Photochemical and Chemical Behaviour of 2,5-Hydroperoxyhydroxy-2,5-dihydrofurans

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From hydroxyhydroperoxides II and III a new bicyclic system, namely the 5,6-dioxabicyclo[2.1.1]hexane VII is obtained by photolysis or by protic acids. Epimer epoxides IV and XI are obtained on reaction with triethylamine.

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Recently, it has been reported that 5-methoxycarbonyl-4-methyl-1-phenyl-2,3,7-trioxabicyclo[2.2.1]hept-5-ene (I) reacts with water to form 2-hydroperoxy-5-hydroxy-3-methoxycarbonyl-2-methyl-5-phenyldihydrofuran (II) which is in equilibrium with 5-hydroperoxy-2-hydroxy-3-methoxycarbonyl-2-methyl-5-phenyldihydrofuran (III) through peroxidic intermediates (1). The only previously reported compound of this series was 2-hydroperoxy-5-hydroxy-2,5-dimethyldihydrofuran but its properties were unreported (2), therefore we considered it interesting to study the reactivity of the 2,5-hydroperoxyhydroxy-2,5-dihydrofurans and in this paper we described the photochemical and chemical behaviour of II and III.

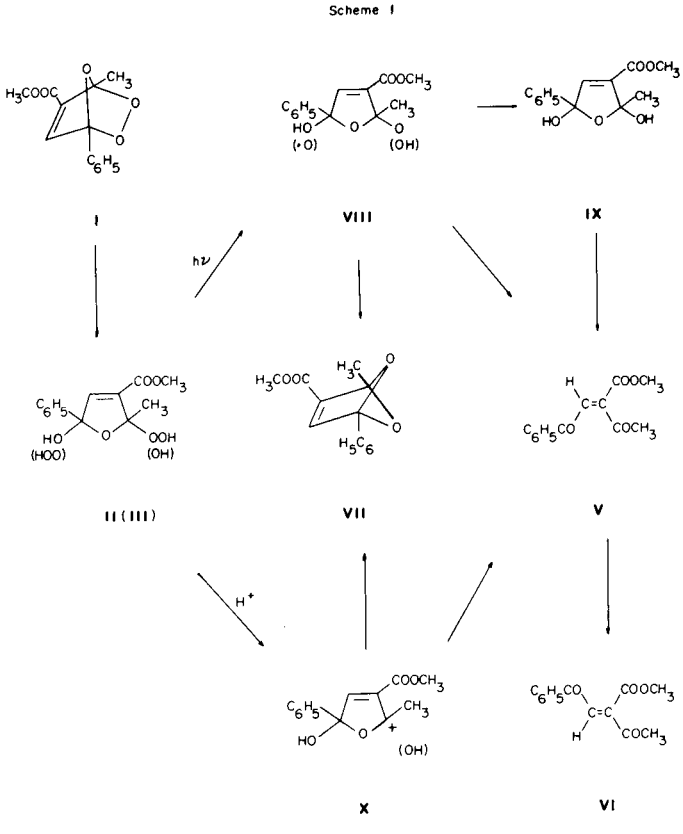
Hydroxyhydroperoxides II and III are not stable enough to be isolated (1), therefore we used the crude mixture of hydrolysis of the *endo*-peroxide I which, on the basis of its ^{1}H nmr spectrum, was composed of II and III (~70%), methyl (*E*)-2-acetyl-3-benzoyl-2,3-epoxypropionate (IV) (~20%), methyl (*E*)-2-acetyl-3-benzoylacrylate (V) and its *Z*-isomer VI (altogether ~10%). Control experiments showed that the compounds different from II and III present in the hydrolysis mixture do not undergo change in the reaction conditions; therefore the yields of the reactions below reported were calculated on the basis of II and III present in the starting mixture.

The photolysis of the mixture of II and III was accomplished in benzene at room temperature using a low pressure mercury lamp (Hanovia 4 W) until the ^{1}H nmr of the reaction mixture showed the complete consumption of the starting II and III. After 24 hours, silica gel chromatography allowed the isolation of acrylates V and VI (1) (~30%) and of 3-methoxycarbonyl-4-methyl-1-phenyl-5,6-dioxabicyclo[2.1.1]hex-2-ene (VII) (~15%). The compound VII, whose structure was assigned on the basis of elemental analysis and spectral data, is the first example of the 5,6-dioxabicyclo[2.1.1]hexane system.

As shown in Scheme I the reaction is envisioned as proceeding by homolytic cleavage of peroxidic bond of II and III to give alkoxy radicals VIII (3). These should be converted, by loss of the hydroxyl radical, into 5,6-dioxabicyclo[2.1.1]hexene VII through intramolecular attack on the hemiacetal carbon and into the acrylate V through a β-scisson (4); the latter partly isomerizes into VI as previously observed (1). Alternatively or simultaneously the alkoxyradicals VIII should lead, as observed in the photoysis of tertiary alkyl hydroperoxides (5), to the bishemiacetal IX which rapidly is converted to the acrylate V.

The compounds V, VI (~40%) and VII (~20%) were also obtained from the mixture of II and III under weakly acidic conditions at 0°. In this case a path involving the ionic intermediate X, as suggested for triarylmethylhydroperoxides (6), is the mode of the reaction (Scheme I).

Scheme I

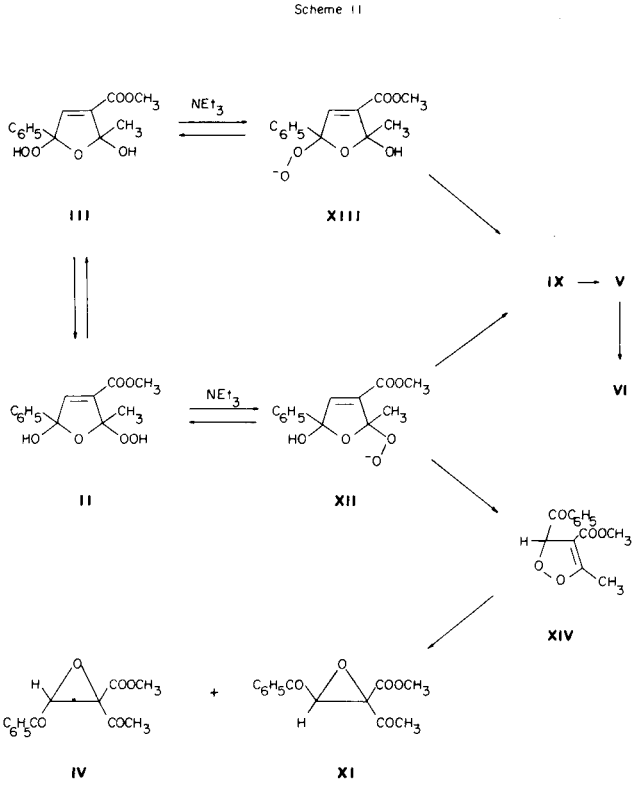


The reaction of the mixture of II and III with triethylamine was carried out in chloroform (1:1 molar ratio of base to hydroxyhydroperoxides II and III). After 30 minutes ^{1}H nmr spectrum showed only the presence of the epimer epoxides IV and XI, the acrylates V and VI and triethylammonium hydroxide. After separation of the

triethylammonium hydroxide, silica gel chromatography of the reaction mixture allowed the isolation of the epoxide IV (1) (~32%), its *Z*-isomer XI 32% and of acrylates V and VI (1) (~10%). The structure of the epoxide XI was assigned on the basis of elemental analyses and spectral data; in particular the *Z*-configuration was supported by the ^{1}H nmr solvent effect (7). In fact the singlet due to acetyl protons, which appeared at δ 2.31 in deuteriochloroform, occurs at δ 1.80 in hexadeuteriobenzene. A series of nuclear Overhauser effect (NOE) difference experiments, performed on a Fourier transform 270-MHz spectrometer with the aid of an ASPECT 2000 microprogram, provided further evidence for the assigned configuration. In fact, in the ^{1}H nmr spectrum of the epoxide XI in deuteriochloroform, irradiation at δ 2.31 ($COCH_3$) caused the enhancement of the signal at δ 4.45 (CH). The structure of triethylammonium hydroxide was assigned on the basis of elemental analyses and spectral data.

A possible mechanism which explains the formation of epimer epoxides IV and XI is shown in Scheme II. An alternative pathway involving epoxidation of acrylates V and VI (8) by XII and XIII can be excluded. In fact when the reaction of II and III with triethylamine was carried out in the presence of ethyl (*E*)-3-acetyl-2-benzoylacrylate (9), neither ethyl (*E*)-3-acetyl-2-benzoyl-2,3-epoxypropionate nor its *Z*-isomer were detected in the reaction mixture.

Scheme II



EXPERIMENTAL

Melting points are uncorrected. The ir spectra were recorded on a Perkin-Elmer 157 spectrophotometer; ^{1}H nmr on a Perkin-Elmer R 12 A or a Bruker W.H. 270 with TMS as an internal standard; ^{13}C nmr on a Bruker W.H. 270 with TMS as an internal standard. Silica gel 0.05-0.20 mm (Merck) and light petroleum bp 30-50° were used for column chromatography. The tlc analyses were carried out on pre-coated plates on silica gel F 254 (Merck).

Preparation of Hydroxyhydroperoxides II and III.

The *endo*-peroxide I (248 mg, 1 mmole) was dissolved in acetone/water (6 ml, 4:1 v/v) precooled at -4° and the solution was kept at -4° for 3 hours. Work up gave a mixture (240 mg), whose ^{1}H nmr spectrum showed the presence of the hydroxyhydroperoxides II and III, the epoxide IV, and the acrylates V and VI. On the basis of the relative areas of the singlets at δ 6.96-7.22 (CH of II and III), 2.33 (CH_3 of IV), 2.47 and 2.49 (CH_3 of V and VI), molar ratio II + III:VI:V + VI was *ca*, 7:2:1. The compounds II,III,IV,V and VI were identified by comparison of the ^{1}H nmr spectrum of this hydrolysis mixture with that of the mixture of the hydrolysis carried out at 0°C (1).

Photolysis of Hydroxyhydroperoxides II and III.

The hydrolysis mixture of I consisting of II and III (212 mg; 0.8 mmoles), IV (54 mg), V and VI (26 mg), was dissolved in benzene (15 ml) and irradiated with a low pressure mercury lamp (Hanovia 4W). After 24 hours, removal of the solvent *in vacuo*, gave a residue formed (^{1}H nmr) by the acrylates V and VI, and the 5,6-dioxabicyclo[2.1.1]hexene VII in addition to the epoxide IV and gummy materials. The residue was chromatographed on silica gel (10 g). Elution with 240 ml of light petroleum/ether (4:1) gave a mixture of V, VI and VII; elution with 120 ml of same solvent gave the epoxide IV (54 mg); elution with ether gave gummy materials (90 mg). The mixture of V, VI and VII by tlc (light petrolum/ether 4:1, uv light) afforded pure acrylates V and VI (82 mg, 30%) and 5,6-dioxabicyclo[2.1.1]hexene VII (27 mg, 15%).

5,6-Dioxabicyclo[2.1.1]hexane VII, recrystallized from light petroleum (bp, 40-70°), gives white crystals, mp 206-208°; ir (chloroform): ν max 1728, 1648 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.75 (3H, s, CH_3), 3.78 (3H, s, OCH_3), 6.72 (1H, s, CH), and 7.20-7.80 (5H, m, C_6H_5); ^{13}C nmr (deuteriochloroform): δ 20.92 (q, CH_3), 52.01 (q, OCH_3), 112.15 and 114.73 (2 × s, C-1 and C-4), 126.91 and 128.47 (2 × d, C-2, C-6 and C-3, C-5 of phenyl group), 128.96 (d, C-4 of phenyl group), 135.71 and 137.24 (2 × s, C-1 of phenyl group and C-3), 140.90 (d, C-2), and 161.79 (CO); m/e 232 (M^+), 217 (M^+-CH_3), 173 (M^+-$COOCH_3$).

Anal. Calcd. for $C_{13}H_{12}O_4$: C, 67.23; H, 5.21. Found: C, 66.83; H, 5.15.

Reaction of Hydroxyhydroperoxides II and III with Hydrochloric Acid.

The hydrolysis mixture of I, consisting of II and III (160 mg, 0.6 mmoles), IV (44 mg) and V and VI (20 mg) was dissolved in acetone (6 ml), treated with 2*N* hydrochloric acid (0.5 ml) and kept at 0°. After 48 hours, in the mixture hydrogen peroxide was detected. Usual work up gave a residue which was partitionated as above described for the photolysis mixture into V and VI (75 mg, 40%), VII (28 mg, 20%), IV (43 mg) and gummy materials (40 mg).

Reaction of Hydroxyhydroperoxides II and III with Triethylamine.

The hydrolysis mixture of I consisting of II and III (170 mg, 0.64 mmoles), IV (45 mg) V and VI (21 mg) was dissolved in chloroform (5.5 ml) and treated with triethylamine (70 mg, 0.64 moles). The reaction was periodically sampled and the samples analyzed by ^{1}H nmr. The reaction was complete within 30 minutes. After removal of the chloroform *in vacuo*, the residue was taken up in carbon tetrachloride and the suspension was filtered to remove the triethyl ammonium hydroxide (50 mg). After evaporation of the solvent, the residue was chromatographed on silica gel (10 g). Elution with light petroleum/ether (4:1) gave the acrylates V and VI (38 mg, 10%) and the epoxide IV (1) (98 mg, 32%). Elution with light petroleum/ether (1:1) gave the *Z*-epoxide XI (50 mg, 32%). Triethylammonium hydroxide is a white solid mp 201-203° from

benzene, ir (chloroform): ν max 3380, 2550 and 2380 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.42 (3H, t, CH_3), 3.15 (2H, q, CH_2).

Anal. Calcd. for $C_6H_{17}NO$: C, 60.45; H, 14.38; N, 11.75. Found: C, 60.01; H, 14.30; N, 11.62.

Epoxide XI, recrystallized from light petroleum (b.p. 40-70°C), gives white crystals mp 73-75°; ir (chloroform): ν max 1765, 1725 and 1703 cm^{-1}; ^1H nmr (deuteriochloroform): δ 2.31 (3H, s, CH_3), 3.65 (3H, s, OCH_3), 4.45 (1H, s, CH), and 7.35-8.05 (5H, m, C_6H_5); ^1H nmr (hexadeuteriobenzene): δ 1.80 (3H, s, CH_3), 3.15 (3H, s, OCH_3), 3.90 (1H, s, CH), and 6.85-7.90 (5H, m, C_6H_5).

Anal. Calcd. for $C_{13}H_{12}O_5$: C, 62.90; H, 4.87. Found: C, 63.01; H, 5.07.

To the hydrolysis mixture of I consisting of II and III (190 mg, 0.72 mmole), IV (50 mg) and V and VI (23 mg) dissolved in chloroform (6 ml), ethyl (*E*)-3-acetyl-2-benzoylacrylate (9) (178 mg, 0.72 mmole) and triethylamine (72 mg, 0.72 mmole) were added. After 30 minutes the solvent was evaporated and after separation of triethyl ammonium hydroxide (60 mg), the residue partitionated as above described into V and VI (40 mg), ethyl (*E*)-3-acetyl-2-benzoylacrylate (170 mg), epoxide IV (108 mg) and its *Z*-isomer XI (57 mg).

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(9) Obtained by reduction with diethyl sulphide of 5-ethoxycarbonyl-1-methyl-4-phenyl-2,3,7-trioxabicyclo[2.2.1]hept-5-ene as will be reported in the near future.