Trans., 1*, 1976, 315. For interconversion of the type azole to azoline, involving a saturated XYZ side chain sequence, see: I. Bata, G. Héja, P. Kiss, and D. Korbonits, *J. Chem. Soc., Perkin Trans., 1*, 1986, 9.

4) See, *e.g.*, 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. For mechanistic investigations on this subject, see: V. Frenna, N. Vivona, G. Consiglio, A. Corrao, and D. Spinelli, *J. Chem. Soc., Perkin Trans. 2*, 1981, 1325; V. Frenna, N. Vivona, A. Corrao, G. Consiglio, and D. Spinelli, *J. Chem. Research*, 1981, (S), 308, (M) 3550; V. Frenna, N. Vivona, A. Caronia, G. Consiglio, and D. Spinelli, *J. Chem. Soc., Perkin Trans., 2*, 1983, 1203; V. Frenna, N. Vivona, G. Macaluso, D. Spinelli, and G. Consiglio, *J. Chem. Soc., Perkin Trans., 2*, 1987, 537; V. Frenna, S. Buscemi, and C. Arnone, *J. Chem. Soc., Perkin Trans., 2*, 1988, 1683.

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

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

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

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

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

10) Kinetic studies and quantum yield measurements for the observed photoreactions will be reported.

11) The composition of equilibrium mixtures, determined by quantitative HPLC analysis, showed values around 10% for **6** and 90% for **7**. (Unpublished results).

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

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

14) Imperial Chemical Industries Ldt., Japan. Kokai, 1978, 37, 695 (*Chem. Abstr.*, 1978, **89**, 146922m).

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