864. *Organic Peroxides. Part X.* The Autoxidation of Ethyl Chaulmoograte: the Course and Stereochemistry of Homolytic Autoxidation.*

By ALWYN G. DAVIES and J. E. PACKER.

The infrared spectrum and chemical properties of the autoxidation product of (—)-ethyl chaulmoograte (III) show it to be an unsaturated hydroperoxide, and not the " oxoxide " (IV) as has been suggested.

The hydroperoxide is essentially optically inactive. The unsaturated alcohol which is formed by reduction of the hydroperoxide with borohydride has been partially resolved, and then hydrogenated to an optically inactive saturated alcohol. It is concluded that the hydroperoxide has at least principally the structure (±)-(V). This appears to be the first demonstration that homolytic autoxidation proceeds with racemisation.

IT has often been suggested that there might exist a family of isolable compounds of the structure (I), isomeric with structure (II) which is commonly accepted for the organic peroxides. These compounds (I) have been called oxoxides,[1] because of their analogy with the sulphoxides and amine oxides These suggestions, however, have not withstood examination, and although the existence of the compounds (I) remains a formal possibility, no example has yet been firmly established.

(I) $R_2O\rightarrow O$ RO·OR (II)

The case has recently been reopened by Bernard [2] who studied the polarographic behaviour of a number of peroxides in buffered 0·5N-aqueous potassium sulphate. One group of compounds (ammonium persulphate, peroxyacetic acid, peroxybenzoic acid, t-butyl peroxybenzoate, the peroxide of cyclohexanone, cumene peroxide, pinene peroxide, the peroxide of ether, and the peroxide of dioxan) showed a reduction wave at 0·0 v. These easily reduced peroxides were assigned the " true peroxide " structure (I). The second group (acetone peroxide, t-butyl hydroperoxide, ethyl hydroperoxide, dibutyl peroxide, the peroxide of acetaldehyde, and hydrogen peroxide) were reduced with more difficulty, at —0·3 to —1·1 v, and were regarded as having the so-called " hydroperoxide " structure (II).

These conclusions have been applied by Baranger and Maréchal [3] in their study of the

---

* Part IX, *J.*, 1958, 4637.

[1] Rieche, " Alkyl Peroxyde und Ozonide," Steinkopff, Dresden, 1931, pp. 97, 161.

[2] Bernard, *Compt. rend.*, 1953, **236**, 2412; *Ann. Chim.* (*France*), 1955, **10**, 315; *Parfumerie, Cosmet., Savon*, 1958, **1**, 467.

[3] Baranger, *J. Inter. Leprosy*, 1948, 49; Baranger and Maréchal, *Compt. rend.*, 1950, **231**, 661; *Bull. Soc. chim. France*, 1957, 782.

autoxidation of ethyl chaulmoograte (III).[†] They assigned to the product the structure (IV), and rejected the possibility that it might be an allylic hydroperoxide (*e.g.*, V) on the basis of the following evidence: (1) The uptake of oxygen was accompanied by an equivalent loss of unsaturation. (2) The product could not be acetylated (RO·OH → RO·OAc), nor could it be alkylated with xanthhydrol or triphenylmethanol (RO·OH → RO·OR′): the reaction with xanthhydrol gave only dixanthen-9-yl peroxide. (3) The polarographic behaviour of the peroxide was typical of Bernard's class of "true" peroxides (I).

We have therefore investigated the structure of the peroxide formed by the autoxidation of ethyl chaulmoograte, because it appeared to be the best authenticated example of a peroxide of the type (I).[‡]

EXPERIMENTAL

Unless otherwise stated, all optical rotations were measured for chloroform solutions.

Analysis.—Peroxides were analysed iodometrically in propan-2-ol solution. Olefinic double bonds were estimated (*a*) by quantitative hydrogenation over platinum oxide, the gas burette described in ref. 7 being modified and the sample added magnetically after the catalyst had been reduced, or (*b*) by Baranger and Maréchal's modification [3] of Hanus's method [4,8] (iodine bromide).

Gas–liquid chromatography of the ethyl chaulmoograte was carried out on a 4 mm. × 1 m. column of silicone grease E 301 on "Celite" at 230° with air (5 c.c./min.) as the carrier gas. We are very grateful to the Analytical Department of Imperial Chemical Industries Limited, Dyestuffs Division, for performing these analyses.

Preparation of Ethyl Chaulmoograte (III).—Ethyl chaulmoograte was obtained from chaulmoogra oil by the following procedure.[9]

Chaulmoogra oil (2 kg.) was saponified for 4 hr. with potassium hydroxide (1 kg.) in boiling ethanol (5 l.). From two reactions, 3·9 kg. of wet acid were obtained. This acid was boiled for 6 hr. in ethanol (4 l.) containing sulphuric acid (150 c.c.), giving 3·2 kg. of mixed ethyl esters. The esters were fractionally distilled at low pressure through a column 95 cm. × 18 mm. packed with Fenske glass helices. The progress of the fractionation was checked by gas–liquid chromatography of the distillate. Two principal fractions were collected: (*a*) crude ethyl hydnocarpate (1343 g.), b. p. 152—156°/*ca.* 0·4 mm., and (*b*) crude ethyl chaulmoograte (1450 g.), b. p. 164—175°/*ca.* 0·2 mm. Fraction (*b*) was saponified for 1 hr. with potassium hydroxide (140 g.) in boiling ethanol (1 l.), and the crude chaulmoogric acid was recrystallised once from ethanol–water (4 : 1 v/v) and twice from ethanol–pentane, giving chaulmoogric acid (432 g.), m. p. 69°, $[\alpha]_D$ +59·3°.

Chaulmoogric acid (300 g.) was heated under reflux in absolute ethanol (1·8 l.) containing concentrated hydrochloric acid (4 c.c.), yielding ethyl chaulmoograte (270 g.), b. p. 143—146°/0·01 mm., $[\alpha]_D$ +51·0° (Found: C, 77·4; H, 11·6. Calc. for $C_{20}H_{36}O_2$: C, 77·8; H, 11·8%). The gas–liquid chromatogram showed only one peak and demonstrated the absence of ethyl hydnocarpate. The infrared spectrum is shown in the Figure.

Ethyl 2′,3′-*Epoxychaulmoograte* (VIII).—Ethyl chaulmoograte (3·91 g.) was mixed with peroxyoctanoic acid (2·13 g.) in benzene, the mixture becoming warm. After 15 hr. the solution was washed three times with ice-cold 10% sodium hydroxide solution and dried (Na_2SO_4). The benzene was removed and the residue was recrystallised from light petroleum at low temperature, giving *ethyl* 2′,3′-*epoxychaulmoograte*, m. p. 30—33°, $[\alpha]_D$ +19·5° (Found:

[†] Baranger and Maréchal suggest that the antileprotic activity of ethyl chaulmoograte is due to the adventitious presence of a small amount of the peroxide formed by reaction with air.

[‡] The "peroxide" formed from the reaction of fluorenone with hydrogen peroxide [4] is, in fact, a complex between the ketone and its *gem*-dihydroperoxide,[5] and not an oxoxide as is often supposed.[4, 6]

[4] Wittig and Pieper, *Ber.*, 1940, **73**, 295.

[5] Criegee, Schnorrenberg, and Becke, *Annalen*, 1948, **565**, 7; Criegee, *Fortschr. chem. Forsch.*, 1950, **1**, 508.

[6] Syrkin and Moiseev, *Russ. Chem. Rev.*, 1960, **29**, 193 (esp. p. 197).

[7] Abraham and Davies, *J.*, 1959, 429.

[8] Norris and Buswell, *Ind. Eng. Chem., Analyt.*, 1943, **15**, 259.

[9] Cf. Gupta and Malkin, *J.*, 1952, 2405.

C, 73·3; H, 11·35. $C_{20}H_{34}O_3$ requires C, 74·0; H, 11·2%). The infrared spectrum is shown in the Figure.

Autoxidation of Ethyl Chaulmoograte.—Ethyl chaulmoograte (80 g.) was shaken under oxygen in a flask connected to a gas burette [7] by flexible tubing. The flask was contained in a large air-bath (a tea chest) kept at *ca.* 35° by a high-pressure mercury lamp, a tungsten-filament lamp, or a hot-plate. The rate of uptake of oxygen, and the nature of the product, were independent of the method of heating: the reactions were always preceded by an induction period and then appeared to be autocatalytic. The relation between the amount of oxygen absorbed (recorded on the gas burette) and the peroxide formed (measured iodometrically) is shown in Table 1.

TABLE 1.

Autoxidation of ethyl chaulmoograte.

O_2 absd. (mol.)	0	0·033	0·056	0·066	0·130
Peroxide formed (mol.)	0	0·033	0·053	0·057	0·099
$[\alpha]_D$ (found)	+51·0°	—	—	+47·9°	+45·6°
$[\alpha]_D$ (calc.[a])	+51·0°	—	—	+47·4°	+43·6°

[a] By assuming that the peroxide is inactive and has a simple dilution effect on the rotation of the ethyl chaulmoograte.

It will be seen that initially all the oxygen is taken up as peroxide but, as the reaction proceeds, some non-peroxide products are formed; if the peroxide is inactive, these impurities appear to be dextrorotatory. It was convenient to continue the oxidation for 12 hr., by which time about 5% of peroxide had been formed, with little or no non-peroxidic products.

Isolation of Ethyl 1'-Hydroperoxychaulmoograte (V).—Alumina was washed once with acetic acid and five times with light petroleum (b. p. 40—60°), and then packed wet into a column 30 × 4 cm. and washed with light petroleum until all the acetic acid was removed. Ethyl chaulmoograte (80 g.), autoxidised to the extent of 5%, in light petroleum (150 c.c.) was then added to the column and eluted with light petroleum.

The presence of the ester in the eluate was indicated by the formation of a translucent spot when a drop of the eluate was allowed to evaporate on filter paper. The peroxide was detected by spraying the paper with an acid ferrous thiocyanate reagent.[10] The peroxide was then eluted with ethanol, and the solvent removed, leaving the peroxide mixed with some aluminium acetate. This was extracted with light petroleum, the extract was washed and dried, and the solvent removed to constant weight, giving *ethyl 1'-hydroperoxychaulmoograte* as a colourless oil [Found: C, 70·8; H, 10·7; peroxidic O, 8·6%; *M* (by iodine bromide), 343, 345; *M* (by hydrogenation of C=C and O–O in a different specimen, see below), 354. $C_{20}H_{36}O_4$ requires C, 70·6; H, 10·7; peroxidic O, 9·4%; *M*, 340·5]. The infrared spectrum is shown in the Figure.

The relation between the purity and the optical rotatory power of specimens from different preparations was as follows (% peroxide; $[\alpha]_D$): 92%, 1·6°; 88%, 4·8°; 81%, 6·8°; 79%, 6·1°.

One preparation was further purified by partition between equal volumes of light petroleum (b. p. 40—60°) and ethanol–water (88 : 12 v/v) in a 25-tube countercurrent separator. The crude peroxide (0·70 g.), 76% pure, $[\alpha]_D$ +5·8° (in EtOH), gave, in tubes 1, 2, and 3 combined, 0·063 g. of peroxide 85% pure, $[\alpha]_D$ +0·8° (in EtOH); and, in tubes 7, 8, and 9 combined, 0·17 g. of peroxide, 75% pure, $[\alpha]_D$ +6·9° (in EtOH).

Ethyl 1'-(1,2-*Dihydro*-1-*methyl*-6,8-*dinitroquinoline*-2-*peroxy*)*chaulmoograte* [by Mr. R. J. STEVENS].—A solution of the hydroperoxide (0·7 g.) in ether was shaken for 2 min. with a solution of 2-ethoxy-1,2-dihydro-1-methyl-6,8-dinitroquinoline [11] (0·4 g.) in acetic acid. The product was twice recrystallised from light petroleum–ether, yielding the yellow *derivative*, m. p. 64·0—64·5° (Found: C, 62·6; H, 7·7; N, 7·3. $C_{30}H_{43}N_3O_8$ requires C, 62·8; H, 7·6; N, 7·3%).

Attempts to prepare the triphenylmethyl derivative (from triphenylmethyl chloride and pyridine) and the xanthen-9-yl derivative (from xanthhydrol in acetic acid) were not successful.

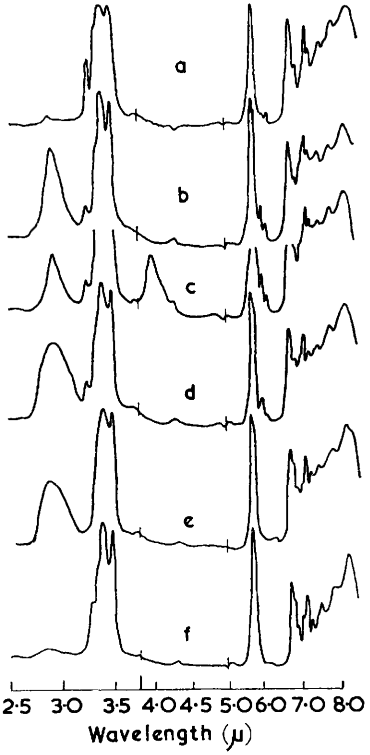
Ethyl 1'-Hydroxychaulmoograte (VI).—The hydroperoxide ($[\alpha]_D$ +6·15° and +4·76° in two experiments) in ten times its volume of ether was mixed with a solution of sodium borohydride in ethanol; the reaction was slightly exothermic. Next day the mixture was washed with acid, and the ethereal layer yielded impure ethyl 1'-hydroxychaulmoograte ($[\alpha]_D$ +5·94° and +4·22°, from the above two samples respectively) as an oil which solidified just below room temperature.

[10] Abraham, Davies, Llewellyn, and Thain, *Analyt. Chim. Acta*, 1957, **17**, 499.

[11] Rieche, Schmitz, and Dietrich, *Chem. Ber.*, 1959, **92**, 2239.

Sodium sulphite and triphenylphosphine were less satisfactory reducing agents.

Ethyl 2′,3′-*Dihydro*-1′-*hydroxychaulmoograte* (VII).—The unsaturated hydroperoxide (89% pure; 0·4232 g.) in ethanol was hydrogenated over platinum oxide at atmospheric pressure and room temperature during 1·5 hr.; 104% of the calculated volume of gas was absorbed (possible unsaturation in the 11% of impurity being ignored), and there was an obvious decrease in the rate of reaction after the reduction was half-complete. The solution was filtered and the alcohol removed under reduced pressure, yielding *ethyl* 2′,3′-*dihydro*-1′-*hydroxychaulmoograte* (from light petroleum), m. p. 33—35° (Found: C, 73·5; H, 11·6. $C_{20}H_{38}O_3$ requires C, 73·5; H, 11·7%). The ester was hydrolysed and the product was recrystallised from aqueous ethanol, giving 2′,3′-*dihydro*-1′-*hydroxychaulmoogric acid*, m. p. 81·5° (Found: C, 72·8; H, 11·5. $C_{18}H_{34}O_3$ requires C, 72·5; H, 11·5%).



Infrared spectra of (a) ethyl chaulmoograte (III), (b) ethyl 1′-hydroperoxychaulmoograte (V), (c) (V) + ethyl 1′-deuteroperoxychaulmoograte, (d) ethyl 1′-hydroxychaulmoograte (VI), (e) ethyl 2′,3′-dihydro-1′-hydroxychaulmoograte (VII), and (f) ethyl 2′,3′-epoxychaulmoograte (VIII).

Hydrogenation of a sample of the hydroperoxy-ester (81% pure), $[\alpha]_D$ +6·8°, gave the crude product, $[\alpha]_D$ −4·0°.

A mixture of ethyl dihydrohydroxychaulmoograte (0·625 g.), phthalic anhydride (0·293 g.), pyridine (0·4 c.c.), and benzene (0·3 c.c.) was kept at 75° for 4·5 hr. The only acid product recovered was phthalic acid. Under the same conditions, cyclopentanol gave *cyclopentyl hydrogen phthalate* (from carbon disulphide–light petroleum), m. p. 61·0—61·5° (Found: C, 67·0; H, 6·2. $C_{13}H_{14}O_4$ requires C, 66·7; H, 6·0%).

Infrared Spectra.—The spectra shown in the Figure were recorded on a Grubb-Parsons model G.S.2A double-beam grating instrument.

Partial deuteration of the hydroperoxy-group was carried out as follows. Ethyl 1′-hydroperoxychaulmoograte (0·329 g.) was mixed with 99% D_2O (0·034 g.), and dioxan was added slowly to give a homogeneous solution. All volatile material was removed under reduced pressure and the product was thoroughly dried. The absorption at 2·90 μ (OH stretching) was found to have diminished and a new peak at 3·95 μ (OD stretching; cf. Ph·CMe₂·O·OD [12]) appeared. This trend was continued by a second similar treatment.

Resolution of 1′-*Hydroxychaulmoogric Acid.*—Crude ethyl 1′-hydroxychaulmoograte was heated under reflux for 1 hr. in ethanol containing a slight excess of concentrated aqueous sodium hydroxide. The product was acidified at 0° with nitric acid, yielding 1′-hydroxychaulmoogric acid. It was slightly soluble in light petroleum and recrystallised from that solvent at $-70°$, but attempts to purify the acid at this stage were unsuccessful.

Equivalent amounts of the crude acid (4·5 g.), $[\alpha]_D$ $+6{\cdot}0°$, and of brucine were dissolved in warm ethyl acetate. After some days at 2°, light buff crystals of the brucine salt had separated; these were filtered off and recrystallised from ethyl acetate. The brucine salt was decomposed with dilute acid and the optically active *1′-hydroxychaulmoogric acid* (0·4 g.) was extracted with ether and recovered, with m. p. 56—58°, $[\alpha]_D$ $+24{\cdot}1°$ (Found: C, 72·2; H, 10·8. $C_{18}H_{32}O_3$ requires C, 72·9; H, 10·9%). An equivalent rotation could be given by a mixture of inactive hydroxychaulmoogric acid (60%) and (+)-chaulmoogric acid (40%) (Calc. for this mixture: C, 74·6; H, 11·1%).

In a second experiment the crude acid, $[\alpha]_D$ $+6{\cdot}5°$ (9 g.), yielded (+)-1′-hydroxychaulmoogric acid, $[\alpha]_D$ $+18{\cdot}0°$.

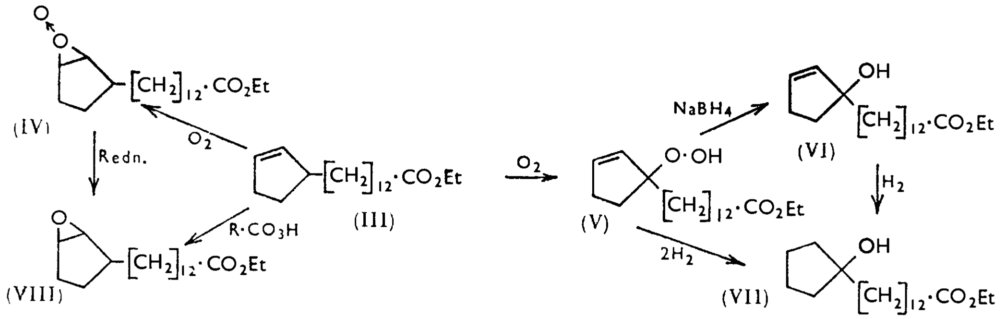
Hydrogenation of (+)-*1′-Hydroxychaulmoogric Acid.*—The (+)-acid (0·2143 g.), $[\alpha]_D$ $+24{\cdot}1°$, in ethanol containing platinum oxide, absorbed 96% of the calculated volume of hydrogen, yielding inactive 2′,3′-dihydro-1′-hydroxychaulmoogric acid. This confirms the view that the reduction had not isolated merely the active impurity from the impure starting material, because the impurity (see above) gives a lævorotatory product on reduction.

In a second experiment the (+)-acid (0·2096 g.), $[\alpha]_D$ $+18°$, absorbed 103% of the calculated volume of hydrogen. The saturated hydroxy-acid which was formed was converted into the ethyl ester and thoroughly dried. The infrared spectrum, particularly the ratio of the heights of the peaks at 2·90 (OH) and 5·75 μ (C=O), confirmed the product as ethyl 2′,3′-dihydro-1′-hydroxychaulmoograte.

DISCUSSION

The Nature of the Peroxide.—Ethyl chaulmoograte (III) was shaken at 35° under oxygen and the peroxide which was formed was periodically analysed iodometrically (Table 1). Up to about 5% autoxidation, essentially all the oxygen is absorbed to form titratable peroxide; further oxidation gives an appreciable amount of non-peroxidic material.

The peroxide was isolated in 92% purity by chromatography on acetic acid-washed alumina: the following evidence shows clearly that the product is a hydroperoxide, and does not have the structure (IV).



The infrared spectrum (see Figure) of ethyl chaulmoograte establishes the absence of the OH group and the presence of the =C–H (3·26 μ) and C=C (6·04 μ) groups. The peroxide shows the presence of an OH group (2·90 μ) which can be progressively changed into an OD group (3·95 μ) if the peroxide is equilibrated with D_2O; the =C–H group (3·26 μ) is still present, and the absorption corresponding to the C=C group (6·04 μ) is stronger than in ethyl chaulmoograte, implying that the double bond is now polarised by a neighbouring polar group. This spectrum is therefore that which would be predicted for a hydroperoxide such as (V) and is not compatible with the requirements of structure (IV) which should show the absence of the OH, =C–H, and C=C groups.

Further support for the hydroperoxide structure came unexpectedly from a study of the C=O absorption of the carboxylic ester group. Ethyl chaulmoograte and its non-peroxidic derivatives decribed below (see Figure) show the presence of this group by a single peak at 5·75 μ; in the hydroperoxy-ester, which we showed to be free from acid, this is accompanied by a slightly smaller peak at 5·82 μ. A similar doublet is obtained if t-butyl hydroperoxide is added to ethyl chaulmoograte and it appears to arise through association between the hydroperoxy- and the carbonyl-group, probably because of the powerful hydrogen-bonding power of the hydroperoxide. An analogous effect has been recorded in the infrared spectrum of acetic acid. At 60° the vapour shows the presence of two peaks at about 5·60 and 5·76 μ, ascribed to the monomer and dimer respectively; at 20° the amount of dimer and its corresponding peak increase in importance, and in the liquid phase, when the acid is fully associated, only one peak is observed, at about 5·83 μ.[13]

The peroxide was reduced with sodium borohydride: the only changes in the spectrum were the disappearance of the peak at 5·82 μ, referred to above, and a slight reduction in the intensity of the OH absorption, as would be expected [14] if a hydroperoxide were being reduced to the corresponding alcohol (*e.g.*, V ⟶ VI). If the peroxide had the structure (IV), the first reduction product might be expected to be the epoxide (VIII). This epoxide was therefore prepared by treating ethyl chaulmoograte with peroxyoctanoic acid, and its spectrum (see Figure) was found to differ from that of the reduced peroxide.

Baranger and Maréchal's strongest evidence for the structure (IV) was perhaps the fact that the autoxidation involved saturation of the 2′,3′-olefinic bond.[3] Using their analytical method (the reaction with iodine bromide) we find in contrast to their results, and in agreement with the infrared evidence described above, that the peroxide contained intact the carbon–carbon double bond. This was confirmed by quantitative hydrogenation of the peroxide; two mol. of hydrogen were absorbed to give a saturated alcohol (*e.g.*, V ⟶ VII) whose infrared spectrum (see Figure) now shows the absence of =C–H and C=C groups.

Rieche and his colleagues [11] have recently shown that characteristic derivatives of hydroperoxides can be obtained by causing them to react with 2-ethoxy-1,2-dihydro-1-methyl-6,8-dinitroquinoline, to give the corresponding 2-alkylperoxy-compounds. We have obtained this derivative of our autoxidation product, confirming again that it is a hydroperoxide.

We conclude therefore that the autoxidation product of ethyl chaulmoograte is a conventional unsaturated hydroperoxide, and that the oxoxide structure (IV) is not correct. Baranger and Maréchal [3] were probably misled because their experiments, particularly the analyses for unsaturation, were apparently carried out, not on the isolated peroxide, but on ethyl chaulmoograte which had been autoxidised to the extent of 22% (and, from our results, would contain an appreciable amount of by-products). They interpreted the fact that the reaction with xanthhydrol gave dixanthen-9-yl peroxide as supporting evidence for the structure (IV). We, on the other hand, regard it as support for an allylic hydroperoxide structure such as (V), which under acid conditions eliminates hydrogen peroxide which is then alkylated by the xanthhydrol; pinane hydroperoxide,[15] 3-methyl-1-phenylallyl hydroperoxide, and 1-methyl-3-phenylallyl hydroperoxide [16] react similarly with triphenylmethanol to give bis(triphenylmethyl) peroxide.

It is less easy to reinterpret Bernard's polarographic results; few of the compounds which he classified as " true peroxides " were isolated, their solubility in water would be very low, and most of the polarographic measurements were carried out on aqueous extracts of the autoxidised oils. Even if his results are accepted at their face value,

---

[12] Simon, Jentzsch, and Menzel, *Chem. Ber.*, 1959, **90**, 1023.

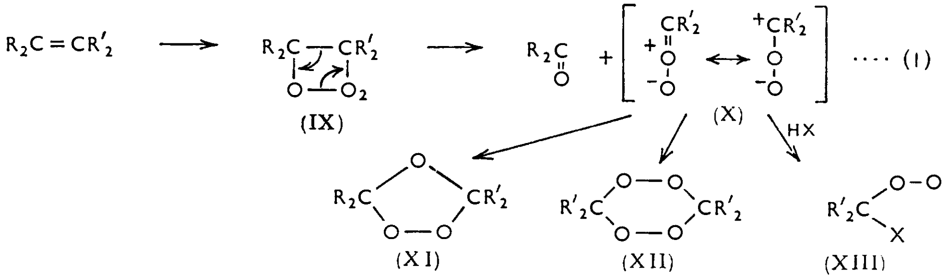
[13] Herman and Hofstader, *J. Chem. Phys.*, 1938, **6**, 534; Davies and Sutherland, *J. Chem. Phys.*, 1938, **6**, 755; Hartwell, Richards, and Thompson, *J.*, 1948, 1436.

[14] Williams and Mosher, *Analyt. Chem.*, 1955, **27**, 517; Khan, *J. Org. Chem.*, 1958, **23**, 606.

[15] M. H. Abraham, personal communication.

[16] Feld, *Chem. and Ind.*, 1959, 1600.

however, they would seem to be an inadequate foundation, without supporting evidence, for proposing the existence of a new class of compounds



···· (1)

We believe that there is still no established example of a stable oxoxide. The best evidence for the formation of this structure appears to be as an unisolated reactive intermediate in the ozonisation of olefins (eqn. 1).[17] The unstable " initial ozonide " * (IX) is assumed to break down to a carbonyl compound and oxoxide (X) which rapidly adds to the carbonyl compound, or to itself, or to a reagent HX, to give a peroxide (XI), (XII), or (XIII) of conventional structure.

The Position of the Hydroperoxy-group and the Stereochemistry of the Autoxidation.— The autoxidation of a hydrocarbon to an alkyl hydroperoxide is generally accepted to proceed by a free-radical chain mechanism (eqns. 2—4).

$$\mathrm{RH} \longrightarrow \mathrm{R}\cdot + [\mathrm{H}\cdot] \qquad (2)$$

$$\mathrm{R}\cdot + \mathrm{O_2} \longrightarrow \mathrm{RO{\cdot}O}\cdot \qquad (3)$$

$$\mathrm{RO{\cdot}O}\cdot + \mathrm{RH} \longrightarrow \mathrm{RO{\cdot}OH} + \mathrm{R}\cdot \qquad (4)$$

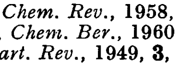
The reaction (4) occurs readily at the α-position to an olefinic double bond (because the radical R• is then resonance stabilised), and more readily at a tertiary carbon atom than at a secondary carbon atom.[19] In the autoxidation of ethyl chaulmoograte, the mesomeric radical (XIV) would thus be expected to be the principal intermediate, and (XV) relatively unimportant.

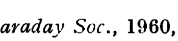
Less is known of the way in which a mesomeric radical such as (XIV) will react with molecular oxygen (eqn. 3) to give the secondary (XVI) or the tertiary (V) hydroperoxide. Much of the older work in the literature would obviously warrant reinvestigation, but there are reasonably well-established precedents for the formation of only the secondary hydroperoxide (eqn. 5),[20] or only the tertiary hydroperoxide (eqn. 6),[21] or both (eqn. 7).[22]

Some preliminary evidence that ethyl chaulmoograte in fact gives the tertiary hydroperoxide (V) as, at least, the principal product was obtained by showing that the corresponding saturated alcohol (VII) could not be esterified with phthalic anhydride in the presence of pyridine under the conditions where cyclopentanol gives the hydrogen phthalic ester; this unreactivity is characteristic of a tertiary alcohol. This structure was

---

* One " initial ozonide " (of *trans*-di-t-butylethylene) has recently been isolated [18] at −75°. It is not yet known whether it has the structure (IXa) or the oxoxide structure (IXb), but the former appears rather more probable.

(IXa)



(IXb)

[17] Reviewed by Bailey, *Chem. Rev.*, 1958, **58**, 5.

[18] Criegee and Schröder, *Chem. Ber.*, 1960, **93**, 689.

[19] See, *e.g.*, Bolland, *Quart. Rev.*, 1949, **3**, 1; *Trans. Faraday Soc.*, 1960, **46**, 358; Russell, *J. Amer. Chem. Soc.*, 1956, **78**, 1047.

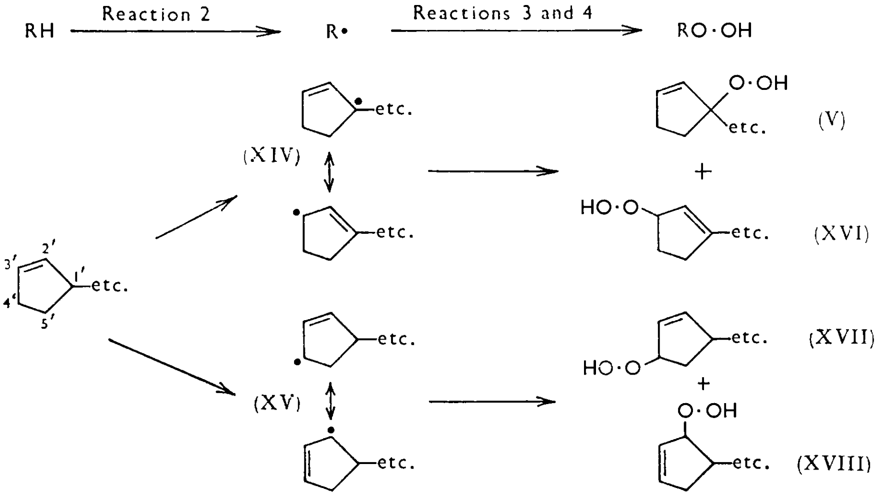
[20] Hoch and Lang, *Ber.*, 1942, **75**, 300.

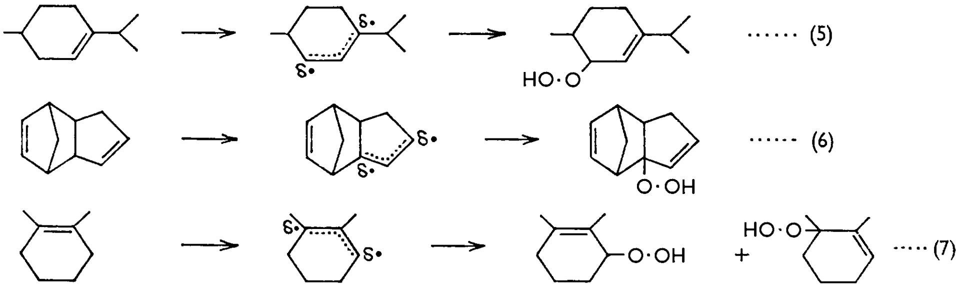
[21] Hoch and Depke, *Chem. Ber.*, 1951, **84**, 386.

[22] Farmer and Sundralingham, *J.*, 1942, 121; Farmer and Sutton, *J.*, 1946, 10.

substantiated by a study of the optical asymmetry of the hydroperoxide and its related compounds.

Ethyl chaulmoograte is optically active, $[\alpha]_D$ +51·0° (in chloroform), by virtue of asymmetry centred on the 1′-carbon atom. As the purity of the derived hydroperoxide increases, its rotatory power decreases. The purest product obtained chromatographically (92% pure) had a specific rotation of +1·6°, and we believe (see below) even this is due to the presence of a non-hydroperoxidic impurity of uncertain structure. This impurity could be further separated by countercurrent extraction, leaving the hydroperoxide (86% pure, from a different preparation), $[\alpha]_D$ +0·8° (in ethanol).*





Reduction of the impure hydroperoxide to the corresponding unsaturated alcohol with sodium borohydride (which may be assumed to proceed with retention of configuration[23]) gave no significant change in the small optical rotation;† this is the result which would be expected if the hydroperoxide was optically inactive, and the impurity was optically active and chemically inert. Hydrogenation of the impure hydroperoxide caused inversion of the sign of rotation (*e.g.*, 81% pure hydroperoxide, $[\alpha]_D$ +6·8° ⟶ $[\alpha]_D$ −4·0°), showing that the impurity was not the parent ethyl chaulmoograte (III)

---

* This essentially zero rotation affords additional evidence against the oxoxide structure (IV), which would be expected to be optically active; a homolytic reaction initiated at the asymmetric (1′) centre, on the other hand, might be expected to give an inactive hydroperoxide (V and/or XVI).

† Again this argues against the oxoxide structure (IV) which might be expected to be reduced to the epoxide (VIII) which we know to have a specific rotatory power of +20°.

[23] Davies and Feld, *J.*, 1956, 665; 1958, 4673; Davies, *J.*, 1958, 3474.

(which would give the symmetrical dihydrochaulmoograte), or apparently the epoxide (VIII) (which we found to be unreactive under these conditions).

Impure ethyl hydroxychaulmoograte, obtained by borohydride reduction of the hydroperoxide, was hydrolysed to the impure hydroxy-acid ($[\alpha]_D$ +6·0° and +6·5° in two experiments). Two recrystallisations of the brucine salts from ethyl acetate gave the pure hydroxy-acids, $[\alpha]_D$ +24·1° and +18·0° respectively. These active acids absorbed the calculated amount of hydrogen to give inactive dihydrohydroxychaulmoogric acid.

The unsaturated hydroxy-acid must therefore be optically asymmetric, the asymmetry being destroyed when the double bond is saturated. This can only mean that the hydroxy-group, and hence the hydroxyperoxy-group, is situated at the junction of the ring and the side-chain, and that the double bond is in the unsymmetrical (2′,3′) position as shown in the structures (VI) and (V).

We conclude that the hydroperoxide which is formed by autoxidation is at least principally, and probably wholly, the tertiary compound (V), and that the reaction involves extensive or complete racemisation. This appears to be the first demonstration of the steric course of a homolytic autoxidation, and the results are clearly compatible with the mechanism outlined in reactions (2)—(4).

We are grateful to Professor E. D. Hughes, F.R.S., and Sir Christopher Ingold, F.R.S., for their interest and encouragement, and to Dr. E. M. Thain and the Director of the Tropical Products Institute for providing facilities for carrying out the counter-current separation. This work was carried out during the tenure (by J. E. P.) of a Commission in the New Zealand Defence Scientific Corps.

William Ramsay and Ralph Forster Laboratories,
University College, London, W.C.1.

[*Received, May* 1*st*, 1961.]