

PHOTOCHEMICAL REARRANGEMENT OF ISOXAZOL-5-YLHYDRAZINES
AND N-(3-METHYL-4-PHENYLISOXAZOL-5-YL)ACETAMIDINE

G. Adembri*, A. Camparini, D. Donati, F. Ponticelli
(Istituto di Chimica Organica dell'Università, Siena, Italy)

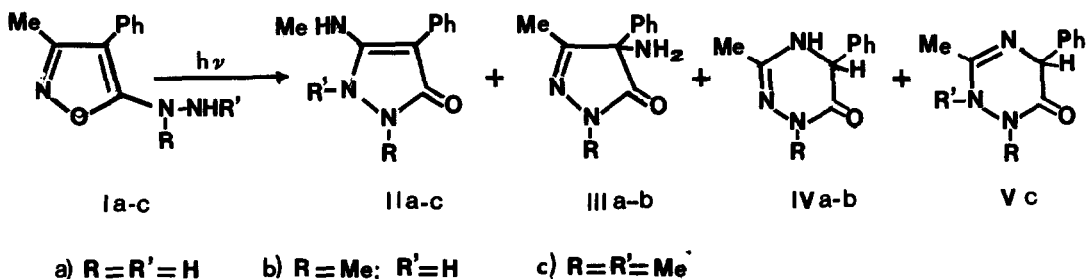
and P. Tedeschi

(Centro di studi del C.N.R. sulla chimica e la struttura dei composti eterociclici e loro applicazioni, c/o Istituto di Chimica Organica della Università di Firenze, Italy)

As reported in our preceding papers (1,2), thermal rearrangement of isoxazol-5-ylhydrazines leads, via the corresponding 2H-azirine-2-carbohydrazides, to 1- and 4-amino-2-pyrazolin-5-ones and to tetrahydro-1,2,4-triazin-6-ones. Different yields were obtained, depending on the types and the positions of the substituents of the isoxazole ring or of the hydrazinic group as well as on the experimental conditions.

The purpose of the present study was to compare the thermal with the photochemical behaviour of the isoxazole derivatives having nucleophilic substituents at the 5- position, owing to the strong synthetic and mechanistic interest in the isoxazole ring transformations (3). Results concerning the photochemical rearrangement of some 3-methyl-4-phenyl derivatives bearing differently substituted hydrazinic or acetamidinic groups at the 5- position, are here reported.

SCHEME 1



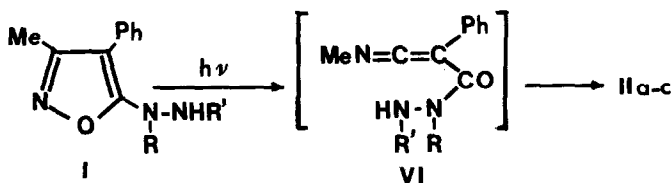
U.V. irradiation of Ia-c (4) caused a rapid disappearance of the starting material. From the crude reaction mixture we were able to isolate two or three of the compounds reported in the scheme 1. The yields of these products, together with those obtained by thermal reaction (2), are shown in the table:

% Yields of photochemical (thermal) products				
Isoxazol-5-yl- hydrazine	II	III	IV	V
Ia	19 (--)	16 (21)	38 (22)	
Ib	16 (--)	40 (60)	30 (26)	
Ic	5 (--)			45 (80)

As evident from the table, U.V. irradiation, beside the products III, IV, V, obtained also by thermal rearrangement, afforded an other type of compound i.e. the 3-methylamino-pyrazolones IIa-c. The structures of these compounds were spectroscopically and synthetically proved (5).

The mechanistic route of the photochemical formation of III, IV, V is supposed to be similar to the thermal one already proposed (2). On the other hand, in order to explain the formation of IIa-c, a methyl shift from the atom at 3-position to the nitrogen of the isoxazole ring is required. The intermediate of the reaction is believed to be the ketenimine VI which may undergo nucleophilic intramolecular attack from the β -hydrazinic nitrogen leading to the final product:

SCHEME 2



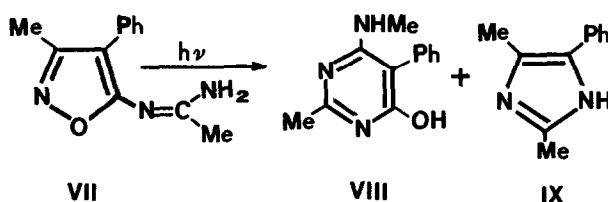
Ketenimines as intermediates are proved to be formed by irradiation of 3-methylbenzoxazole (6), of 3-methyl-4,5,6,7-tetrahydro-1,2-benzisoxazole (7) and of 3,5-dimethylisoxazole (8), and to add subsequently nucleophilic reagents as water, alcohols or amines.

In the case of the isoxazolylhydrazines, the presence of an external nucleophile as C_2H_5OH or piperidine during the irradiation, did not prevent the formation

of IIa-c and the addition products on the ketenimine were not isolated, owing to the easier intramolecular cyclization.

In order to infer the generality of the photochemical 1,2-shift of the 3-methyl in other isoxazole derivatives, we synthesized (5) and irradiated in a polar aprotic solvent the acetamidine VII obtaining the 4-methylaminopyrimidine VIII and the imidazole IX in 17% and 43% yield respectively (4) (Scheme 3).

SCHEME 3



The structure of VIII was established on the basis of spectroscopic data and confirmed by synthesis (5); the structure of IX was proved by comparison with an authentic sample (9). The occurrence of compound VIII is easy understood on the basis of the same reaction path leading to compounds IIa-c, as shown in Scheme 2.

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References and Notes

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- 3) T. Nishiwaki, Synthesis, 20 (1975) and references cited therein.
- 4) A solution of compounds Ia-c in anhydrous ether or absolute ethanol was irradiated by a low pressure mercury lamp in a quartz reaction vessel. A solution of VII in CHCl_3 was irradiated by the light of a medium pressure mercury lamp filtered by a CuSO_4 aqueous solution. In both cases N_2 was allowed to bubble through the solution. The progress of the reaction was monitored

by TLC and stopped after the disappearance of the starting material.

5) Compound IIa: M.p. 225-226°C (ethanol/ether); IR(KBr) 3440, 3300-2300, 1580, 1530 cm^{-1} ; NMR (DMSO- d_6) δ 2.74(d, J=5Hz, 3H), 6.29(q, J=5Hz, 1H), 6.90-7.70 (m, 5H), 9.00(br. s, 2H) ppm.

Compound IIb: M.p. 168-170°C (chloroform/light petroleum); IR(KBr) 3220, 3150-2400, 1630, 1570, 1515 cm^{-1} ; NMR (CDCl₃) δ 2.77(d, J=5Hz, 3H), 3.21(s, 3H), 4.05(s, 1H), 4.33(br. s, 1H), 7.05-7.45 (m, 5H) ppm.

Compound IIc: M.p. 180-182°C (sublimed in vacuo); IR(KBr) 3250, 1640, 1605, 1580, 1550 cm^{-1} ; NMR (CDCl₃) δ 2.73(d, J=5.5Hz, 3H), 2.97(s, 3H), 3.12(s, 3H), 4.80(q, J=5.5Hz, 1H), 7.13-7.53 (m, 5H) ppm.

Compound VII: M.p. 150-151°C (benzene); IR(nujol mull) 3340, 3120, 1670, 1600, 1580 cm^{-1} ; NMR (CDCl₃) δ 2.03(br. s, 3H), 2.28(s, 3H), 5.90(br. s, 2H), 7.12-7.52 (m, 5H) ppm.

Compound VIII: M.p. 275-276°C (DMSO/water); IR(KBr) 3430, 3270, 3180-2200, 1620, 1590, 1575 cm^{-1} ; NMR (DMSO- d_6) δ 2.21(s, 3H), 2.77(d, J=4.8Hz, 3H), 5.72(q, J=4.8 Hz, 1H), 7.10-7.54(m, 5H), 11.85(br. s, 1H) ppm.

Satisfactory elemental analyses were obtained for all new compounds. Synthetic details will be given in our full manuscript.

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