*M. L. Graziano, M. R. Iesce and R. Scarpati**

Institute of Organic and Biological Chemistry, University of Naples, 80134 Naples, Italy

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Trisubstituted oxazoles I react at -15° with singlet oxygen to give dioxazoles III and imino-anhydrides V which rearrange at room temperature to triamides VI. The intermediate ratio (III/V) is sensitive to the reaction temperature. It is likely that at room temperature triamides VI are essentially formed *via* imino-anhydrides V.

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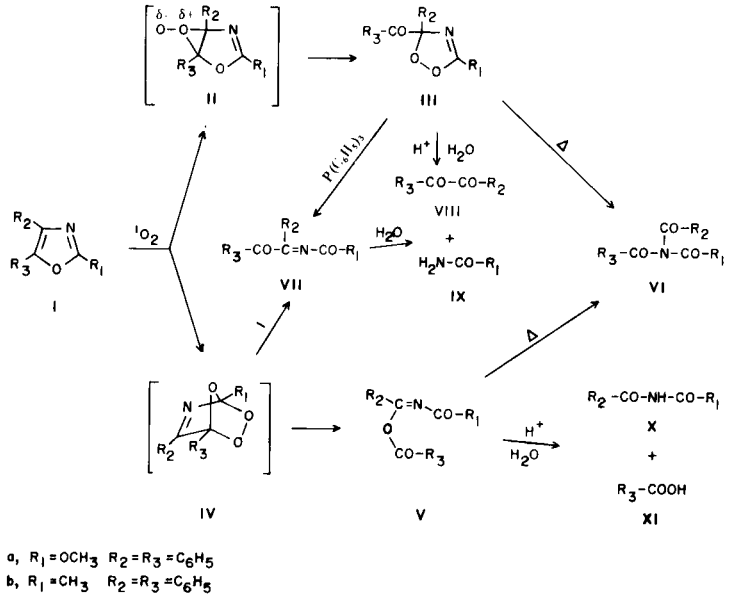
In a previous paper (1) we reported that the fully substituted 5-alkoxyoxazoles and 2,4-dialkoxyoxazoles I react with singlet oxygen to give 3*H*-1,2,4-dioxazoles III, diacylcarbamates VI and imines VII and we suggested that the reaction follows two distinct pathways. The singlet oxygen attacks either the electron-rich C_4-C_5 double bond of the oxazoles by 1,2-addition to give the unstable peroxirane intermediates II which rearrange into dioxazoles III, or attacks the oxazole-diene system by 1,4-addition to give the unstable *endo*-peroxides IV which partly rearrange into diacylcarbamates VI, *via* imino-anhydrides V, and partly form imines VII, *via* diradicals (2) (Scheme).

In order to test the generality of this behaviour, the photosensitized oxygenation of trisubstituted oxazoles in which the C_4-C_5 double bond is not activated by alkoxy groups was investigated.

2-Methoxy-4,5-diphenyloxazole (Ia) was photooxygenated at 0° in anhydrous chloroform using methylene blue as a sensitizer. The reaction was complete within 3 hours; during this time we observed, by ^{1}H nmr at 0°, the disappearance of the methoxy signal of Ia and the emergence of two new methoxy singlets at δ 3.73 and 3.59 with relative areas *ca.* 10:1. The ^{1}H nmr spectrum remained unchanged either by addition of triphenylphosphine (3) or by keeping the mixture at 0°; on warming at 35° a new methoxy signal at δ 3.69 due to methyl *N*,*N*-dibenzoylcarbamate (VIa) emerged while the one at δ 3.73 declined. When the conversion was complete (3 hours) silica gel chromatography allowed the isolation of VIa in 93% yield, benzil (VIIIa) in 5% yield and methyl carbamate (IXa). Compounds VIIIa and IXa were clearly formed by hydrolysis during the separation procedure of the product which showed the methoxy singlet at δ 3.59. Structure VIa was assigned on the basis of elemental and spectral analyses. When 2*N* hydrochloric acid in acetone was added to the oxidation mixture kept at 0°, methyl *N*-benzoylcarbamate (Xa) was obtained in 93% yield, in addition to VIIIa, IXa and benzoic acid (XIa). Therefore, on the basis of the previous results (1,2), the singlet at δ 3.73 is to be assigned to imino-anhydride Va and the singlet at δ 3.59 to imine VIIa.

When the sensitized photooxidation of Ia was carried out at -15°, the ^{1}H nmr spectrum of the oxidation mixture, after the signals of the starting material had disappeared (3 hours), in the range of the methoxy absorption showed three singlets at δ 4.25, 3.73 (imino-anhydride Va) and 3.59 (imine VIIa) with relative areas *ca.* 2:3:0.3. When the oxidation mixture was heated at 35° for 3 hours, inspection of the ^{1}H nmr spectrum showed only the presence of diacylcarbamate VIa and imine VIIa in *ca.*

SCHEME



a, R_1 = OCH_3 R_2 = R_3 = C_6H_5
b, R_1 = CH_3 R_2 = R_3 = C_6H_5

5:0.3 molar ratio. Therefore, on the basis of the above and previous results (1), the singlet at δ 4.25 can be assigned to $=C\text{-}OCH_3$ of the dioxazole IIIa. The chemical behaviour of the oxidation mixture, kept at -15°, provided further evidences for the assigned structure IIIa (4); in fact mild acid hydrolysis followed by silica gel chromatography allowed the isolation of carbamate Xa (from Va) and benzil VIIIa (from IIIa and VIIa), in *ca.* 3:2 molar ratio, in addition to benzoic acid XIa (from Va) and carbamate IXa (from IIIa and VIIa). Addition of triphenylphosphine gave a mixture which, on the basis of its ^1H nmr spectrum, proved to be composed of Va and VIIa in *ca.* 3:2.3 molar ratio.

These results clearly indicate that the 1,2-addition of singlet oxygen to the oxazole system is possible also when the C_4-C_5 double bond is not directly activated by alkoxy groups and that this reaction takes place preferentially at low temperatures.

The above and the previously reported (1) results suggested that the sensitized photooxygenation of alkyl, phenyltrisubstituted oxazoles should be reinvestigated. The original observation was that at room temperature the products were triamides (5). These compounds were suggested to be derived from the initial 1,4-addition of singlet oxygen on the basis of the results obtained when labeled singlet oxygen was added to an unsymmetrical trisubstituted oxazole (6). As these results are accomodated also by the dioxazole intermediate III, we examined the behaviour of 2-methyl-4,5-diphenyloxazole Ib by methylene blue-sensitized photooxidation at 0° in order to detect transient intermediates. After 4 hours the ^1H nmr spectrum of the Ib oxidation mixture, in the high-field region, showed three signals at δ 2.18 (s), 2.34 (s) and 2.48 (s), with relative areas *ca.* 3:1:1. When the oxidation mixture was heated at 35° for 10 minutes, inspection of the ^1H nmr spectrum showed only the presence of triamide VIb (singlet at δ 2.48), the structure of which was assigned by comparison (ir and nmr) with an authentic sample (5). Therefore, the singlets at δ 2.18 and 2.34 are to be assigned to dioxazole IIIb and imino-anhydride Vb. The composition of the mixture, deduced on the basis of the thermal rearrangement, was confirmed by the results obtained from mild acid hydrolysis of the oxidation mixture kept at -15°. Silica gel chromatography of the hydrolysis mixture allowed the isolation of benzil VIIIb (from IIIb) and diamide Xb (from Vb) in *ca.* 3:1 molar ratio in addition to triamide VIb, acetamide IXb (from IIIb) and benzoic acid XIb (from Vb).

Final attribution of the signals at δ 2.18 and 2.34 was performed by gradual addition of triphenylphosphine to the oxidation mixture kept at -15°. Examination of the reaction mixture, by ^1H nmr, showed the emergence of a singlet at δ 2.21, due to imine VIIb (7), whereas the singlet at δ 2.18 gradually disappeared and the singlet at δ 2.34 remained unchanged. Hence the singlet at δ 2.18 is to be assigned to dioxazole IIIb (8) and the singlet at δ 2.34 to imino-anhydride Vb.

The above results point out that, by dye-sensitized photooxidation of Ib at 0°, triamide VIb is partly formed *via* dioxazole IIIb, showing that the presence of alkoxy groups on the oxazole system is not essential in order that the 1,2-addition takes place.

On the other hand, when the Ib oxidation was carried out at -15°, the ^1H nmr spectrum of the reaction mixture showed the presence of dioxazole IIIb, imino-anhydride Vb and triamide VIb in *ca.* 4:1:0.5 molar ratio. However, in this case a decrease in temperature also appears to increase the IIIb/Vb ratio. Therefore, it is very probable that at room temperature the 1,4-addition is the main reaction and triamide VIb is formed essentially *via* endoperoxide IVb as Wasserman suggested (5,6).

EXPERIMENTAL

Melting point is uncorrected. Ir spectrum was recorded on a Perkin-Elmer 157 spectrophotometer; ^1H nmr on a Perkin-Elmer R12A spectrometer with TMS as the internal standard. Silica gel 0.05-0.20 mm (Merck) was used for column chromatographies. Light petroleum refers to the fraction b.p. 30-50°. Chloroform used in the oxidation reactions was anhydrous and ethanol free.

Photosensitized Oxidation of Ia.

Into a 2% solution of Ia (500 mg.) (9) in chloroform, after addition of 7 mg. of methylene blue, dry oxygen was bubbled. The solution was cooled with ice-water and irradiated with a halogen-superphot lamp (Osram 650 W). The solution was periodically sampled and the samples analyzed by ^1H nmr. The reaction was complete within 3 hours. Analysis of the ^1H nmr spectrum of the reaction mixture, on the basis of the relative areas of the methoxy signals of the photoproducts, showed the presence of imino-anhydride Va and imine VIIa in *ca.* 10:1 molar ratio. The ^1H nmr spectrum remained unchanged by addition of triphenylphosphine at 0°.

An aliquot of the solution (12.5 ml.) was kept at 35°; after 3 hours inspection of the ^1H nmr spectrum showed Va completely changed to diacylcarbamate VIa. The solvent was removed *in vacuo* and the residue chromatographed on silica gel (20 g.). Elution with light petroleum/ether (19:1), (9:1) and (4:1) gave VIIIa (5%), VIa (93%) and trace amounts of IXa. The latter compound and VIIIa were identified by comparison (ir and ^1H nmr spectra) with authentic samples. Diacylcarbamate VIa is a white solid, m.p. 84-86° from light petroleum b.p. 40-70°, ir ν max (chloroform): 1755, 1725 and 1705 cm^{-1} (-CO-N-); ^1H nmr (deuteriochloroform): δ 3.69 (3H, s, OCH_3), 7.40-8.00 (10H, m, $2C_6H_5$).

Anal. Calcd. for $C_{16}H_{13}NO_4$: C, 67.84; H, 4.63; N, 4.95. Found: C, 67.76; H, 4.71; N, 4.84.

A second aliquot (12.5 ml.) was immediately treated with 2*N* hydrochloric acid in acetone solution and kept at 0°. After 24 hours, usual work up gave a mixture which was chromatographed on silica gel (20 g.). Elution with light petroleum/ether (19:1), (9:1), (4:1) and ether gave VIIIa (5%), XIa (80%), trace amounts of IXa and diamide Xa [93%; identified by comparison (ir and ^1H nmr spectra) with an authentic sample (10)].

When during the irradiation (Ia, 250 mg.; methylene blue, 4

mg.) the solution was cooled at -15°; the reaction was complete within 3 hours. The ^{1}H nmr spectrum of the reaction mixture showed the presence of IIIa, Va and VIIa in *ca.* 2:3:0.3 molar ratio. An aliquot of the solution (3 ml.) was kept at 35°. After 30 minutes inspection of ^{1}H nmr spectrum showed that IIIa was completely changed to VIa, whereas Va was changed only partially. The ^{1}H nmr spectrum of the reaction mixture, recorded after 3 hours, showed only the presence of VIa and VIIa in *ca.* 5:0.3 molar ratio.

A second aliquot (6 ml.) was treated at -15° with 2*N* hydrochloric acid in acetone solution and kept at -15°. After 24 hours, usual work up gave a mixture which was chromatographed on silica gel (10 g.). Elution with light petroleum/ether (19:1), (9:1), (4:1) and ether gave VIIIa (40%), XIa (45%), IXa (13%) and Xa (57%).

A third aliquot (3 ml.) was treated at -15° with triphenylphosphine (60 mg.); the ^{1}H nmr spectrum of the reaction mixture showed only the presence of Va and VIIa in *ca.* 3:2.3 molar ratio.

Photosensitized Oxidation of Ib.

Oxidation was accomplished on a 2% solution of Ib (500 mg.) (11) in chloroform, as described above for Ia, cooling the solution with ice-water. The reaction was complete within 4 hours. Analysis of the ^{1}H nmr spectrum of the reaction mixture, on the basis of the relative areas of the methyl signals of the photoproducts, showed the presence of IIIb, Vb and VIb in *ca.* 3:1:1 molar ratio. An aliquot of the solution (5 ml.) was kept at 35°; inspection of the ^{1}H nmr spectrum after 10 minutes showed IIIb and Vb completely changed to VIb which was identified by comparison (ir and ^{1}H nmr spectra) with an authentic sample (5).

A second aliquot (10 ml.) was treated at -15° with 2*N* hydrochloric acid in acetone solution and kept at -15°. After 24 hours usual work up gave a mixture which was chromatographed on silica gel (15 g.). Elution with light petroleum/ether (19:1), (9:1), (4:1), (1:1) and ether/methanol (19:1) gave VIIIb (58%), XIb (10%), VIb (18%), Xb (19%) and IXb (50%).

A third aliquot (10 ml.) was treated at -15° with triphenylphosphine (75 mg.); the ^{1}H nmr spectrum of the reaction mixture showed the presence of the methyl signals of IIIb, Vb, VIb and VIIb in *ca.* 1.5:1:1:1.5 molar ratio. After adding more triphenylphosphine (150 mg.) at -15°, the ^{1}H nmr spectrum of the reaction mixture showed only the methyl signals of Vb, VIb and VIIb in *ca.* 1:1:3 molar ratio. The mixture was kept at 35°; after 10 minutes the ^{1}H nmr spectrum showed the presence of VIb and VIIb in *ca.* 2:3 molar ratio. Evaporation of the solvent *in vacuo* afforded a mixture which was chromatographed on silica gel (40 g.). Elution with light petroleum/ether (19:1), (4:1) and ether/methanol (19:1) gave triphenylphosphine, VIIIb (58%), VIb (38%), triphenylphosphine-oxide and IXb (50%).

When, during the irradiation, the solution was cooled at -15°, the reaction was complete within 4 hours. The ^{1}H nmr spectrum showed the presence of IIIb, Vb and VIb in *ca.* 4:1:0.5 molar ratio.

Acknowledgments.

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