Tetrahedron Letters, Vol.22, No.24, pp 2277 - 2280, 1981
Printed in Great Britain

0040-4039/81/242277-04$02.00/0

A STUDY ON THE TRANSITION STATE IN THE PHOTOOXYGENATIONS BY AROMATIC AMINE N-OXIDES

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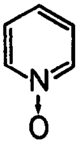
Summary: Oxygen-atom transfer process in the photolysis of aromatic amine N-oxides was suggested to involve the primary oxygen-atom elimination from N-oxides to give "oxene" follwed by its reactions with the oxygen-acceptors.

Biological oxygen-atom transfer reactions catalyzed by monooxygenases involve epoxidation of olefins, hydroxylation of alkanes and of arenes, and N- and S-oxidations1). Considerable interest has been recently shown in chemical systems which mimic the behaviours of such enzyme reactions. Of these, the most satisfactory mechanistic model examined was the photolysis of aromatic amine N-oxides, demonstrating oxenoid nature of their reactions2). Mechanistic aspects of this reaction, however, have not been thoroughly clarified. Recently a report on stereochemical and mechanistic study in this area has appeared3) and it prompted the present paper of our work concerning the transition state of the oxidant generated in the photolysis of pyridine N-oxide (1) and of pyridazine N-oxides 2, 4 and 54).

A priori, the oxygen-atom transfer reaction was expected to proceed either by a); an interaction of the photoexcited N-oxide or its rearrangement product with the acceptor followed by oxygen transfer, or by b); elimination of the oxygen-atom from the photoexcited N-oxide to give "oxene" 5) (atomic oxygen) followed by its reaction with the acceptor. In order to gain an insight into the mechanism of the oxygenation process, effects of oxygen-acceptor addition on the photoreaction of N-oxides were examined.

3-Methylpyridazine 2-oxide (2) was irradiated6) with and without addition of oxygen-acceptors (cyclohexane, cyclohexene or anisole) and the consumption rate of 2 in each irradiation was determined by gas chromatography (OV-17, G-SCOT capillary column, 30 m x 0.28 mm), using diethylterephthalate as the internal standard.

The results obtained from the irradiations using cyclohexene as oxygen-acceptor are summarized in Fig. 1 in which conversions (%) of 2 as pure solution and as the solutions in the presence of either 4 or 8 equimolar quantities of cyclohexene were plotted vs irradiation time. This figure shows that conversion rates of 2 are apparently regardless of the addition of cyclohexene, in spite of the fact that cyclohexene was oxidized to its epoxide and cyclohexanone in at least 20 % of total yields. Addition of cyclohexane or anisole as the oxygen acceptors have resulted also in no remarkable effect on consumption of 2. The fact suggested that an oxygen transfer mechanism to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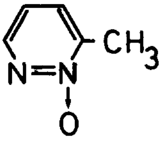
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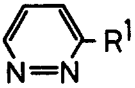
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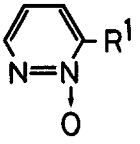
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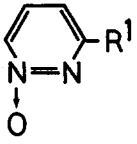
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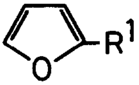
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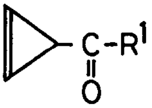
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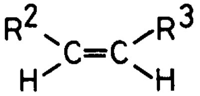
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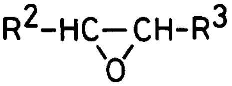
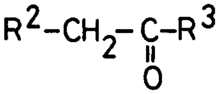

9a : *cis*
9b : *trans*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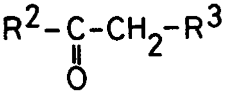
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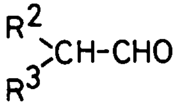
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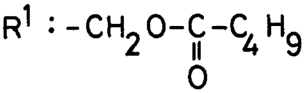

$R^1 : -CH_2O-C(=O)-C_4H_9$

$R^2 : -C_6H_{13}$ $R^3 : -C_{10}H_{21}$

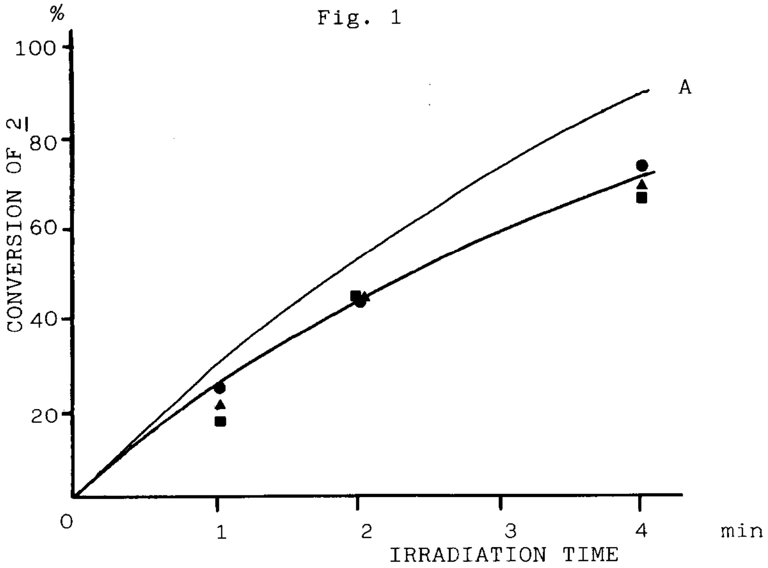


Fig. 1

● : 0.03 M of 2, ▲ : 0.03 M of 2 + 0.12 M of cyclohexene, ■ : 0.03 M of 2 + 0.24 M of cyclohxene. Curve A: an expected conversion rate of 2 in the mechanism involving 20 % of path **a** process in addition to self-conversion (●).

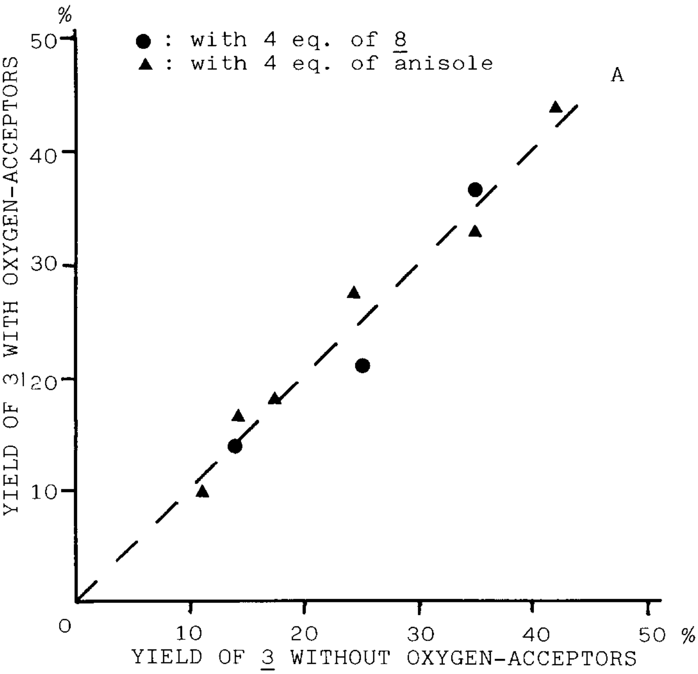
require a primary interaction between the photoexcited N-oxide and the substrate could probably be excluded and that the transition state of the process should involve some oxidant generated from the conversion of N-oxide.

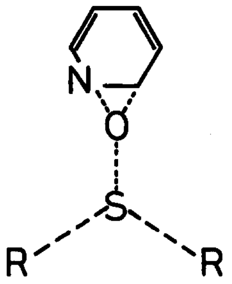
Another experiment to distinguish between path a and b was carried out using 3-vareloyloxymethylpyridazine 2-oxide (4). Compound 4 afforded, on irradiation in $CH_2Cl_2$6), the deoxygenation product 3 and rearrangement products such as 6 and 7 whose structures were eluciated by GC-MS7). Irradiation of 4 in the presence of *cis* -octadec-7-ene (8)8) or of anisole gave also the same products 3, 6 and 7 as well as a mixture of 9a, 9b, 10a, 10b and 11 or a mixture of hydroxyanisoles respectively, as the oxygenated products9). Several experiments to irradiate 4 as pure solutions and as the solution in the presence of four equivalent amounts of oxygen-acceptors (8 or anisole) were carried out in parallel runs to compare the respective yields of deoxygenation product 3. Their yields were determined by gas chromatography and those of 3 (maximum ca 45 %) and of the total oxygenated products in the respective irradiation were summarized in the Table in which the yields of each line (in each experiment) were obtained under comparable irradiation condition. In Fig. 2 yields of 3 with oxygen-acceptors were plotted vs those without oxygen-acceptors in each experiment. Since the plots to be obtained in the mechanism in which the yields of 3 are regardless of the presence of the oxygen-acceptors should follow the line A, the result indicates that the deoxygenation was not affected by addition of oxygen-acceptors in spite of the fact that formations of oxygenated products were almost proportional to the yields of 3.

Table

	Irradiation Condition				
	4	4 + 8		4+Anisole	
	Products %				
Exp. No	3	3	9+10+11	3	Hydroxy-anisoles
1	11	10	6	-	-
2	14	17	-	14	7
3	17	18	12	-	-
4	24	28	19	-	-
5	25	-	-	21	12
6	35	33	-	37	17
7	42	44	-	-	-

Fig. 2

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A similar result was obtained also in the photolysis of 3-vareloyloxymethylpyridazine 1-oxide (5) in the presence of 8, although the yields of deoxygenation and of oxygenated products were lower than the case of 4 affording higher yields of rearrangement products of 5.

Since photooxygenation of 8 with 1, 2, 4, or 5 under the same irradiation condition resulted in the formation of 9a, 9b, 10a, 10b and 11 in almost the same ratio, the same kind of reactive oxygen species should be generated from all of these N-oxides.

Although a previous paper[3)] proposed a transition state such as 12 in the sulphoxide formation by photochemical oxygen-atom transfer from various aromatic amine N-oxides, all these data mentioned above would suggest that the operation of path b involving a primary oxygen-atom elimination from N-oxide to give "oxene" (atomic oxygen) followed by its reactions with oxygen-acceptors is more likely, at least, in olefin epoxidations and aromatic hydroxylations.

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6. The photolyses were conducted with 450 watt high pressure mercury lamp (UM-452, Ushio Electric Inc.)using pyrex immersion well. 0.03 M solution of the N-oxides (2, 4 or 5) in CH_2Cl_2 (0.5 ml) was taken in a quartz tube (5 mm diameter) and the tube was settled at a fixed position. Photolysis under the same condition was repeated several times to gain reproducible values.
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9. 9a, b and 11 were identified with authentic specimens spectroscopically as well as on their chromatographic behaviours. Compounds 10a, b were obtained as an unseparable mixture (ca 1 : 1, determined by GC-MS) whose analytical and spectral data were in accord with these structures.

(Received in Japan 3 March 1981)