Ozonolysis of cis- and trans-1,4-Dichlorobut-2-ene. Non-concerted Formation of Primary Ozonides [1]

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The ozonolysis of cis- or trans-$CH_2Cl \cdot CH=CH \cdot CH_2Cl$ (1) performed at $-10\ ^{\circ}C$ in a participating solvent (CD_3OD) has been found to lead to non-concerted formation of primary ozonides (9). The heterolysis of these unusually stable primary ozonides to the corresponding alkoxy peroxide (11) and aldehyde (12) was monitored and the data have been tentatively rationalized by assuming neighbouring halogen participation which actually increases the stability of the Criegee zwitterionic intermediate (6).

The mechanism of the ozonolysis of alkenes is still being actively investigated in order to clarify the many aspects which are not fully understood [e.g. the nature of the transition states leading from the primary (2) to the final (5) ozonides]. Very little information is available on the nature of the interaction of ozone with olefins bearing halogen substituents. It is known that these substituents generally deactivate the double bond, but investigations have generally been concerned with the electrophilic nature [2] of ozone attack on the double bond rather than the role of the halogen. The recently reported ozonolysis of trans-2,3-dichlorobut-2-ene in non-participating solvents [3] has given new insight into the course of the ozonolysis of halogenated double bonds, since the ratio between the carbonyl (3) and Criegee zwitterion (4) moieties obtained by cleavage of the (undetected) primary ozonides (2) was found to be unexpectedly higher than unity. This has been tentatively attributed to side reactions involving dimerization of the unstable zwitterion. We therefore investigated 1,4- rather than 2,3-dichloro derivatives in order to assess the increase, if any, in stabilization of the zwitterionic intermediate (6) as a result of neighbouring halogen participation.

Results and Discussion

The ozonolysis of the title olefins, performed at 24 $^{\circ}C$ in non-participating solvents, confirms some preliminary observations.[4] No definite stereoselectivity is observed in the production of the ozonides (7) starting from either cis- or trans-$CH_2Cl \cdot CH=CHCH_2Cl$(1) [neat or in solvents such as C_6D_6, CCl_4, $CFCl_3$, CD_2Cl_2, CD_3COCD_3, or $(CD_3CO)_2O$], the cis : trans ratios of the products being ca. 1 in each case † providing the comparison is made for the same solvent. On increasing the polarity of the solvent (e.g. from benzene to acetic anhydride, see above) a slight increase in the total amount of α-chloroacetaldehyde together with small amounts of oligomers are found (see Experimental section). These effects may be attributed to increased solvent participation in the transition state which affects the recombination (see Scheme) of the zwitterion and aldehyde moieties to the final ozonide.[8]

A completely different situation arises when the ozonolysis of cis- or trans-olefin (1) is performed in CD_3OD at $-10\ ^{\circ}C$; the spectroscopic and chemical evidence (reported in detail in the Experimental section) show the formation of the primary ozonides (9). In the n.m.r. spectra a substantial upfield shift ($\Delta\delta$) of the methine proton signals is observed compared to those of the ozonides (7), and the multiplicities were as expected.[9] In the i.r. spectra, the observed C–O and O–O–O (both antisymmetric and symmetric) frequencies and the O–O–O bending vibration agree fairly well with recent findings.[10] Final confirmation was obtained on reductive cleavage of the ozonides (9) with a Grignard reagent, which

yielded the corresponding α-diols, identified by comparison with authentic samples.

The formation of primary ozonides in participating solvents is not unprecedented, although there are very few reports in the literature.[11] Much more intriguing is the apparent lack of stereospecificity in their formation, as implied by the preliminary n.m.r. results in Table 1 and supported by the more detailed data in Table 2.

According to reported chemical [12] and spectroscopic [9] analyses, the 1,3-dipolar cycloaddition of ozone to an olefin is generally considered to be a concerted, and therefore stereospecific, orbital-symmetry-allowed reaction; this has also been indicated by thermochemical considerations.[13] However, it has been reported recently [14] that although non-concerted routes to ozonide are usually minor, under some experimental conditions they can become the major pathway. With some halogen-substituted olefins,[2] in addition to steric retardation of cycloaddition as a likely cause of the observed anomalies, another explanation [2,15] has been suggested; this involves the reversible initial formation [16] of a π-complex (8) which can

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† It may be inferred in analogy with the reported anomalous behaviour of cis-but-2-ene [5] that for the cis primary ozonide
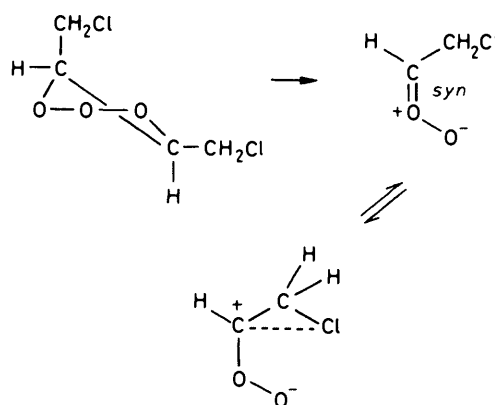
an axial rather than equatorial CH_2Cl substituent is preferentially incorporated into the zwitterion moiety. Since axial substituents favour the production of syn-zwitterions which react with aldehydes to give preferentially trans final ozonides, the observed lack of stereoselectivity is not totally unexpected. On this basis however it is difficult to assess whether the syn-carbonyl oxide is more stabilized than its anti-stereoisomer [6] by a probable halogen participation which induces a more efficient charge delocalization of the corresponding zwitterionic carbocation. The reported relative efficiency of the CH_2Cl group in stabilizing zwitterions via inductive and mesomeric effects [7] does not clarify this point.

**Table 1.** N.m.r. results [a] for the ozonolysis of 1,4-dichlorobut-2-ene (1) in CD_3OD at $-10\,°C$

Expt.[b]		Conversion	Ratio [d] of	Product ratios	
no.	Reactant [c]	(9) : (1)	stereoisomers	(12) : (9)	(11) : (9)
1	trans-(1) *	0.42	0.85		
2	trans-(1) †	0.40	0.82	0.14	0.13
3	cis-(1) *	0.44	1.20		
4	cis-(1) †	0.39	1.16	0.15	0.16

[a] All the results were determined *in situ* by evaluating the ratios of specific integrated CH peak areas. [b] The experiments were performed by treating O_3 (30.0 mmol) with excess of alkene (50.0 mmol: 5 ml of solvent). [c] The spectra were taken at $-10\,°C$ either * immediately, or † after 8 h at 24 °C. [d] The reported ratios refer to the high (δ 4.68) to low (δ 4.80) field integrated CH peak areas of (9).

Table 2. Heterolysis of primary ozonides (9) in CD_3OD at 24 °C. Summary of results [a] determined by n.m.r. and conventional techniques

Expt.	Reaction	Conversion	Ratio [b] of	Product ratios		
no.	time	(9) : (1)	stereoisomers	(12) : (9)	(11) : (9)	(7) [c] : (9)
1	d	0.42	0.85			
2	20 h	0.38	0.76	0.26	0.26	
3	3 days	0.28	0.66	0.51	0.44	0.28
4	e	0.20	0.60	0.30	0.58	0.45

[a] Unless otherwise indicated, all the results were determined as in Table 1. [b] The ratios [*meso-* to ($\pm$)-] of isomers of 1,4-dichlorobutane-2,3-diol obtained by reductive cleavage with a Grignard reagent are reasonably different [expt. 1, 0.36; expt. 2, 0.30; expt. 3, 0.20; expt. 4, 0.12]. Since the overall yields of glycols were low (see Experimental section), the ratios obtained by this procedure do not reflect the ratios of stereoisomers (9). [c] The formation of final ozonides (7) has been independently confirmed, as reported in the Experimental section, through their partial isolation and characterization. [d] Same as expt. 1, Table 1. [e] Same as expt. 3 but after partial solvent removal and 2 more days at 24 °C.
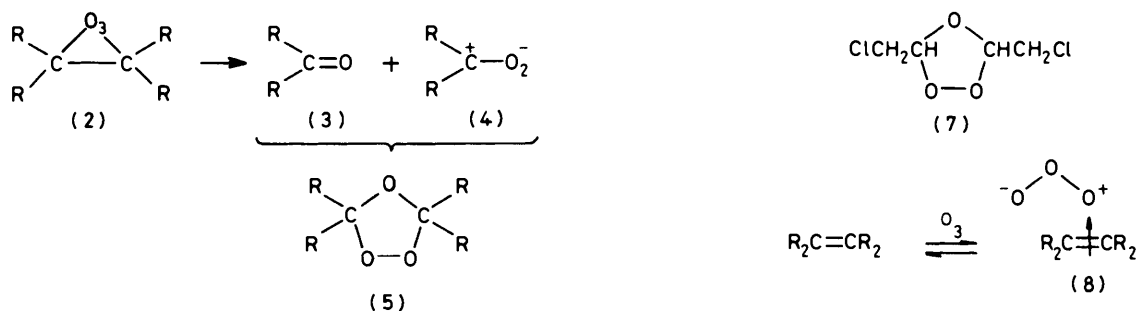
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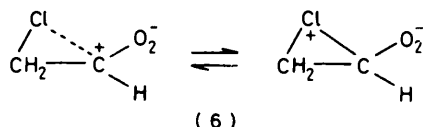
subsequently take part in the cycloaddition step. The cited anomalies are apparently more justified if they are attributed to resonance effects of the halogen substituents which affect the reversible formation of complex (8). In order to explain the observed lack of stereospecificity in product formation [17] from the olefin (1), an intramolecular, stabilizing halogen participation has already been postulated to occur in the transition state. If this is the case, it may be assumed that any neighbouring halogen participation which occurs before the cycloaddition step may cause partial isomerisation of (1), thus contributing to the reported lack of stereospecificity.
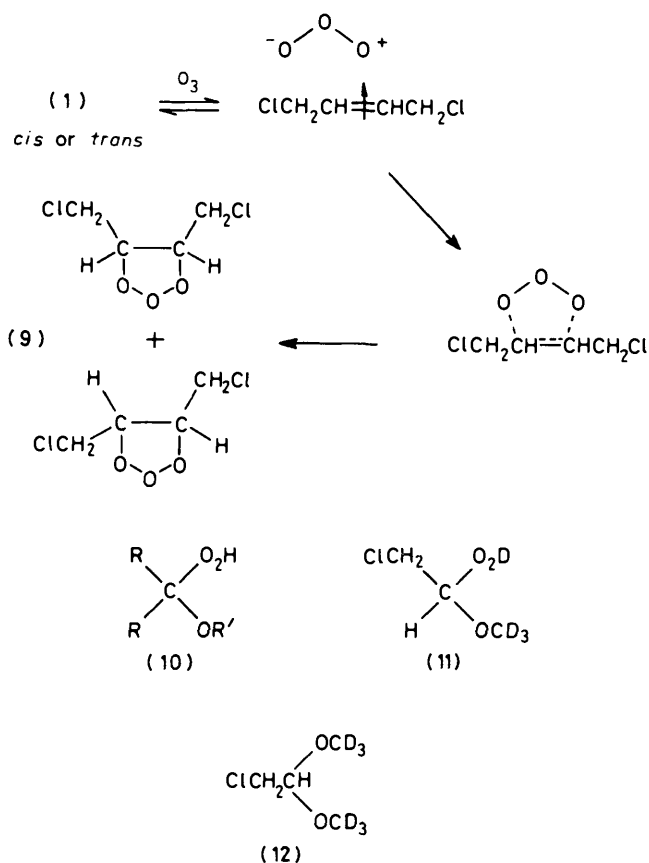
Some of the earliest evidence for the existence of Criegee zwitterions (4) came from scavenging reactions of these ions with alcohols [18] to form the corresponding hydroperoxides

(10). We carried out preliminary * n.m.r. investigations which suggested the incipient formation of the alkoxy peroxide (11) and aldehyde (12). Re-examination of experiments 1 and 3 (Table 1) after 8 h at room temperature (experiments 2 and 4, respectively) gave further n.m.r. evidence which supported this observation (see Experimental section).

In order to assess any increase in stabilization of the zwitterionic intermediate (6) due to participation of a neighbouring halogen, the heterolysis of (9) in CD_3OD was more extensively investigated by n.m.r. at 24 °C (see Table 2). At this temperature, on increasing the reaction time (Figure) the methine peak areas of the primary ozonides (9), centred at δ 4.68 and 4.80, steadily decreased while a concomitant increase was observed for the methine peak areas of the alkoxy peroxide (11) and the aldehyde (12), centred at δ 4.95 and 4.50 respectively.

The data summarised in Table 2 require an explanation since the observed primary ozonide decomposition is unusually slow. It may be observed that: (i) while with *trans*-2,3-

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* It has been reported [19] that in MeOH some primary ozonides rearrange to cyclic peroxides by a different route from the Criegee mechanism.

(1)

cis or trans

O_3

$ClCH_2CH=CHCH_2Cl$

(9)

+

$ClCH_2CH=CHCH_2Cl$

(10)

(11)

(12)

Figure. Heterolysis of primary ozonides (9) in CD_3OD. The n.m.r. spectrum of experiment 1 (Table 1) after 3 days at 24 °C (δ relative to internal $SiMe_4$)

(13)

(14a)

(14b)

(15a)

(15b)

(15c)

dichlorobut-2-ene in non-participating solvents [3] the carbonyl (3) to zwitterion (4) reported ratios are much higher than unity, in this case the same ratio [which may be taken as the aldehyde (12) to alkoxy peroxide (11) ratio] is much closer to 1 (see Table 2, experiment 2); (ii) the observed formation of the final ozonides (see Figure and Table 2, experiments 3 and 4) implies recombination of carbonyl and zwitterion moieties to a minor extent which, owing to the solvent nucleophilicity, would normally be prevented. These results seem to suggest that the halogen acts as an internal nucleophile and may compete effectively with solvent molecules (cf. the reported [20] formation of halogenonium ions via 1,4-halogen participation in nucleophilic solvents) in stabilising the developing zwitterionic carbocation. Accordingly, charge dispersal to the bridged halogen atom may lead to a more stabilized zwitterion (6), thus increasing the chances of interaction with the aldehyde moiety to yield the final ozonides (7).

The following n.m.r. data provide additional evidence for the intermediacy of the stabilized zwitterion (6). By repeating the same heterolysis in MeOH under comparable experimental conditions to those reported in Table 2, a faster collapse of the primary ozonides (9) is observed (see Experimental section). However, as far as the in situ formation of the non-deuteriated alkoxy hydroperoxide (11) is concerned, and relative to the same pure hydroperoxide isolated from the same reaction mixture by vacuum distillation, we have found that: (i) while the methine hydrogen of the pure distilled compound yields a neat triplet, the methine hydrogen observed in situ appears as a doublet of triplets suggesting the formation of two isomeric hydroperoxides (the same effect occurs in CD_3OD: see Figure, δ 4.96); (ii) the hydroperoxy proton observed (δ 5.90) in situ is clearly less deshielded than the corresponding proton (δ 9.54) in the distilled compound (see Experimental section).
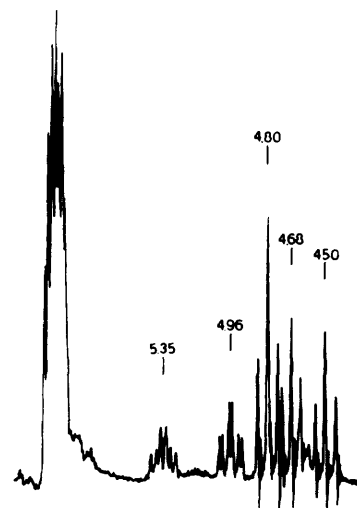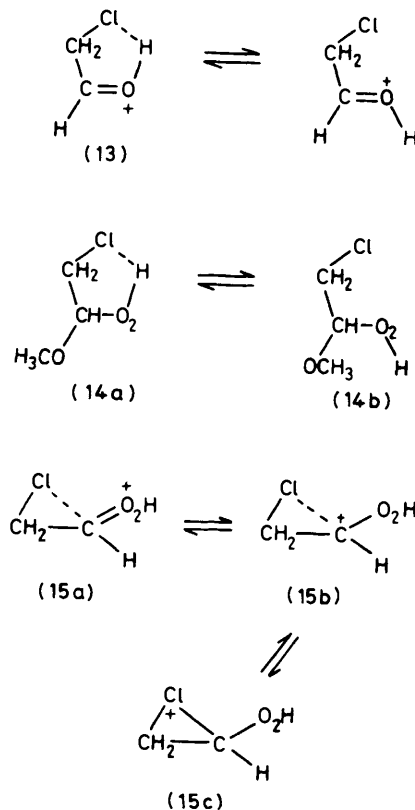
The latter results are reminiscent of some recent observations [21] with protonated α-chloroacetaldehyde, which is shown to yield two isomeric species. One of these species, (13), with a less deshielded O^+H proton (0.5 p.p.m. to higher field) and more deshielded methylene protons, is explained in terms of hydrogen bonding (between the proton on oxygen and the chlorine atom) which delocalizes the positive charge to the halogen.

In our case, although it is more complex and unprecedented, it may be assumed that two isomeric hydroperoxides (14), which normally are not distinguishable owing to fast

exchange of the non-protonated O_2H group, can be differentiated when generated in CH_3OH or CD_3OD by heterolysis of the primary ozonides (9). However, the degree of deshielding observed for the hydroperoxide proton compared with that of the O^+H proton of the aldehyde can hardly be accounted for only in terms of intramolecular hydrogen bonding. Rather, it can be explained by assuming that: (i) a much greater positive charge delocalization to halogen is associated with the immediate precursors [e.g. protonated zwitterionic intermediates (15)] of the isomeric hydroperoxides (14); and (ii) this greater positive charge delocalization, as a stabilizing factor, actually retards the formation, by heterolysis of the ozonides (9), of the isomeric peroxides (14) in solution.

Experimental

N.m.r. spectra were obtained on a Varian 100 or 270 spectrometer equipped with a variable-temperature controller, with Me_4Si as internal reference. I.r. spectra were recorded on a Perkin-Elmer Model 225 instrument with conventional cells (and compensation cells in the reference beam) fitted with KBr or CsBr windows. The low-temperature spectra were recorded after depositing vapours on CsBr windows [10] in a conventional low-temperature cell. Qualitative and quantitative gas chromatographic analyses were performed on a Carlo Erba Model GT 200 gas chromatograph. The ozone source was a laboratory ozonizer of the type described by Bonner [22] using pure dry oxygen as the feed gas.

cis- *and* trans-1,4-*Dichlorobut-2-ene* (1).—cis-Olefin (1) was synthesized according to the procedure of Bobbitt [23] while the *trans*-isomer (1) was obtained from Fluka. Gas chromatographic analyses (2.5% SE 30 on 60—80 mesh DMCS Chromosorb W) showed that the cis-isomer was contaminated with ca. 3% of an unknown impurity and a trace of the *trans*-isomer, while *trans*-(1) contained only a trace of the cis-isomer and no other impurities.

α-*Chloroacetaldehyde.*—The aldehyde was prepared by periodate oxidation of α-chlorohydrin; [24] water removal was performed by azeotropic distillation as reported by Trippett *et al.*[25]

Isopropyl Bromide.—Obtained commercially from Merck-Schuchardt, it was distilled (b.p. 60 °C 759 mmHg) under nitrogen immediately before use.

Isopropylmagnesium Bromide.—The required amount of magnesium turnings was placed in the reaction flask and after the system had been thoroughly flushed with dry nitrogen, small quantities of the required halogen compound in sodium-dried diethyl ether were added under a reduced nitrogen flow. Initiation of the reaction was effected by the addition of several drops of ethyl bromide followed by gentle warming. To the moderately stirred mixture was added isopropyl bromide at a rate such that gentle refluxing was maintained. Stirring was continued after the addition of halide had been completed and the reaction mixture was allowed to stand overnight before use.

1,4-*Dichlorobutane-2,3-diol.*—The isomers were prepared from cis- or trans-(1) by the method of Emmons *et al.*[26] and analyzed by gas chromatography (2.0% TPA Carbowax 20 M-Chromosorb G 100—200 mesh).

α-*Chloroacetaldehyde Dimethyl Acetal.*—The aldehyde derivative was obtained commercially by Aldrich.

Ozonolysis Procedures.—Ozone concentration at a gas flow rate of 20 l/h was ca. 5.5 wt% and was normally determined iodometrically. The ozonolysis vessels were generally equipped with a gas inlet tube, a pneumatic sampling device, a solid CO_2-alcohol-cooled condenser and a dropping funnel for the addition of reagents. Cold traps (-80 °C) were put in the gas line before and after the reaction vessel to prevent moisture from entering. The ozonolyses were run to ca. 45% completion in order to prevent autoxidation of aldehydes to peracids.

Ozonolysis of (1) *in Non-participating Solvents.*—On treatment of excess of cis- or trans-(1) [50.0 mmol; neat or dissolved in 5 ml of C_6D_6, CCl_4, $CFCl_3$, CD_2Cl_2, CD_3COCD_3, or $(CD_3-CO)_2O$] at 24 °C with ozone (30.0 mmol), the ozonides (7) were obtained in cis : trans ratios of ca. 1 : 1 (evaluated by integrating the n.m.r. CH peak areas). Comparison with the i.r. and n.m.r. data obtained in CD_2Cl_2 [$v_{max.}$ 2 950, 1 430, 1 360, 1 105, 1 032, and 990 cm^{-1}; n.m.r. cis- (7) δ 5.44 (t, J 5.0 ± 0.5 Hz, 2 H), 3.64 (d, J 5.0 ± 0.5 Hz, 4 H); trans- (7) δ 5.55 (t, J 5.0 ± 0.5 Hz, 2 H), 3.54 (d, J 5.0 ± 0.5 Hz, 4 H)], which coincide fairly well with prior observations,[4] shows that increasing the solvent polarity leads to slight increases in the total amount of free α-chloroacetaldehyde (independently confirmed through its 2,4-dinitrophenylhydrazone derivative; from 3.6 mmol in benzene to 7.7 mmol in acetic anhydride) and oligomer formation occurs to a minor extent as evidenced by a weak n.m.r. absorption on the low-field side of the CH ozonide peak.

Ozonolysis of (1) *in* CD_3OD *and Reaction with Isopropyl Grignard Reagent.*—After completing the addition of O_3 (30.0 mmol) to a solution of cis- or trans-(1) (50.0 mmol) in CD_3OD (5 ml) at -10 °C, as reported in Table 1, the following i.r. and n.m.r. data were obtained. $v_{max.}$ 1 120 (asymm. CO), 1 210 (symm. CO), 970 (asymm. O_3), 1 055 (symm. O_3), and 760 cm^{-1} (O_3 bend); δ 4.68 (t, J 5.5 Hz, 2 H), 3.48 (d, J 5.5 Hz, 4 H), 4.80 (t, J 5.5 Hz, 2 H), 3.58 (d, J 5.5 Hz, 4 H).

The reductive cleavage of (9) was generally performed as follows. After completing the addition of O_3 as reported above, the solvent was carefully removed under reduced pressure while keeping the reaction mixture at low temperature. An excess of an ethereal solution of isopropylmagnesium bromide (200 mmol in 150 ml) was added dropwise to the residue and the temperature of the reaction mixture was not allowed to rise above -80 °C. After 2 days at 10 °C, considerable solid material had separated while nothing had condensed in the solid CO_2-alcohol cooled trap. The reaction mixture was then refluxed for 90 min, cooled to -15 °C and carefully hydrolysed with aqueous ammonium chloride (35.0 g in 150 ml). After exhaustive extraction with diethyl ether of the neutralized aqueous layer, the combined ethereal phases were dried (Na_2SO_4), the ether removed, and the residue (which gave a positive test for α-glycol with periodic acid) was analyzed by gas chromatography and found to contain a mixture of 1,4-dichlorobutane-2,3-diol isomers (the yields never exceeded ca. 20%).

Heterolysis of Primary Ozonides (9) *in* CH_3OH. *Isolation of 2-Chloro-1-methoxyethyl Hydroperoxide.*—Experiment 1 of Table 1 was repeated in CH_3OH under the same experimental conditions. After 20 h at 24 °C a faster cleavage of (9) was observed relative to the heterolysis performed in CD_3OD (Table 2, experiment 2), as evidenced by the following ratios of products: (12) : (9) = 0.50 and (11) : (9) = 0.61. After the solvent had been removed, the ozonides (9) had almost disappeared; accordingly, relative to unconverted olefin (1), in

analogy with the trend observed in Table 2 (see experiment 4), the following ratios were evaluated: (11):(1) = 0.72 and (7):(1) = 0.61. The pure non-deuteriated peroxide (11) was obtained (1.05 g, 8.30 mmol) by vacuum distillation (50.5 °C, 1 mmHg) from the residue; δ 9.54 (bs, O_2H) (cf. δ 5.90 for in situ O_2H), 4.92 (t, CH), 3.68 (t, CH_2), and 3.57 (s, CH_3). Strongest i.r. bands: $v_{max.}$ 3 370, 1 430, 1 360, 1 180, 1 110, 1 055, 1 000, 970, and 765 cm⁻¹. Minor deviations or anomalies in these assignments may be due to the relative stability of pure hydroperoxides containing electron-releasing groups [27] together with the active oxygen assay obtained in this case (ca. 90%).

Although isolation of the final ozonides (7) from the peroxide derivative before vacuum distillation of the latter proved unsuccessful, their presence could be further inferred in the residue obtained after complete solvent removal (24 °C; 1 mmHg) on the basis of some characteristic i.r. frequencies ($v_{max.}$ 2 950, 1 105, and 1 032 cm⁻¹).

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