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On the Preparation and Characterisation of *p*-Dioxanyl Hydroperoxide

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p-Dioxanyl hydroperoxide has been prepared in crystalline form and characterised by analysis, iodometric titration, NMR, IR, and mass spectra and also by reductive degradation.

Hydroperoxides are considered to be initial products in the autoxidation of organic compounds.[1,2] In aliphatic ethers the hydroperoxy group becomes attached to the carbon adjacent to the ether oxygen affording unstable peroxidic hemiacetals.[3–5] If the ether oxygen forms part of a 5- or 6-membered ring system, the resulting cyclic peroxydic hemiacetals appear to be more stable.[5] Several representatives of this type of compounds have been isolated after autoxidation or photo-oxidation of the corresponding cyclic ethers, usually by distillation of the reaction mixtures under reduced pressure. Thus, 2-tetrahydrofuryl hydroperoxide has been obtained by oxidation of tetrahydrofuran with air [6–9] and *p*-dioxanyl hydroperoxide by photooxidation of *p*-dioxane with oxygen.[10,9] Both compounds were described as colourless liquids boiling under 0.01 mm Hg at 45—50° and 45°, respectively.[9] Moreover, a number of hydroperoxides have been prepared from phthalanes, isochromanes, and homoisochromanes.[5] The closely related cyclic acetals, acetaldehyde-ethyleneglycolacetal,[11] benzaldehyde-ethyleneglycolacetal,[5] as well as other 1,3-dioxolanes [12] and 1,3,5-trioxanes [13] react similarly with oxygen yielding the corresponding cyclic hydroperoxy *ortho*-diesters.

In view of the general utility of peroxidic compounds for specific oxidations the present study was carried out on the preparation, properties and characterisation of crystalline *p*-dioxanyl hydroperoxide (I).

A rapid stream of air was passed through freshly distilled, peroxide-free dioxane (925 g) refluxing on a steam bath. After 48 hours the solution contained about 1.2 % hydroperoxy compound (iodometric titration). The solvent was removed under reduced pressure and a colourless oil (20.5 g) was obtained which partially crystallised on standing in a refrigerator. The crystals were

filtered off (11.0 g, 0.87 %) and repeatedly recrystallised from ethylacetate-hexane yielding colourless prisms melting between 53 and 56°.

The compound gave on analysis C 39.86, H 6.85 and O 53.18 % ($C_4H_8O_4$ requires: C 40.02, H 6.66 and O 53.31 %) and liberated 97 % of the theoretical quantity of iodine from an acidified potassium iodide solution. It is soluble in water and the common polar solvents (methanol, ethanol, acetone, ethyl acetate, diethylether, chloroform) but almost insoluble in non-polar solvents (benzene, carbon tetrachloride, hexane).

The IR-spectrum (KBr) shows a relatively sharp OH stretching vibration band at 3346 cm^{-1} and a double peak in the 1390—1370 cm^{-1} region, probably attributable to the in-plane OH bending vibration. The position of the band at 3346 cm^{-1} indicates strong intramolecular hydrogen bonding. This hydrogen bond proves sufficiently strong to withstand fission in dioxane, which would lead to intermolecular hydrogen bond formation, and is essentially unaffected by dilution. Two further bands, at 1120 and 1075 cm^{-1} can be correlated with the C—O antisymmetric stretching modes and a weaker peak at 890 cm^{-1} may be due to the O—O vibration.

In the NMR spectrum (Fig. 1) the hydroxyl proton exhibits a signal (1 H) at $\delta=9.77$ ppm. The triplet centered at 5.04 ppm (1 H) is due to the proton on the carbon atom which carries the hydroperoxy group (C_2). This proton couples with the protons on C_3 giving rise to a spectrum of the ABX type ($J_{AX}+J_{BX}=5.7$ cps). The signals of the protons on C_3 form the AB part centered at 3.75 ppm and are included in the methylene multiplet. They could be located by spin decoupling of the C_2 proton and by INDOR irradiations [14] with the observation fields resting on the lines at 5.01 and 5.07 ppm.

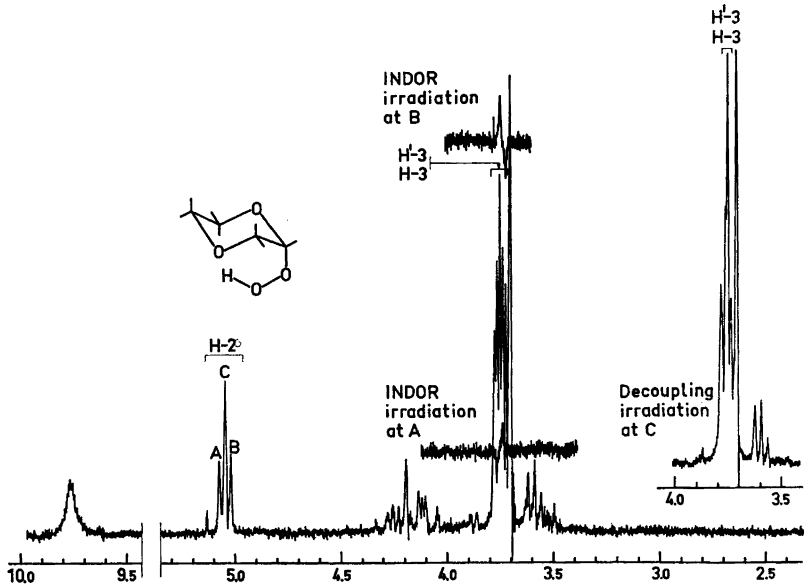


Fig. 1. NMR spectrum of *p*-dioxanyl hydroperoxide (I).

The symmetrical triplet pattern of the signal exhibited by the C_2 proton indicates two weak interactions with the vicinal protons. This can be rationalised in terms of an axial-equatorial and an equatorial-equatorial coupling and implies that the chair form having the hydroperoxy function axially orientated is strongly favoured. This preferred axial orientation of the hydroperoxy group may be due to hydrogen bonding between the hydroperoxy group and the oxygen atom in 4-position, as well as to the interaction between the C—OOH dipole and the dipole due to the unshared electrons of the adjacent dioxane ring oxygen.

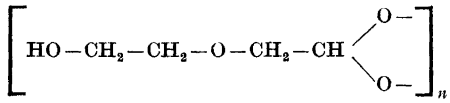
The latter explanation had been advanced to interpret the preferred conformation with axially orientated substituents in *trans*-2,3- and *trans*-2,5-dihalo-*p*-dioxanes [15] and in glycosides [16] and glycosyl halides [17–19] ("anomeric effect").[20,21]

Fig. 4 shows the mass spectrum of compound I. The base peak at $m/e=87$ is probably due to the dioxanyl fragment $C_4H_7O_2^+$ (oxonium ion) formed by loss of the hydroperoxy radical ·OOH. Strong peaks are present at $m/e=73$, 45, 31, 29, and 15. The first of these can be attributed to the aldehydic oxonium ion $OHC-CH_2-O^+=CH_2$ arising through transfer of hydrogen from C_6 to the hydroperoxy group with cleavage of the 1,2-bond followed by rupture of the 2,3-bond. The others may possibly be ascribed to the arrangement products $CH_3-CH=O^+H$, $CH_2=O^+H$, $HC\equiv O^+$ and $CH_3^{\cdot}$, respectively. The molecular ion peak ($m/e=120$) amounts to 1.3 % of the base peak.

The crystalline compound (I) decomposed slowly, even when kept at 0°, producing a colourless liquid composed of at least eight components. Attempts to separate these components chromatographically have been unsuccessful so far because of their instabilities and similar chromatographic behaviour. At room temperature the conversion into the oily liquid proceeds faster and at 100° it is essentially complete after 3 h. No violent decomposition of the pure compound has so far been observed.*

The hydroperoxidation of dioxane was carried out under a variety of conditions. Refluxing temperature, abundant supply of air (or oxygen) and illumination (daylight or UV) were found necessary for an extensive reaction. The use of benzophenone as a sensitizer increased the rate of reaction at room temperature to a considerable extent.[9] Attempts to improve the yield of the hydroperoxy compound by prolonging the reaction time were unsuccessful. Under the conditions employed (see p. 3183) the content of *p*-dioxanyl hydroperoxide reached a maximum after about 48 h, when the decomposition caused by the acidity of the compound and of its decomposition products

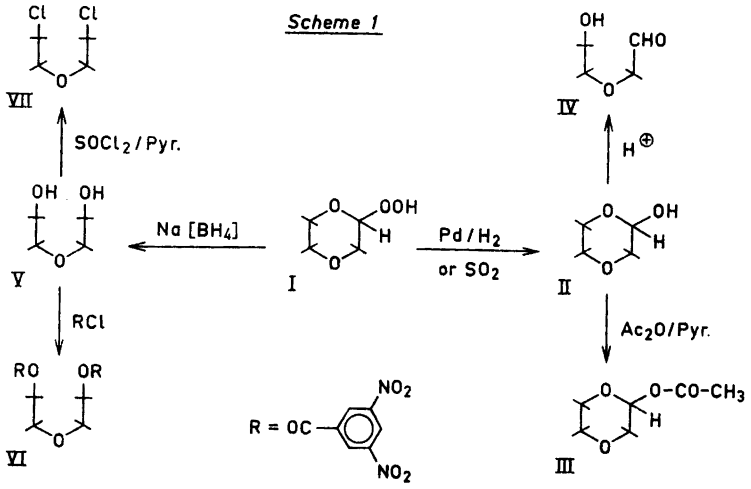
* However, care should be taken, when technical grade dioxane is distilled. In the distillation residues the hydroperoxy compound I will accumulate and on prolonged heating possibly produce explosive alkylideneperoxides of the type (*cf.* Ref. 8)



counter-balanced the formation. The products of decomposition have not been characterised.

The following reactions have been carried out with compound I (see Scheme 1).

Scheme 1



Catalytic reduction with hydrogen and palladium or reduction with sulphur dioxide yielded the cyclic hemiacetal II (*p*-dioxan-2-ol)[22,23] which was characterised by analysis, NMR and IR spectra, as well as by conversion into its acetate (III)[24,25] and ring opening to the hydroxy-aldehyde IV.[26]

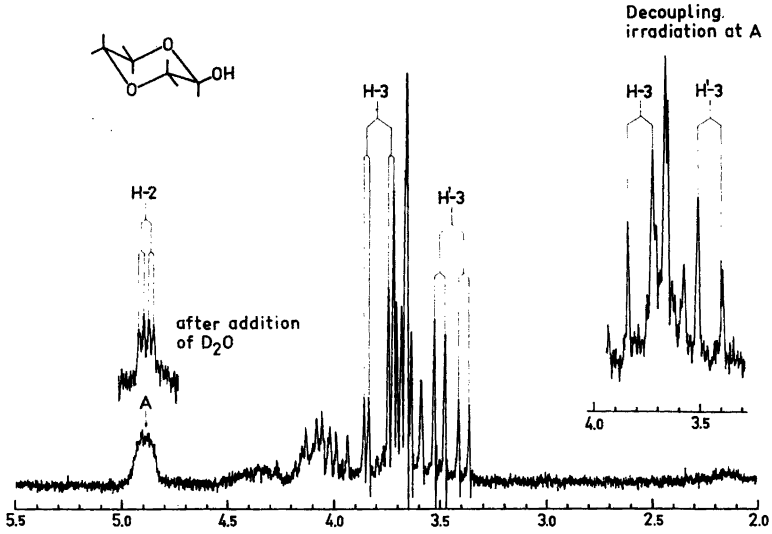


Fig. 2. NMR spectrum of *p*-dioxan-2-ol (II).

The NMR spectrum for *p*-dioxan-2-ol (II) is shown in Fig. 2. The hydroxyl proton exhibits a weak and broad signal at about 4.33 ppm. On addition of D_2O this signal disappears, whereas the signal due to the C_2-proton (1 H) at 4.87 ppm is resolved into four lines. These lines form the X part of an ABX-system, the remaining two quartets of which are centered at 3.77 and 3.45 ppm. Their signals could be located in the methylene multiplet by spin decoupling of the C_2-proton at 4.87 ppm, whereby the two quartets collapsed into two doublets (see Fig. 2). The broad signal of the C_2-proton and the distinct difference between the vicinal couplings (J_{AX}=2.2 cps and J_{BX}=5.0 cps) may be associated with an equatorial-axial and a diaxial coupling, respectively, and suggest that the chair conformation having the hydroxyl group equatorially orientated predominates in the conformational equilibrium. Evidently, there is no possibility for strong hydrogen bonding between the hydroxyl group on C_2 and the oxygen in 4-position. Furthermore, the interaction of the C_2—OH dipole with the atomic dipole due to the *p* electrons of the oxygen in the 1-position may be expected to be weak (*cf.* the small "anomeric effects" on free hydroxyl groups, Ref. 16, p. 376).

The observed vicinal couplings (2.2 and 5.0 cps) are in good agreement with the values for corresponding methyl-2-deoxy-pyranosides (*e.g.* methyl-2-deoxy-β-D-*threo*-pentapyranosides, 1.9 and 5.0 cps, respectively).[27] The equatorial orientation of the hydroxyl group on C_2 is also supported by the chemical shift of the axial C_2-proton (δ=4.87 ppm) the resonance of which appears at higher field than the signal of the equatorially orientated C_2-proton in *p*-dioxanyl hydroperoxide (δ=5.04 ppm, see above) (*cf.* Ref. 28).

The NMR spectrum for *p*-dioxan-2-ol acetate (III), shown in Fig. 3, bears strong resemblance to that of *p*-dioxanyl hydroperoxide (Fig. 1). As with the latter, the C_2 and C_3 protons give rise to an ABX-pattern ($J_{AX}+J_{BX}$=3.8 cps). Compared to the signal of the C_2-proton in compound

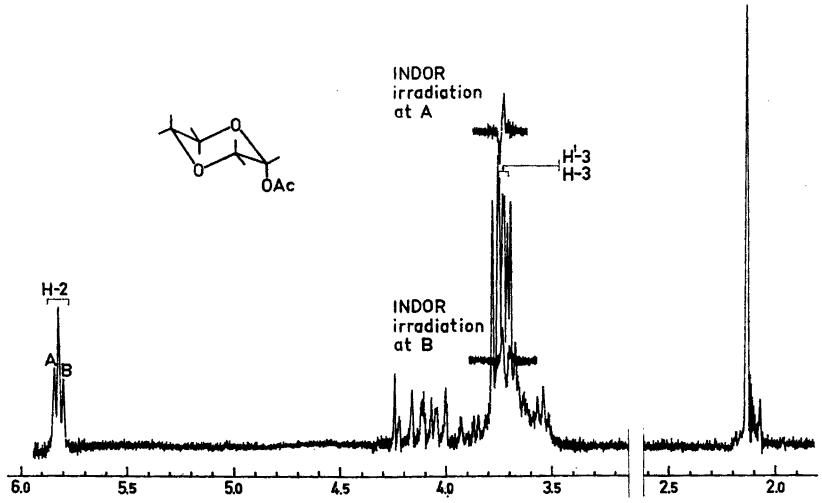


Fig. 3. NMR spectrum of *p*-dioxan-2-ol acetate (III).

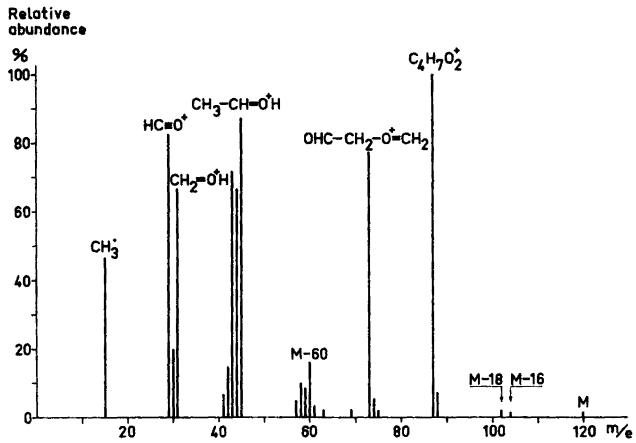


Fig. 4. Mass spectrum of *p*-dioxanyl hydroperoxide (I).

II the resonance of the C_2-proton in compound III, a symmetrical triplet (1 H), is displaced by 0.96 ppm to lower field (δ=5.83 ppm). This shift may be attributed partly to the stronger deshielding effect of the acetoxy group as compared with that of the hydroxyl group [29] and partly to the equatorial orientation of the C_2-proton.[28]

Thus, the spectrum of *p*-dioxan-2-ol acetate (Fig. 3) in common with that of *p*-dioxanyl hydroperoxide (Fig. 1) shows a preponderant contribution of the chair conformer having the substituent on C_2 axially orientated. The different conformation of the acetate III compared with that of the parent hemiacetal II must be ascribed to a stronger dipole-dipole interaction ("anomeric effect") in the former compound (see above).

INDOR-irradiations at the frequencies of the outer signals of the triplet at 5.83 ppm permitted the location of four of the strongest resonances for the C_3-protons (2 doublets centered at 3.73 and 3.75 ppm). On spin decoupling of the C_2-proton these doublets collapsed into 2 singlets. The acetyl protons of compound III resonate at 2.14 ppm.

The IR spectrum of *p*-dioxan-2-ol (II) contains a broad, intense OH stretching band between 3500 and 3200 cm^{-1}, indicative of strong intermolecular hydrogen bonding. The IR spectrum of the acetate III shows stretching vibration bands at 1733 cm^{-1} (C=O) and 1235 cm^{-1} (C—O).

Reduction of compound I with sodium borohydride gave diethyleneglycol (V) which was identified by NMR and IR spectra, and by preparing the bis-3,5-dinitrobenzoate (VI) and the β,β'-dichloro-diethylether (VII). The NMR and IR spectra of compounds V—VII were identical with those of authentic samples, all the NMR spectra showing characteristic symmetrical A_2B_2-patterns.

EXPERIMENTAL

All melting points are corrected. Extracts were dried over sodium sulphate and concentrated under reduced pressure.

Thin-layer chromatography was performed on silica gels G and HF_{254} using a mixture of chloroform-ethyl acetate (1:1) as solvent. The chromatograms were developed with iodine vapour or conc. sulphuric acid to reveal all the components or with solutions of potassium iodide (5 %) and of starch (0.5 %) to specifically locate hydroperoxy compounds.

NMR spectra were obtained on a Varian HA-100 (compounds I—III) and on a Varian A-60 spectrometer (compounds V—VII). Solutions in deutero-chloroform (about 10 %) were used with tetramethylsilane as internal reference. The spin decoupling and INDOR [14] experiments were carried out using a Hewlett Packard Model 202C Audio Oscillator.

The preparation and properties of *p*-dioxanyl hydroperoxide (I), as well as all NMR and IR spectra are described on pp. 3183—3188.

Reactions of p-*dioxanyl hydroperoxide.* a) *Reduction with sodium sulphite.* A precooled aqueous solution (30 ml) of $Na_2SO_3.7\ H_2O$ (2.5 g) was added dropwise to a cooled solution of compound I (1.0 g) in water (5 ml) with stirring. The solution was repeatedly extracted with ether and the combined ether extracts were carefully dried. After evaporation chromatographically pure p-*dioxan-2-ol (II)* remained. (0.56 g, 64.7 %) (Found: C 46.02; H 7.70; O 46.27. Calc. for $C_4H_8O_3$: C 46.17; H 7.69; O 46.14).

b) *Catalytic reduction.* Compound I (1.0 g) was dissolved in ethanol (80 ml) and catalytically hydrogenated (Pd on charcoal). After purification by thin-layer chromatography compound II was obtained as a colourless liquid (0.48 g, 55 %) identical with the product prepared according to a) (analysis, NMR, and IR spectrum).

p-*Dioxan-2-ol acetate (III).* *p*-Dioxan-2-ol (II) (0.25 g) prepared according to a) or b) (see above) was acetylated with acetic anhydride (2 ml) in pyridine (2 ml). The crude product was purified by preparative thin-layer chromatography using ethyl acetate as solvent. (160 mg, 45.6 %) (Found: C 49.27; H 6.83; O 44.06. Calc. for $C_6H_{10}O_4$: C 49.34; H 6.84; O 43.82).

5-Hydroxy-3-oxapentanal-o,p-*dinitrophenylhydrazone.* A solution of *p*-dioxan-2-ol (II) (0.4 g) in water (5 ml) containing 1 drop of conc. hydrochloric acid was heated on a steam bath for 1 h. The hydroxyaldehyde IV formed was converted into its *o,p*-dinitrophenylhydrazone by adding a solution of 2,4-dinitrophenylhydrazine hydrochloride in dilute acetic acid. Recrystallisation of the crude precipitate from 50 % ethanol yielded yellow plates (0.67 g, 61 %), m.p. 139—140°, lit. 136°.[26]

c) *Reduction with sodium borohydride.* To a solution of compound I (4.0 g) in water (10 ml) an aqueous solution (20 ml) of sodium tetrahydrido-borate (3.5 g) was added dropwise. After 2 h the precipitate of borate was filtered off and the filtrate passed through a cation exchanger of type Dowex 50W—X8 in the H^+-form. The eluate was evaporated to dryness and the residue freed from boric acid by repeated dissolution in methanol and concentration under reduced pressure. The yield of crude *diethyleneglycol* was 3.33 g (94.3 %). The product was distilled under reduced pressure (0.1 mm Hg) at 60—70° to give chromatographically pure compound V (2.23 g, 63 %).

Heating compound V (0.55 g) with 3,5-dinitrobenzoyl chloride (3.45 g) yielded the bis-3,5-dinitrobenzoate (VI) (2.3 g, 90 %) which after repeated recrystallisation from chloroform-hexane melted at 153—154°. Mixed m.p. with an authentic sample showed no depression.

Treatment of compound V (0.25 g) with thionylchloride (0.85 ml) in pyridine (0.30 ml) afforded crude *β,β'*-dichloro-diethylether (VII) (0.26 g, 76 %) which was purified by thin-layer chromatography. (Found: C 33.77; H 5.44; O 11.34; Cl 49.49. Calc. for $C_4H_8OCl_2$: C 33.61; H 5.59; O 11.19; Cl 49.60).

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