

## Stereochemistry of Olefin and Fatty Acid Oxidation. Part 2.<sup>1</sup> Photosensitised Oxidation of Hexene and Hepta-2,5-diene Isomers

By Edwin N. Frankel, Robert F. Garwood, John R. Vinson, and Basil C. L. Weedon,<sup>\*,†</sup> Department of Chemistry, Queen Mary College, Mile End Road, London E1 4NS

The stereochemistry of the photosensitised oxidation of hex-1-ene, *cis*- and *trans*-hex-2-ene, *cis*- and *trans*-hex-3-ene, and of the three geometrical isomers of hepta-2,5-diene, has been investigated by the reduction or hydrogenation of the hydroperoxides produced and analysis of the resulting allylic or saturated alcohols. The isomeric distribution of hydroperoxides from hexene isomers is that expected from the concerted ene reaction of singlet oxygen with the parent olefin oriented so as to favour the *cis*, cyclic process. In contrast to autoxidation, photosensitised oxidation of hepta-2,5-diene isomers produces a mixture of conjugated (67–70%) and nonconjugated (30–33%) hydroperoxides. The conjugated products formed are explicable in terms of the conformations of the parent dienes which have the least steric interactions.

PHOTOSENSITISED oxidations have attracted much attention because of the accumulating evidence that singlet oxygen is implicated in many biochemical processes,<sup>2</sup> in aging,<sup>2c,3</sup> and in environmental pollution.<sup>4</sup> It has also been suggested that singlet oxygen plays a role

The configuration of the shifted allylic double bond varied significantly according to the configuration of the starting isomer. Photosensitised oxidation of hex-*trans*-3-ene resulted in a larger proportion of 3-hydroperoxyhex-*cis*-4-ene (17–20%) than that formed from the

TABLE 1

Allylic alcohols formed by reduction of the hydroperoxides from the photosensitised oxidations of hexenes (5–10% oxidation, 1% Rose Bengal, 50% ethanolic solution)

Hexenes	Temp. (°C)	Hexenol product (weight %)						
		<i>cis</i> -3-en-2-ol	<i>trans</i> -3-en-2-ol	<i>cis</i> -4-en-3-ol	<i>trans</i> -4-en-3-ol	<i>cis</i> -2-en-1-ol	<i>trans</i> -2-en-1-ol	1-en-3-ol
<i>trans</i> -3	50	0	0	20	80	0	0	0
<i>trans</i> -3	25	0	0	17	83	0	0	0
<i>cis</i> -3	50	0	0	5	95	0	0	0
<i>cis</i> -3	25	0	0	2	98	0	0	0
-1-ene	50	0	0	0	0	22	78	0
-1-ene	25	0	0	0	0	18	82	0
<i>trans</i> -2	50	8	27	0	0	0	0	65
<i>trans</i> -2	25	9	32	0	0	0	0	59
<i>cis</i> -2	50	0	29	0	0	0	0	71
<i>cis</i> -2	25	0	34	0	0	0	0	66

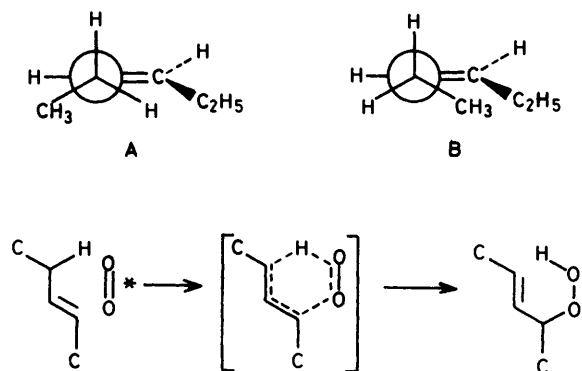
in initiating the autoxidation of unsaturated fatty acids.<sup>5</sup> Although singlet oxygenation of olefins has been studied extensively, there are various mechanistic aspects of this important reaction that have not yet been completely settled.<sup>6</sup>

In the first part of this series, the stereochemistry of the autoxidation of hexene and hepta-2,5-diene isomers was explained in terms of the conformation of the parent olefins.<sup>1</sup> In this paper we report the use of the same model systems to investigate the products of photosensitised oxidation. The hydroperoxides were unambiguously identified and analysed, after reduction to unsaturated and saturated alcohols, with reference to the authentic samples reported in Part 1.

**Hexenes.**—Oxidations in ethanolic solution at 25 and 50 °C were photosensitised in the presence of Rose Bengal (Table 1). Analysis of allylic alcohols produced by reduction showed that the positional hydroperoxide isomers formed are those expected from the concerted ene reaction of singlet oxygen with the parent olefins. Temperature had little effect on the product distribution.

<sup>†</sup> Present address: The University of Nottingham, University Park, Nottingham NG7 2RD.

*cis*-isomer (2–5%). The formation of as much as 98% *trans*-hydroperoxide from hex-*cis*-3-ene may be explained by the required orientation A for the *cis*, cyclic process that has provided a consistent explanation for other

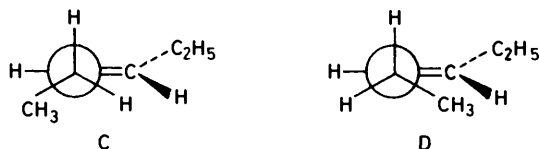


photosensitised hydroperoxidations of di- and tri-substituted olefins.<sup>6d</sup>

The significantly larger proportion of 3-hydroperoxyhex-*cis*-4-ene formed by photosensitised oxidation of

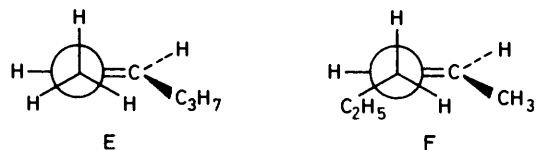
hex-*trans*-3-ene is probably due to the reduced interactions in the corresponding conformers C and D, compared to those in A and B, in hex-*cis*-3-ene.

Hex-1-ene produced only 1-hydroperoxyhex-2-ene (Table 1). The relatively high proportion of the *cis*-hydroperoxide (18–22%) may also be explained by



the low steric interactions with the vinylic hydrogens in the starting olefin.

In hex-2-ene, the predominant hydroperoxide produced by photosensitised oxidation is that in which the double bond has migrated to the terminal position. In contrast, this isomeric hydroperoxide was a minor product of free radical autoxidation<sup>1</sup> where hydrogen abstraction occurred preferentially from the secondary position. For photosensitised oxidation, the three equivalent conformers E leading to 3-hydroperoxyhex-1-ene assume greater importance than the conformers (*e.g.* F) which lead to 2-hydroperoxyhex-3-ene.



The formation of *cis*- and *trans*-isomers of 2-hydroperoxyhex-3-ene from hex-*trans*-2-ene, and only the *trans*-isomer from hex-*cis*-2-ene, may be explained on the same grounds as suggested for the corresponding hex-3-ene isomers.

The factors influencing the reactivity of various olefins toward singlet oxygen have been discussed extensively.<sup>6</sup> With unsymmetrically substituted olefins, Markovnikoff-directing effects are almost completely absent and secondary and tertiary products are formed in nearly equal amounts.<sup>7</sup> The results reported here for hexene isomers support previous work which indicated that

TABLE 2

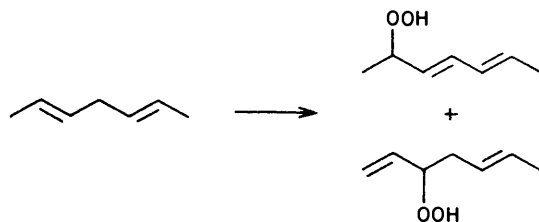
Heptanols formed by hydrogenation of hydroperoxides from the photosensitised oxidations of hepta-2,5-dienes (5–10% oxidation, 25 °C, 1% Rose Bengal, 50% ethanolic solution)

Heptadienes	Heptanol product (weight %)	
	2-ol	3-ol
<i>cis</i> -2, <i>cis</i> -5	70	30
<i>cis</i> -2, <i>trans</i> -5	67	33
<i>trans</i> -2, <i>trans</i> -5	69	31

singlet oxygen tends to attack an olefin in its most favourable conformation, and are consistent with a vast amount of evidence favouring a concerted ene reaction.<sup>8</sup>

**Hepta-2,5-dienes.**—On photosensitised oxidation, all three diene stereoisomers produced 2- and 3-hydro-

peroxy-dienes, as indicated by the heptanols obtained on subsequent catalytic hydrogenation (Table 2). The main isomer (67–70%) corresponds to the conjugated 2-hydroperoxyhepta-3,5-dienes formed by autoxidation (Scheme 1). The other isomer, constituting up to 33%



SCHEME 1

of the total, corresponds to the nonconjugated 3-hydroperoxyhepta-1,5-dienes which would be expected from the ene mechanism.<sup>6</sup> This product distribution is in marked contrast to that of autoxidation in which the conjugated isomers were formed almost exclusively. The higher proportion of conjugated hydroperoxide isomers formed by photosensitised oxidation indicates that the double bond moves preferentially into the 3,4-position and not the terminal position as was found with hex-2-ene (Table 1). Although the same steric effects apply, the shift to the 3,4-position may be favoured by the development of a conjugated diene system.

TABLE 3

Isomeric hepta-3,5-dien-2-ols formed by reduction of the hydroperoxides from the photosensitised oxidations of hepta-2,5-diene<sup>a</sup>

Heptadienes	Heptadien-2-ol product (weight %)			
	<i>cis</i> -3, <i>cis</i> -5	<i>cis</i> -3, <i>trans</i> -5	<i>trans</i> -3, <i>cis</i> -5	<i>trans</i> -3, <i>trans</i> -5
<i>cis</i> -2, <i>cis</i> -5	0	0	70	30
<i>cis</i> -2, <i>trans</i> -5	3	4	32	61
<i>trans</i> -2, <i>trans</i> -5	0	9	0	91

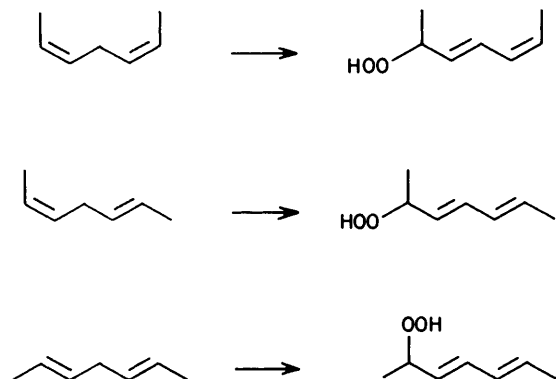
<sup>a</sup> For conditions see Table 2.

The stereochemistry of the conjugated diene hydroperoxides was determined by analysis of the dienols obtained on subsequent reduction (Table 3). The relative proportions of the main *trans,cis*- and *trans,trans*-isomers are explicable in terms of the conformations and steric interactions in the parent dienes. The main conjugated products formed are those expected from the conformation of hepta-2,5-diene isomers with the least steric interactions (Scheme 2).

The other conformers of hepta-2,5-dienes<sup>1</sup> can be neglected because in the *cis,cis*-isomer they would produce *cis,cis*-conjugated hydroperoxides which were not detected. In the *cis,trans*-isomer other conformers may play a minor part and account for the small percentages of *trans,cis*- and *cis,cis*-isomers detected. Similarly, in the *trans,trans*-isomer the formation of 9% *cis,trans*-conjugated diene hydroperoxide may be rationalised by the intervention of the conformers shown in Scheme 3.

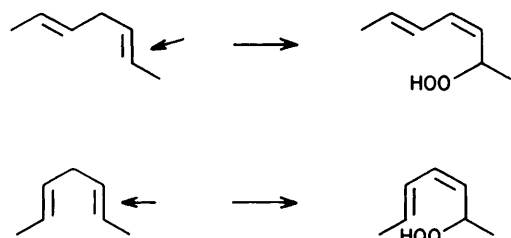
There remains the question of explaining the formation of as much as 30% *trans,trans*-conjugated hydroperoxide

from the hepta-*cis*-2,*cis*-5-diene. In previous work<sup>8</sup> on the photo-oxygenation of undeca-*cis*-4,*cis*-7-diene with chlorophyll at 30 °C, the formation of the conjugated 4-hydroperoxy-*trans*-5,*cis*-7-diene and the unconjugated



SCHEME 2

5-hydroperoxy-*trans*-3,*cis*-7-diene was reported in the ratio 3 : 2, in agreement with the present work. Further sensitised irradiation caused the isomerisation of the *trans*,*cis*-conjugated hydroperoxide to a mixture containing up to 60% *trans*,*trans*-conjugated hydroperox-



SCHEME 3

ides.<sup>8</sup> According to some reports<sup>9</sup> the singlet oxygenation of methyl linoleate gives conjugated and unconjugated hydroperoxides in approximately equal amounts, but other reports<sup>10</sup> show a product ratio which favours the conjugated hydroperoxides. Chan *et al.*<sup>11</sup> have reported a 1,5-hydroperoxy-shift during thermal isomerisation of methyl linoleate hydroperoxides. This free-radical 1,5-rearrangement was accompanied by isomerisation of the *trans*,*cis*- to *trans*,*trans*-hydroperoxides. In our previous experiments<sup>1</sup> no rearrangement products were observed during a period similar to that in which the diene was autoxidised. However, in the present work *trans*,*cis*- to *trans*,*trans*-isomerisation may have been promoted during photo-oxygenation in the same way as observed by Clements *et al.* with undeca-

*cis*-4,*cis*-7-diene.<sup>8</sup> Further experiments are needed to determine whether or not this isomerisation involves a free-radical process promoted by photo-oxidation.

## EXPERIMENTAL

The preparation of unsaturated substrates and hydroxy-products by unequivocal methods was described in Part 1.<sup>1</sup>

*Photosensitised Oxidation.*—A 50% solution of the olefin in ethanol containing 1% Rose Bengal was stirred under oxygen and illuminated by a 150-W tungsten filament bulb. Samples taken at 5–10% oxidation were either reduced with triphenylphosphine or catalytically hydrogenated over Raney nickel and analysed by g.l.c.<sup>1</sup>

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