

PHOTOLYSIS OF 2-ORTHO-NITROPHENYL-5-ARYLOXAZOLES --

A NEW ROUTE TO 2-AROYL-1H-4-QUINAZOLINONES

Ioan A. Silberg*

Institute of Chemistry, str. Donath 65-103, Cluj, Romania

Rodica Macarovici

Institute of Medicine and Pharmacy, Cluj

Nicolae Palibroda

Institute of Stable Isotopes, Cluj

(Received in UK 12 February 1976; accepted for publication 7 March 1976)

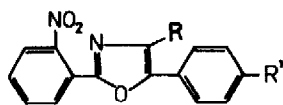
The photochemistry of azoles represents a very promising research field,¹ with interesting - but still largely unexplored - synthetic perspectives. We wish to report herewith a new heterocyclic ring-interconversion reaction of preparative value, leading to 2-acyl-1H-4-quinazolinones, a rather poorly investigated class of compounds, accessible so far only via many-step syntheses.^{2,3}

We observed that the readily available⁴ 2-o-nitrophenyl-4-bromo-5-phenyloxazole (Ib) and its -5-p-bromophenyl analogue (Ic) are sensitive to light. Thus, unlike their m- and p-nitrophenyl isomers, Ib and Ic turned reddish on exposure to diffuse light, even in the solid state, with the appearance of C=O and N-H bands in the IR spectrum; when the irradiation was carried out in benzene solutions with a 400 W high-pressure Hg lamp at $\sim 70^\circ$, Ib gave a 70% yield of IIa, m. 176° , and Ic yielded 80% IIb, m. 252° . However, Ia gave only small amounts of IIa, a fact which stresses the importance of the presence of a Br atom in position 4 of the oxazole.

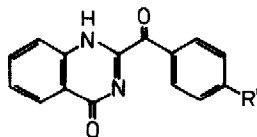
To establish the structure of IIa, its IR spectrum was recorded in CHCl_3 solutions; two ν C=O bands (1677 and 1718 cm^{-1}) and a sharp N-H absorption (3365 cm^{-1}) were present, whereas NO_2 bands were missing. NMR-spectra

(80 MHz, CDCl_3) confirmed the existence of the N-H group and showed that the remainder of the protons were attached to aromatic rings. The molecular ion appeared in the mass spectrum at m/e 250, indicating the molecular formula $\text{C}_{15}\text{H}_{10}\text{N}_2\text{O}_2$, in agreement with elemental analyses; this implies a structure with 12 DBE. The intense peaks at m/e 105 and 77 (shifted to 183/185, resp. 155/157 in the mass spectrum of IIb) point out the presence of benzoyl-, resp. *p*-bromobenzoyl groups in the molecule. The formation of a hydrazone and a phenylhydrazone, which showed only the low frequency C=O band in the IR spectra, demonstrated the existence of only one keto group with normal reactivity.

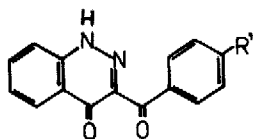
Since the known elements of structure (two benzene rings and two C=O groups) up to 10 DBE, it appeared to us that the three isomeric structures



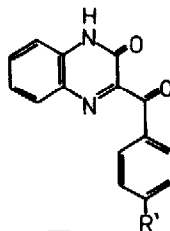
Ia R = R' = H
 Ib R = H; R' = Br
 Ic R = R' = Br



II a R' = H
 II b R' = Br



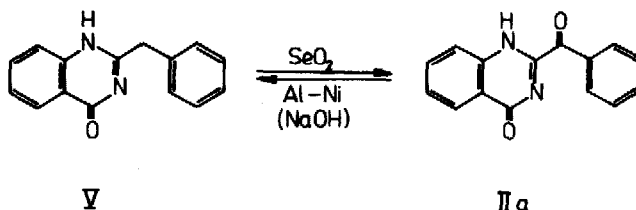
III



IV

(II-IV) - in which the remaining CN_2H unit was used to assemble an additional ring containing a double bond - are the only ones that reasonably account for the above mentioned physical and chemical properties. Structure IV was excluded by a comparison with the properties reported for 2-benzoyl-4H- β -quinoxalinone;⁵ the remarkable tendency of 2-acyl-quinoxaline hydrazones to cyclize, yielding pyrazolo-derivatives ("flavazoles"^{5,6}), substantially discredited formulation III (which also possesses a β -dicarbonyl moiety) since our hydrazones failed to cyclize even under vigorous conditions.

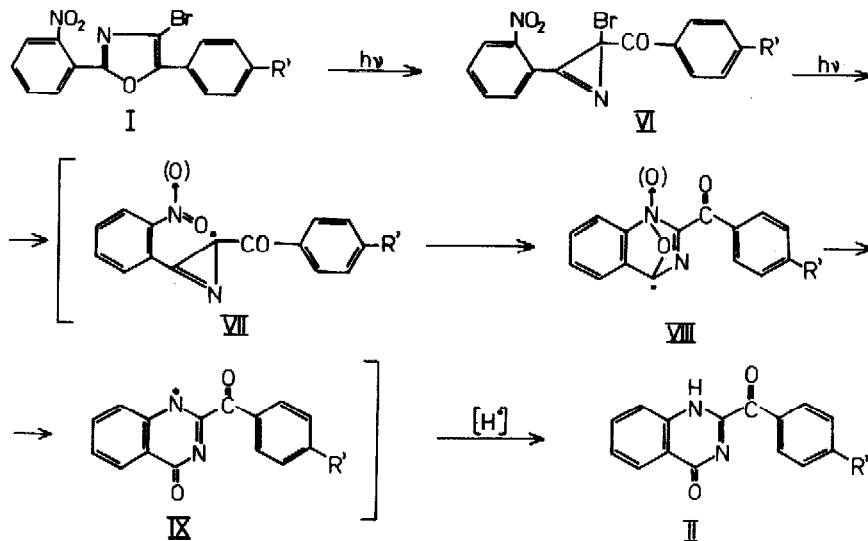
Consequently, an independent synthesis of IIa was carried out, following essentially the route described by Patel.³ Thus, by condensing anthranilic acid with phenylacetyl chloride and by subjecting the obtained amide to the action of formamide at 165-75° for 2 hrs., we prepared 2-benzyl-1H-4-quinazolinone (V), which was oxidized in excellent yield with SeO₂ in iso-AmOH to a



compound identical (m. p., TLC, and IR) with IIa. On the other hand, by treating IIa with 1:1 Al-Ni alloy in 10% aq. NaOH at 30-40°, we carried out the selective reduction of the exo-keto-group, obtaining a compound identical with V prepared by the Patel method. In the case of IIb, formation of V is accompanied by the typical dehalogenation induced by the Al-Ni alloy. It is of interest to emphasize that the ring carbonyl remained unaffected in the reduction, an observation which finds a parallel in the failure to reduce 4-pyridone by means of the same reagent.⁷

It was thus demonstrated that the products of the irradiation of 2-*o*-nitrophenyl-5-aryloxazoles (I) are the 2-*o*-nitrophenyl-1H-4-quinazolinones (II), formed by loss of the bromine atom from position 4, and of an oxygen atom, followed by the acquisition of an H atom from the reaction medium. We tentatively put forward the mechanism shown in the scheme for this reaction.

The first step is represented by the well-known¹ isomerization of oxazoles (I) into 1-azirines (VI), followed by the breaking of the labile C-Br bond on the azirine ring. We assume that the existence of the radicalic center at carbon in VII might trigger an antarafacial cycloaddition of the N=O group to the C-C bond of the azirine ring, the latter being broken in a conrotatory fashion. The intermediate VIII would be expected to yield the quinazolinonyl radical IX which captures an H atom from the reaction medium. It is possible that the nitro group is retained in VII, and the loss of oxygen occurs after - or simultaneously with - the cyclization to VIII. Careful mass-



spectrometric examination of the crude reaction mixture revealed no bromine-containing compounds in the case of Ib and we concluded that bromine is expelled in form of volatile products, probably as HBr.

Attempts to generalize this reaction by varying both the ortho substituent on the 2-phenyl ring and the nature of the heterocyclic moiety, are under way in our laboratory.

REFERENCES

1. S. T. Reid, Advan. Heterocycl. Chem. **11**, 1 (1970) and references therein; A. Lablach-Combiar and M.-A. Remy, Bull. Soc. Chim. Fr. **1971**(2), 679.
2. N. D. Heindel, V. B. Fish and Th. F. Lemke, J. Org. Chem. **33**(11), 3997 (1968); T. Sasaki, T. Yoshioka and Y. Suzuki, Bull. Chem. Soc. Japan **44**, 185 (1971).
3. V. S. Patel and S. R. Patel, J. Indian Chem. Soc. **42**, 531 (1965); *ibid.* **45**, 167 (1968); R. K. Thakkar and S. R. Patel, Bull. Chem. Soc. Japan **42**, 3198 (1969).
4. R. Macarovici and M. Ionescu, Rev. Roumaine Chim., in the press.
5. V. D. Romanenko and S. I. Burmistrov, Khim. Geterosikl. Soedin. **1973**(6), 852.
6. H. Dahn and J. Nussbaum, Helv. Chim. Acta **52**, 1661 (1969).
7. I. A. Silberg and K. W. Lienert, unpublished.