HETEROCYCLES, Vol 14, No 3, 1980

A NEW METHOD FOR SYNTHESIS OF LACTAM

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Abstract — 2-Substituted 3-oxo-3,4-dihydroquinoxalines were oxidized with H_2O_2 to 2,3-dioxo-1,2,3,4-tetrahydroquinoxaline. This oxidation of the imino bonding in the heterocycles to the lactam was assumed to proceed via the various peroxides, but not via the oxaziranes.

The oxidation of Shiff bases (imines, $R_1R_2C{=}NR_3$) with peracid gives oxaziranes,[1,2,3] which are further converted to amides with ferrous ion and by pyrolysis (at 300°C).[2] The oxaziranes are also obtained from hydroperoxides, which are produced by the reaction of Shiff bases with H_2O_2[4] (Chart 1-a). We now report a novel one-step oxidation of imino bonding in heterocycles to lactam with H_2O_2 (Chart 1-b). 2-Substituted 3-oxo-3,4-dihydroquinoxalines were used as the heterocycles (Chart 2).

A solution of 2-methyl-3-oxo-3,4-dihydroquinoxaline (I)[5] (3.1 mmol) and H_2O_2[6] (31 mmol) in AcOH

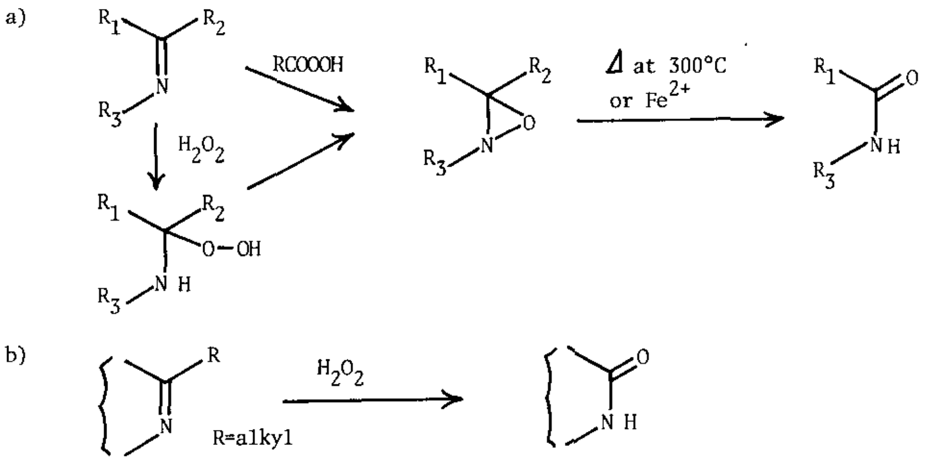


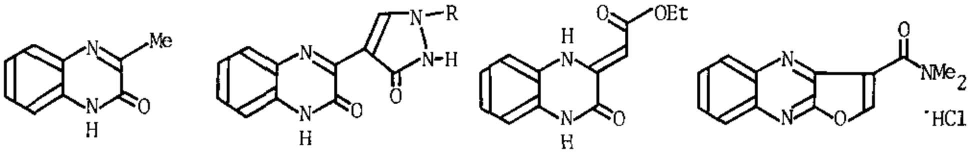
Chart 1

(30 ml) was heated on a water bath to afford 2,3-dioxo-1,2,3,4-tetrahydroquinoxaline (V),[7] in 6% yield. A similar reaction of 4-(3'-oxo-3',4'-dihydroquinoxaline-2'-yl)pyrazolones (IIa-c)[8] (3.3 mmol) with H_2O_2 (165 mmol) in AcOH (100 ml) brought about V, in 40% yield. 2-Ethoxycarbonylmethylene-3-oxo-1,2,3,4-tetrahydroquinoxaline (III)[9] (4.3 mmol) and 3-(N,N-dimethylaminocarbonyl)furo-[2,3-*b*]quinoxaline (IV)[8] (3.6 mmol) also gave V in the presence of 10-fold molar amount of H_2O_2, in 60% and 65% yields, respectively. From the above reaction mixture, the oxaziranes and a moiety other than quinoxaline were not obtained.

As shown in Table I, it is evident that the yield of V is low when 2-substituent in the quinoxaline ring is methyl group, but its yield is improved when the 2-substituent includes α,β-unsaturated bonding (C=C). This may indicate that the addition of H_2O_2 to I, II, IIIa,[9] and IV[8] produces the peroxides (Ii),[10] (IIi), (IIIi), and (IVi) as the respective intermediates, as shown in Chart 3. However, these peroxides were not isolated, presumably due to ease of decomposition. Compound V may be formed from these peroxides in a radical or concerted mechanism.[11,12]

On the other hand, the mechanism via the oxaziranes should be eliminated in the above reactions, since ferrous ion or heating at a higher temperature was necessary for the formation of the amide from the oxazirane, even if the oxazirane was produced. Furthermore, when the solution of the oxazirane was heated near 100°C for a long time, the nitrone was brought about.[2]

In conclusion, it is of interest that the oxidation of the imino bonding in the heterocycles with H_2O_2 generates the lactam via the peroxides, but not via the oxaziranes.



(I)

(IIa) R=H
(IIb) R=Me
(IIc) R=C_6H_5

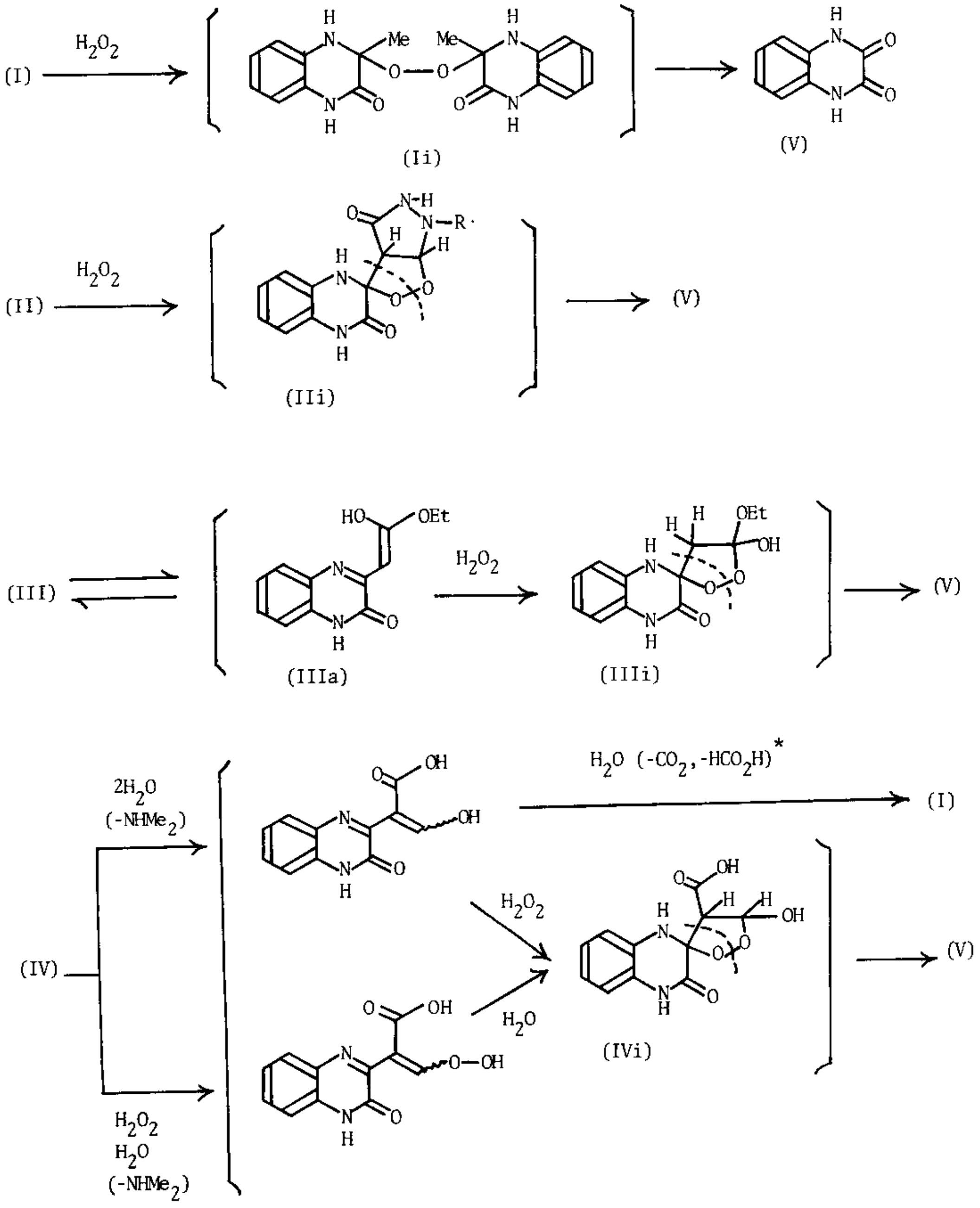
(III)

(IV)

Chart 2

Table I

Compound	Molar ratio of H_2O_2	Reaction time	Yield of V (%)
I	10-fold	1 hr	6
II	50-fold	3 hr	40
III	10-fold	1 hr	60
IV	10-fold	1 hr	65



* reference No.8

Chart 3

References and Footnotes

1. W. D. Emmons, *J. Amer. Chem. Soc.*, 1956, **78**, 6208.
2. Idem, ibid., 1957, **79**, 5739.
3. E. Schmitz, *Angew. Chem. internat. Edit.*, 1964, **3**, 333.
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5. C. L. Lees and H. N. Rydon, *J. Chem. Soc.*, 1955, 303.
6. 30% solution of H_2O_2 in H_2O was employed.
7. Spectral and physical data of V were identical with the sample prepared by the reaction of *o*-phenylenediamine with diethyl oxalate.
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12. The mechanism like the Baeyer-Villiger reaction was denied, since it did not lead to the formation of compound V.

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Received, 22th December, 1979