1,2-Dioxolane *versus* 1,2-Dioxane Formation in the Cyclization of an α,ω-Diene Hydroperoxide under Polar and Free Radical Conditions

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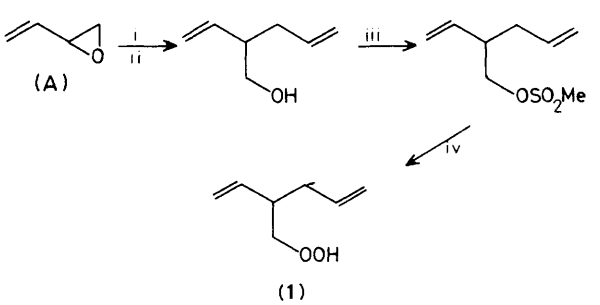
Radical cyclizations of 3-hydroperoxymethylhexa-1,5-diene occur exclusively at the C-1,C-2 double bond to afford 1,2-dioxolanes stereospecifically, whereas electrophile-induced cyclizations additionally yield products derived from attack at the C-5,C-6 double bond.

Studies of the radical[1] and polar[2] cyclizations of unsaturated hydroperoxides have played an important part in establishing a basis for understanding the oxidation of polyunsaturated substrates. 1,2-Dioxolanes and 1,2-dioxanes have been obtained by both mechanisms, but there is scant evidence regarding the relative ease of formation of the two ring sizes. Thus, to the best of our knowledge, no kinetic data are available, and internal competitions have invariably involved *exo versus endo*[3,4] cyclizations. We report here the preparation of the first diene hydroperoxide capable of forming both 1,2-dioxolane and 1,2-dioxane by the favoured *exo* mode, and the results of its cyclization under free radical conditions and by reaction with electrophiles.

3-Hydroperoxymethylhexa-1,5-diene (**1**)† was prepared by the route shown in Scheme 1. The conversion of butadiene monoxide (A) into alcohol was regiospecific and quantitative. The yield of hydroperoxide from mesylate was only 14%, but the reaction was clean.



Scheme 1. *Reagents:* i, excess of $CH_2{=}CHCH_2MgBr$; ii, aq. NH_4Cl; iii, $MeSO_2Cl$, pyridine; iv, 30% H_2O_2, KOH.

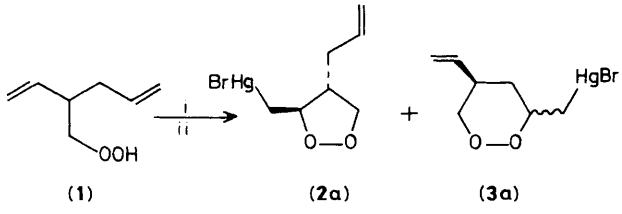
† All new compounds had satisfactory elemental analyses and/or mass spectra, and ^1H and ^{13}C n.m.r. spectra consistent with the proposed structures.

Polar cyclization of diene hydroperoxide (**1**) with mercury(II) nitrate[2] afforded a *ca.* 2 : 1 mixture of *trans* (see below) dioxolane (**2a**)† and mainly *cis* (by ^1H n.m.r. spectroscopy) dioxane (**3a**)† (Scheme 2).

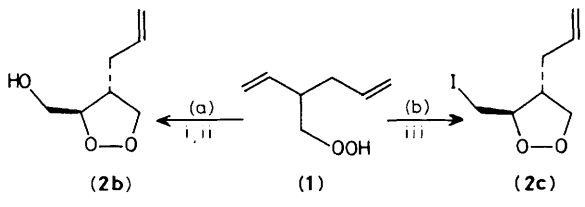
On the other hand, t-butoxyl-initiated radical cyclization[1] afforded only one peroxidic product, the hydroxy-substituted dioxolane (**2b**)† (Scheme 3, a). We assign the *trans* configuration to this product by analogy with the result for the parallel cycloperoxyiodination (see below).

The yield of isolated dioxolane (**2b**) was only 10%, but the conclusion that radical cyclization of diene hydroperoxide (**1**) is both regio- and stereo-specific was supported by its reaction with *N*-iodosuccinimide (NIS). We have provided evidence that this reagent brings about cycloperoxyiodination by a free radical chain mechanism,[5] and dioxolane (**2c**)† (54%) was the sole cyclization product (Scheme 3, b).

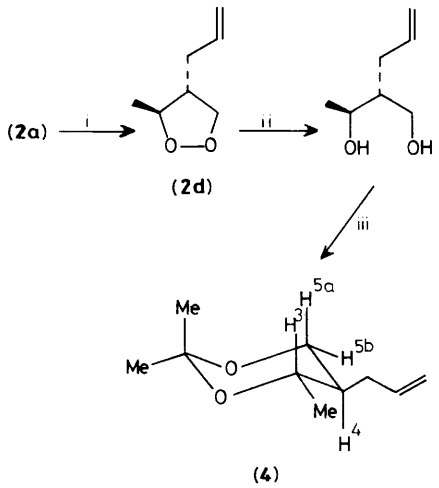
The configurations of the dioxolanes (**2a**) and (**2c**) were shown to be the same by interconversion *via* iododemercur-



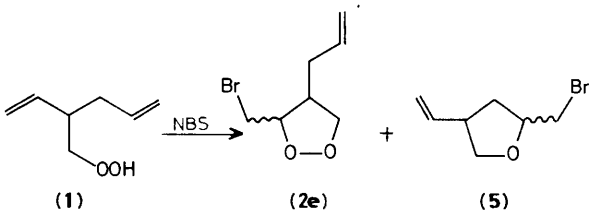
Scheme 2. *Reagents:* i, $Hg(NO_3)_2{\cdot}0.5H_2O$; ii, aq. KBr.



Scheme 3. *Reagents:* i, $(Bu^tOOCO)_2$, O_2; ii, Ph_3P; iii, NIS.



Scheme 4. *Reagents:* i, $NaBH_4/OH^-$; ii, Zn/NH_4Cl; iii, $Me_2C(OMe)_2$, p-$MeC_6H_4SO_3H$ catalyst.



Scheme 5

iation.[6] The configuration was established as *trans* by converting the mercurial (**2a**) into the 1,3-dioxane (**4**) [Scheme 4; numbering as in original (**2a**); *cf.* ref. 7], for which analysis of the 400 MHz ^1H n.m.r. spectrum gave $J_{3,4}$ 10.1, $J_{4,5a}$ 11.4, and $J_{4,5b}$ 5.1 Hz. Thus, the 5-*exo* cyclization of the peroxyl radical derived from diene hydroperoxide (**1**) exhibits parallel stereoselectivity to that of the 4-methylhex-5-enyl radical, in agreement with the predictions of Beckwith *et al.*[8]

Cycloperoxybromination by reaction with *N*-bromosuccinimide (NBS) is mainly a polar process.[5] Consistent with this, diene hydroperoxide (**1**) yielded not only dioxolane (**2e**),† but also the tetrahydrofuran derivative (**5**), in a ratio of *ca.* 2 : 1, both products being mixtures of *cis*- and *trans*-isomers (Scheme 5). Formation of cyclic ether (**5**) can be rationalised by the intermediacy of a *gem*-dialkylperoxonium ion.[9]

Whereas mercuriodioxane (**3a**) could conceivably arise *via* isomerisation of the initially formed mercuriodioxolane,‡ conversion of bromodioxolane (**2e**) into the tetrahydrofuran derivative (**5**) under the reaction conditions used is extremely unlikely. It seems probable, therefore, that polar cyclization is generally less regiospecific than radical cyclization. However, both mechanisms favour formation of the five-membered ring with a *trans*-disposition of the 3,4-substituents.

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‡ The product ratio was changed to *ca.* 1 : 1 by increasing the reaction time from 0.75 to 24 h, but extensive decomposition also took place.