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The ozonolysis of 2-phenyloxazoles having the good leaving group as an anion at C-5 position gave mainly *N*-benzoylisocyanate (**2**) with the formation of carbon dioxide.

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In the course of investigations about the ozonolysis of oxazoles, we have observed three types of ozonolysis reactions, the formation of acid anhydrides [1-3], *N*-acylamides [4] and *N*-acylisocyanates [5], depending on the position of the substituent group. From these facts in a previous paper [5] a consistent reaction mechanism was proposed where the key step of the formation of the ozonolysis products was the bond cleavage of the C-H bond on the oxazole ring with the elimination of a proton. Especially, the bond cleavage at C-5 position governed the formation of the ozonolysis products prior to those at the C-2 and C-4 position. Under these circumstances, we were very interested in the ozonolysis of oxazoles such as 5-bromo- and 5-ethoxy-2-phenyloxazoles, which seemed to cause the bond cleavage easily at C-5 position with the elimination of an anionic species.

When 5-bromo-2-phenyloxazole (**1a**) was treated with an excess ozone-oxygen stream in dichloromethane at -78° , the reaction mixture was colored an intense orange. In the ir spectrum of this ozonolysis mixture, the absorptions of isocyanate and carbon dioxide appeared at 2250 and 2350 cm^{-1} . After treatment of this ozonolysis product with *p*-anisidine, *N*-benzoyl-*N'*-*p*-methoxyphenylurea (**4**) and *N*-formylbenzamide (**3**) were detected on hplc in 65 and 35% yield, respectively. Since **3** was inert to *p*-anisidine and **4** was generally formed from *N*-benzoylisocyanate (**2**) by the treatment with *p*-anisidine,

the main products from **1a** by ozonolysis were found to be **2** and carbon dioxide. In addition, the minor product was found to be **3**, where the formation of bromine was anticipated. Actually, the intense orange color of the ozonolysis product disappeared by the addition of styrene to afford 1,2-dibromo-1-phenylethane in 34% yield.

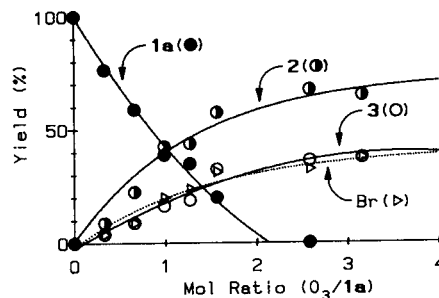
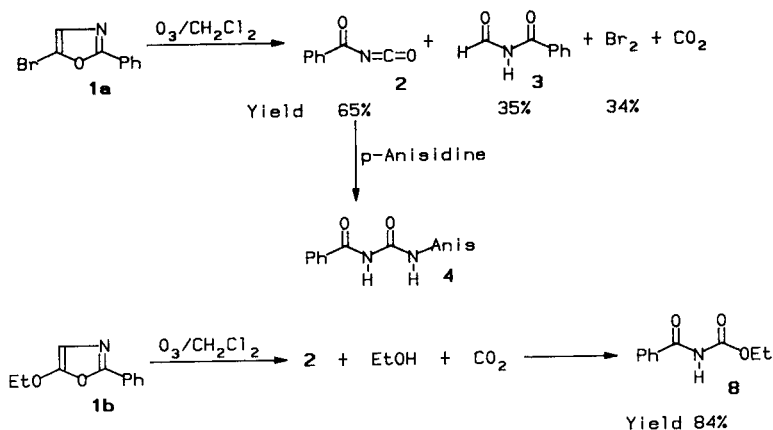


Figure 1

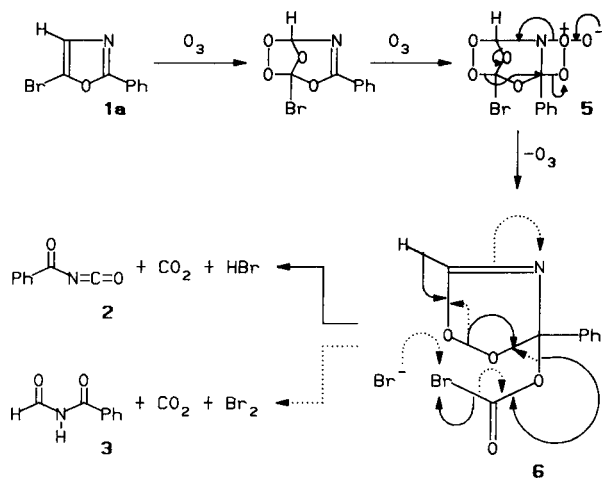
In order to clarify the reaction profile of **1a** with ozone, **1a** was added to the appropriate amount of dichloromethane saturated with ozone at -78° and after standing for 1 hour the residual substrate and **3** were monitored by hplc summarized in Figure 1. Also the resulting **2** and bromine were monitored by hplc after treatment with *p*-anisidine and styrene. Figure 1 showed that **1a** consumed 2 molar amounts of ozone and the yield of **3** was parallel with that of bromine. On the basis of

Scheme 1



these results, the ozonolysis mechanism of **1a** was proposed as shown in Scheme 2. The diozonide **5**, which was initially formed from **1a** by the attack of 2 molar amounts of ozone, was isomerized into the 1,2,4-dioxazoline form **6**. By C-H bond cleavage at the C-5 position of **6** accompanied with the elimination of bromide anion, **2**, carbon dioxide and hydrogen bromide were formed. Further the resulting bromide anion reductively attacked the bromine atom of another molecule of **6** to afford **3**, carbon dioxide and bromine. When **1a** was treated with ozone in methanol or ethanol, the formation of **3** was depressed by the deactivation of bromide anion and **2** was predominantly formed. The resulting **2** was instantly quenched by solvent to give methyl (**7**) and ethyl *N*-benzoylcarbamate (**8**) in 82 and 84% yield, respectively.

Scheme 2



Since ethoxy group was a good leaving group as an anion but inert to the reductive elimination, the ozonolysis of 5-ethoxy-2-phenyloxazole (**1b**) in dichloromethane at -78° gave **2**, ethanol and carbon dioxide through the reaction mechanism similar to that of **1a**. Further the resulting **2** and ethanol immediately reacted to afford **8** in 84% yield.

In conclusion, the ozonolysis of 2-phenyloxazoles having a good leaving group as an anion at C-5 position gave mainly *N*-benzoylisocyanate (**2**).

EXPERIMENTAL

Melting points were uncorrected. The nmr spectra were obtained on a JEOL FX-100 (100 MHz) spectrometer in deuteriochloroform with tetramethylsilane as an internal standard. The ir spec-

tra were recorded on a JASCO A-3 Infrared spectrometer. The hplc was run on a JASCO BIP-1 high pressure liquid chromatograph on Megapak SIL-C₁₈ column with aqueous methanol.

Materials.

5-Bromo-2-phenyloxazole (**1a**) was prepared according to the method described in the previous paper [6]. 5-Ethoxy-2-phenyloxazole (**1b**) was prepared by the method of Kondrat'eva [7].

Ozonolysis of **1a**.

The ozone-oxygen stream was bubbled into a solution of **1a** (1 mmole) in dichloromethane (20 ml) at -78° . When the reaction mixture changed to intense orange, bubbling was stopped and excess ozone was removed by the bubbling of argon. The ir absorptions of ozonolysis mixture were observed at 3350, 2350, 2250, 1730, 1680 cm^{-1} . After treating with *p*-anisidine and styrene for 1 hour at room temperature, the reaction mixture was diluted with water, extracted with dichloromethane. The organic layer was washed with aqueous sodium hydroxide, dried over anhydrous magnesium sulfate, and concentrated. From the residue, **3**, **4** and 1,2-dibromo-1-phenylethane were identified by hplc in 35, 65 and 34% yield, respectively. In the cases of ozonolysis in methanol and ethanol, **7** and **8** were obtained in 82 and 84% yield without any post-treatment, respectively.

Stoichiometric Study.

Since a saturated solution of ozone in dichloromethane at -78° contained 0.04 mole/l according to Rubin [8], an appropriate amount of dichloromethane was bubbled with a stream of ozone-oxygen and was saturated with ozone by the change to blue. To this ozone solution was added **1a** in dichloromethane (5 ml) with an unreactive standard compound. After treatment with *p*-anisidine and styrene, the residual mixture was monitored by hplc. The results are summarized in Figure 1.

Ozonolysis of **1b**.

Ozonolysis of **1b** was performed according to the conditions described above. The resulting ozonolysate was allowed to warm to room temperature for 3 hours and then concentrated. The product was identified to be **8** with the authentic sample in 84% yield.

REFERENCES AND NOTES

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