Stereochemistry of Olefin and Fatty Acid Oxidation. Part 1. Autoxidation of Hexene and Hepta-2,5-diene Isomers

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The stereochemistry of the autoxidation 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 determined by the reduction of the hydroperoxides produced and analysis of the resulting allylic alcohols. The relative proportions of the isomeric hydroperoxides are explicable in terms of the conformations of the parent olefins which are capable of giving delocalised radicals on hydrogen abstraction.

ALTHOUGH the autoxidation of oleic and linoleic acids and related compounds has been studied extensively, many features of the mechanism remain obscure. The literature on the stereochemistry of olefin and fatty acid autoxidation has been particularly confusing, and much of the evidence presented has been far from clear.[1] The possibility of resolving some of this confusion motivated this investigation with chemical model systems. Initially we selected simple olefins which on autoxidation, followed by mild reduction of the resulting hydroperoxides, afford mixtures of unsaturated alcohols that can be unambiguously identified and analysed by reference to authentic samples of all the isomeric products. The mono-olefins chosen include hex-1-ene, *cis*- and *trans*-hex-2-ene, and *cis*- and *trans*-hex-3-ene. The diene systems were the *cis,cis*-, *cis,trans*- and *trans,trans*-isomers of hepta-2,5-diene. Hex-*cis*-3-ene is a model for oleic acid, and hepta-*cis*-2,*cis*-5-diene a model for linoleic acid. Subsequent papers in this series will deal with the photosensitised oxidation of these olefins and with the autoxidation of these fatty acids.

Hex-trans-3-*ene*.—After autoxidation (5—10%) at 25 and 50 °C in the presence of a cobalt catalyst, analysis of the allylic alcohols obtained on reduction showed that almost half of the initial hydroperoxides contained isomers in which the double bond retained its original position and *trans*-configuration (Table 1). In the remaining products, the double bond was shifted to the adjacent 2-position giving *ca.* 40% of the *trans*- and 11—13% of the *cis*-isomer. The same hydroperoxide distribution was obtained by autoxidation (50 °C) catalyzed by manganese acetate [48% (2), 12% (3), 40% (4)], azobis(isobutyronitrile) (ABIN) [47% (2), 13% (3), 40% (4)], and u.v. light [48% (2), 11% (3), 41% (4)].

TABLE 1

Allylic alcohols formed by reduction of the hydroperoxides from the cobalt acetate catalysed autoxidations of hexenes (5—10% oxidation, 0.05% catalyst)

Hexenes	Temp. (°C)	Products (weight %) (1)	(2)	(3)	(4)	(5)	(6)	(7)
trans-3	50	0	48	13	39	0	0	0
trans-3	25	0	47	11	42	0	0	0
cis-3	50	26	23	11	40	0	0	0
cis-3	25	33	16	8	43	0	0	0
Hex-1-ene	50	0	0	0	0	9	43	48
Hex-1-ene	25	0	0	0	0	9	50	41
trans-2	50	8	31	0	37	0	12	12
trans-2	25	6	35	0	48	0	12	9
cis-2	50	9	29	19	18	7	6	12
cis-2	25	7	32	26	13	8	4	10

It is generally accepted that autoxidation of olefins involves abstraction of hydrogen from the α-position(s), and subsequent reaction of the resulting delocalised allylic radical(s) with atmospheric oxygen to give hydroperoxides.[1] Three conformers of hex-*trans*-3-ene may be considered from which hydrogen abstraction results in delocalisation of the electron without further rotation about carbon–carbon bonds (Scheme 1). Each of the radicals thus formed (I, II, and IIA) can, by reaction with oxygen at either end of the three carbon system, lead to two possible products. Radicals (II) and (IIA) lead to identical products (2a) and (3a) and only differ by rotation about a carbon–carbon single bond. [Similarly an *s-cis*-isomer of radical (I) is obtained by hydrogen

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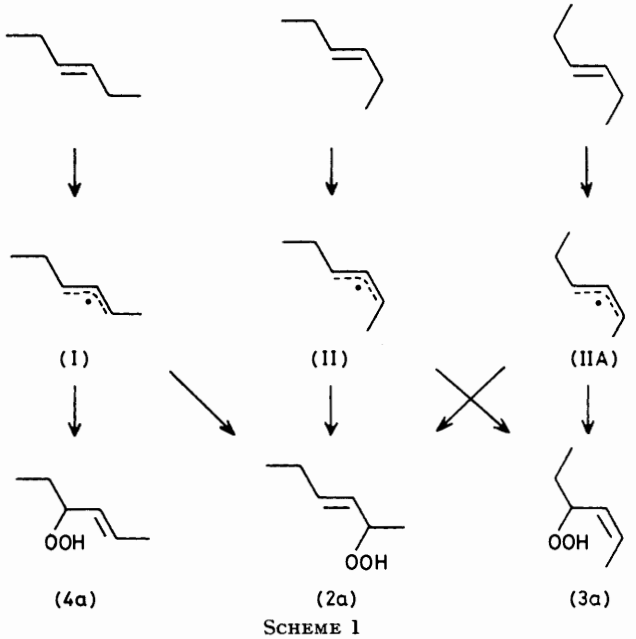
abstraction from the other α-site with the second conformer illustrated.] Radicals (I) and (II) both yield 2-hydroperoxyhex-*trans*-3-ene (2a) by attack of oxygen at the carbon atom from which hydrogen abstraction occurred. However, attack at the alternative position of (I) gives 3-hydroperoxyhex-*trans*-4-ene (4a). The nearly equal proportions of the positional isomers (2a) and (4a), as shown by the analysis of the derived alcohols (Table 1), indicates that attack of oxygen is equally probable at either end of the delocalised radical. The preferential formation of the *trans*-(4a) over the *cis*-isomer (3a) of 3-hydroperoxyhex-4-ene may be explained by the greater degree of steric interaction in radical (II) than that in radical (I). Similar interactions would occur in the starting olefin, and in the transition state leading to



SCHEME 1

the radical, so that radical (I) would be preferred over radicals (II) and (IIA). The higher ratio of *trans* : *cis* isomers observed at 25 °C (8.1 : 1) than at 50 °C (6.7 : 1) is consistent with the expected larger proportion at higher temperatures of higher energy conformations leading to radicals (II) and (IIA). Alternatively, if hydrogen abstraction from the 2-position occurs more readily from the more extended system yielding radical (I), a lower *trans* : *cis* ratio is expected at higher than at lower temperatures.

Hex-cis-3-*ene*.—Autoxidation produced predominantly *trans*-allylic hydroperoxides, but the yields of *cis*-isomers were significant (up to 41%) (Table 1). Similar results were obtained by autoxidation catalyzed at 50 °C by ABIN [25% (1), 25% (2), 11% (3), and 40% (4)], or u.v. light [25% (1), 25% (2), 12% (3), and 38% (4)]. The amount of 2-hydroperoxyhex-*cis*-3-ene (1a) was significantly larger at 25 than at 50 °C. The identification of the *trans*-hydroperoxide in which the double bond is retained in its original position suggests that a defined stereochemistry is lost in the radical intermediate. Alternative explanations might be that the olefin isomerises under the conditions of autoxidation, that the mixture of allylic alcohols used in the analysis changes composition, or that the allylic hydroperoxides, once formed, then isomerise. These possibilities were investigated, as described below, and rejected.

Careful examination of the recovered hexenes showed that no *cis–trans* isomerisation had occurred under the conditions of the autoxidation. Little isomerisation was detected after the hexenols had been exposed under either oxygen or nitrogen to a cobalt catalyst for a period similar to that used in the autoxidation of the hexenes (Table 2). To check the stereochemical stability of the

TABLE 2

Rearrangement of hexenols [0.05% $Co(Ac)_2$, 50 °C, 3 d]

	Hexenol product (weight %)			
Hexenols	*trans*-3-en-2-ol	*cis*-3-en-2-ol	*trans*-4-en-3-ol	*cis*-4-en-3-ol
Under oxygen				
trans-3-en-2-ol	99	0	1	0
cis-3-en-2-ol	3	97	0	0
trans-4-en-3-ol	2	0	98	0
cis-4-en-3-ol	4	0	1	95
Under nitrogen				
trans-3-en-2-ol	99	0	1	0
cis-3-en-2-ol	3	95	2	0
trans-4-en-3-ol	1	0	99	0
cis-4-en-3-ol	4	0	1	95

hydroperoxides themselves, hex-*cis*-3-ene was autoxidised at both 25 and 50 °C and the influence of reaction time, and of keeping the reaction mixture under nitrogen for 3 days, was investigated. No significant changes in the isomer distribution were detected (Table 3).

TABLE 3

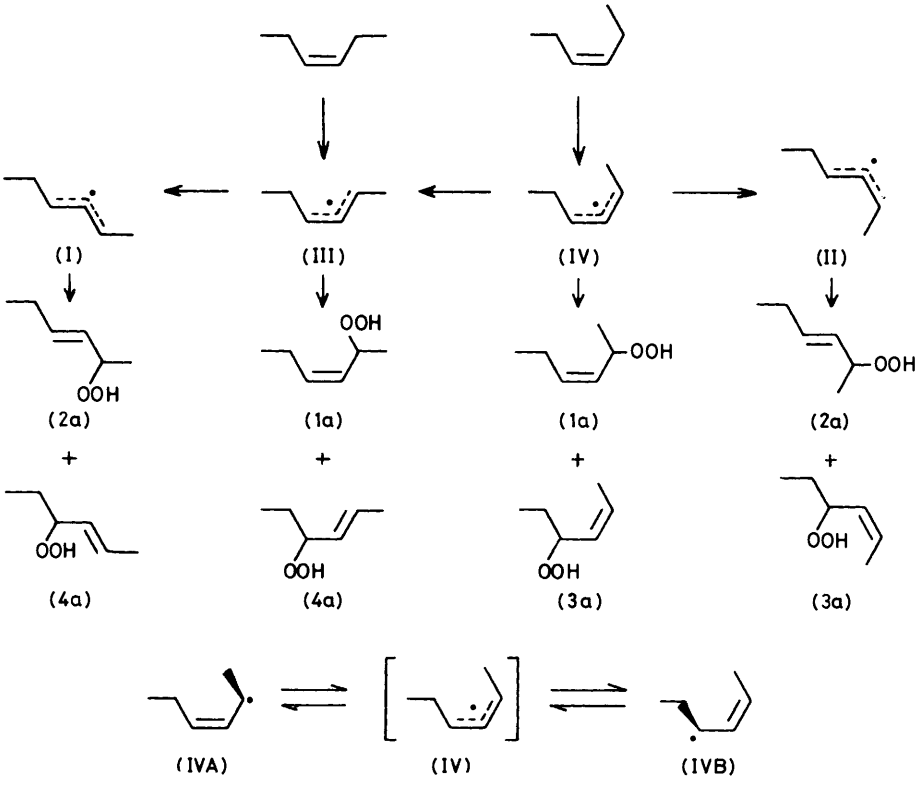
Time dependence of hex-*cis*-3-ene cobalt acetate catalysed autoxidations: allylic alcohols formed after reduction of the hydroperoxides

	Hexenol product (weight %)			
Conditions (% autoxidation)	*trans*-3-en-2-ol	*cis*-3-en-2-ol	*trans*-4-en-3-ol	*cis*-4-en-3-ol
ca. 5% at 50 °C	23	26	40	11
ca. 10% at 50 °C	24	25	41	10
ca. 5% at 25 °C	16	33	43	8
ca. 5% at 25 °C, then N_2 at 25 °C (3 d)	17	33	42	8
ca. 5% at 25 °C, then N_2 at 50 °C (3 d)	20	30	44	6

The formation of all four isomers (Table 1) can most readily be explained by the presence of radical intermediates (III) and (IV) which lose their defined stereochemistry, particularly at elevated temperatures (Scheme 2). If rotation about the 3,4-bond occurs, four isomeric allylic radicals are involved, two of which are identical with (I) and (II) from hex-*trans*-3-ene (Scheme 1). Loss of the defined stereochemistry by (III) or (IV) or both would explain the formation of 2-hydroperoxyhex-*trans*-3-ene (2a).

Examination of a model of intermediate (IV) shows serious crowding of hydrogen atoms which is relieved if the three-carbon system is twisted from the planar form.

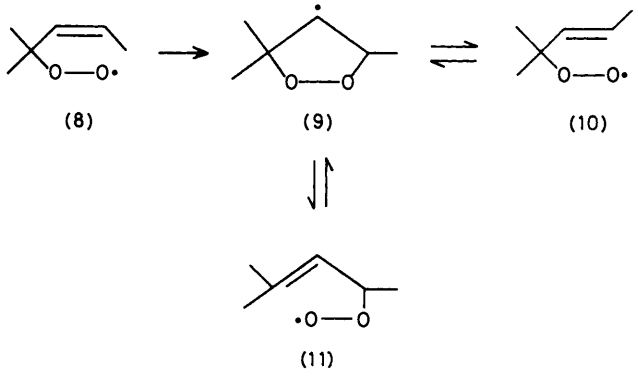
However, such twisting would decrease and ultimately result in the loss of the resonance energy of the delocalised radical. In the extreme case, radical (IV) may be viewed as two separate, nonplanar, nondelocalised radicals (IVA) and (IVB), in equilibrium with each other, *via* the planar delocalised form (IV). In the nondelocalised radicals (IVA) and (IVB), rotation about the carbon–carbon single bond allows isomerisation to occur. The deviation from planarity in these radicals would be the consequence of relief of steric strain by twisting, resulting in greater stability than that resulting from the gain in resonance energy afforded by the planar allyl radical. The higher *cis* : *trans* ratio for 2-hydroperoxyhex-3-ene at 25 than at 50 °C can be correlated with a less probable interconversion of radicals at lower temperatures.



SCHEME 2

Some loss of defined stereochemistry of allylic products has been observed in other free radical reactions. *cis–trans* Isomerisation is produced in allylic halogenations with t-butyl hypochlorite and photoinitiated allylic radicals.[2] Chlorination of pent-*cis*-2-ene on C-1 gave some *trans*-isomers at 100 but not at 40 °C. However, chlorination on C-4 gave 43% *trans*-isomer at 40 °C. These results were explained by assuming that steric hindrance in higher olefins may decrease the stability of *cis*-allyl radicals which isomerise to the *trans*-form. Thus, 4,4-dimethylpent-*cis*-2-ene reacted to give approximately equal amounts of *cis*- and *trans*-1-chloro-4,4-dimethylpent-2-ene at 40 °C.

In another study,[1b] oxidation of but-*cis*-2-ene produced a mixture of 34% *cis*- and 66% *trans*-hydroperoxides, whereas but-*trans*-2-ene produced 90% *trans*-hydroperoxides. Here, the stereochemistry of the *cis*- and *trans*-allyl radicals was thought to be preserved until their reaction with oxygen. When peroxy-radicals are formed, steric hindrance in the *cis*-hydroperoxides should facilitate *trans*-isomerisation. Our results showing the relative stability of hydroperoxides (Table 3) are not consistent with this view. In a further study[1c] the formation of 2-hydroperoxy-2-methylpent-*trans*-3-ene by

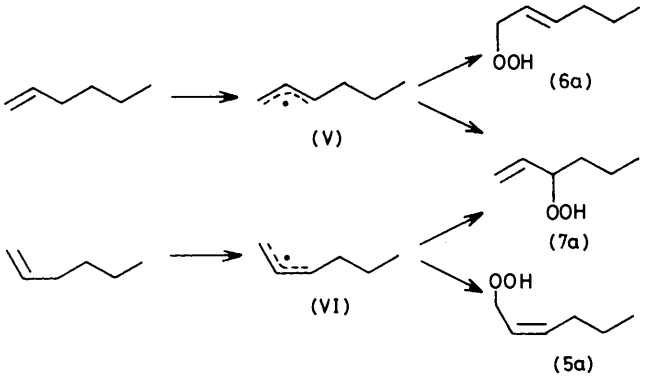


SCHEME 3

autoxidation of the *cis*-olefin was explained either by rearrangement of the *cis*-peroxy-radical (8) *via* a cyclic peroxide (9), which is in equilibrium with both the

trans-peroxy-radical (10) and the allylic isomer (11) (Scheme 3), or by rearrangement of a *cis*-allylic radical prior to reaction with oxygen.[3]

Hex-1-ene.—The three products of autoxidation, *cis*- and *trans*-1-hydroperoxyhex-2-ene (5a) and (6a), and 3-hydroperoxyhex-1-ene (7a) (Table 1) are consistent with a mechanism of hydrogen abstraction giving two



SCHEME 4

delocalised radicals (V) and (VI) (Scheme 4). The results indicate a small preference for attack at C-1 to give 1-hydroperoxyhex-2-ene (5a) and (6a). As expected, the rearranged double bond is mainly in the *trans*-form. In the analogous free radical chlorination of pent-1-ene, there was also observed a preferential (60–70%) formation of 1-chloropent-2-ene; [2] predominant factors suggested to explain this result were steric hindrance, favouring reaction at C-1, and equilibration of all isomers producing the more highly substituted olefin.

Hex-2-ene.—The products from hex-*trans*-2-ene can be explained on the basis of the three expected allylic radicals which are the same as the principal reactive intermediates from hex-*trans*-3-ene [(I), Scheme 1], hex-*cis*-3-ene [(III), Scheme 2], and hex-1-ene[(V), Scheme 4].

(I) ⟶ (2a) + (4a)
(III) ⟶ (1a) + (4a)
(V) ⟶ (6a) + (7a)

The products from hex-*cis*-2-ene require the same radicals as those produced from hex-1-ene [(V) and (VI), Scheme 4], hex-*cis*-3-ene [(III), Scheme 2], and hex-*trans*-3-ene [(II), Scheme 1].

(V) ⟶ (6a) + (7a)
(VI) ⟶ (5a) + (7a)
(III) ⟶ (1a) + (4a)
(II) ⟶ (2a) + (3a)

Hydrogen abstraction from a methylene group, producing intermediate (II), appears to be favoured over that from a methyl group, producing (V) and (VI). This preference for hydrogen abstraction from the secondary position is calculated to be 3.16 : 1 at 50 °C and 3.75 : 1 at 25 °C, and may be due to the lower C–H bond dissociation energy of a methylene group. A similar effect was noted[3] in the chlorination of pent-2-ene by t-butyl hypochlorite where the ratio of secondary to primary abstraction was 2.54 : 1 at 100 °C and 5.27 : 1 at −78 °C.

Hepta-2,5-diene.—On autoxidation all three stereoisomers of the diene produced conjugated 2-hydroperoxy-3,5-dienes, as shown by the dienols obtained on subsequent reduction (Table 4). Catalytic hydrogenation

TABLE 4

Allylic alcohols formed by reduction of the hydroperoxides from the cobalt acetate catalysed autoxidations of hepta-2,5-dienes (5—10% oxidation, 0.05% catalyst)

		Heptadien-2-ol product (weight %)			
Heptadienes	Temp. (°C)	*cis*-3, *cis*-5	*cis*-3, *trans*-5	*trans*-3, *cis*-5	*trans*-3, *trans*-5
cis-2,*cis*-5	75	0	0	10	90
	50	0	0	35	65
	25	0	0	48	52
cis-2,*trans*-5	75	0	5	10	85
	50	trace	3	17	80
	25	3	3	22	72
trans-2,*trans*-5	75	0	10	0	90
	50	0	8	0	92
	25	0	6	0	94

of the hydroperoxides gave a mixture of heptanols consisting mainly (>95%) of the 2-isomer with traces of the 4-, 1-, and 3-isomers (*ca.* 1%). Clearly only very small amounts of unconjugated diene hydroperoxides are present in the autoxidation reaction mixture.

The *cis*,*cis*-diene gave the *trans*-3,*cis*-5- and *trans*-3, *trans*-5- conjugated diene hydroperoxides which are analogous to the products reported from the structurally equivalent linoleic acid.[4] Autoxidation catalysed by a free radical initiator (ABIN) or cobaltous acetate gave the same isomer distribution as the control samples with no added catalyst (Table 5). As with linoleic acid, the

TABLE 5

Isomeric hepta-3,5-dien-2-ols from oxidations of hepta-*cis*-2,*cis*-5-diene followed by reduction of the hydroperoxides

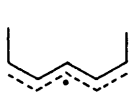
		Heptadien-2-ol product (weight %)	
Conditions	Temp. (°C)	*trans*-3, *cis*-5	*trans*-3, *trans*-5
ABIN [a]	75	10	90
No catalyst	75	9	91
ABIN [a]	50	34	66
No catalyst	50	33	67
No catalyst	25	50	50

[a] Azobis(isobutyronitrile), 1%.

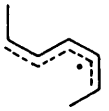
ratio of *trans*,*cis*- to *trans*,*trans*-products increased as the autoxidation temperature was lowered, 89—91% *trans*,*trans* being formed at 75 °C and equal proportions of *trans*,*cis* and *trans*,*trans* being formed at 25 °C.

The stereochemistry of the conjugated diene hydroperoxides produced can be accounted for in a similar manner to the products from autoxidation of the hexenes. Three conformers of the *cis*,*cis*-diene isomer may be considered from which corresponding delocalised heptadienyl radicals would be produced by hydrogen

abstraction. Of the three planar radicals (VII), (VIII), and (IX), (VII) produces a *trans*-3,*cis*-5-conjugated product with the *trans*-bond nearest the hydroperoxide. Radicals (VIII) and (IX) can be neglected because of their steric interactions, and because they would produce



(VII)



(VIII)

(IX)

cis,*cis*-conjugated hydroperoxides which were not found among the autoxidation products. It is interesting to note that only the conformation analogous to (VII) could be detected in e.s.r. studies on the pentadienyl radical itself at ambient temperatures.[5,6]

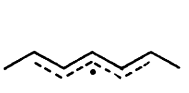
The stability of the hepta-3,5-dien-2-ols and the products of the autoxidation toward stereomutation was investigated in the same manner as that of the hexenols and products from hex-3-ene autoxidation (Table 3). Little rearrangement occurred during a period similar to that in which the diene was autoxidised. Thus, the variation in stereochemistry in the hydroperoxides is unlikely to be due to stereomutation of the 2-hydroperoxyhepta-*trans*-3,*cis*-5-diene to 2-hydroperoxyhepta-*trans*-3,*trans*-5-diene.

However, it has been shown that the corresponding *trans*,*cis* conjugated diene 9- and 13-hydroperoxides, obtained from the autoxidation of methyl linoleate, undergo allylic rearrangement at 40 °C, and that the process is accompanied by extensive stereomutation to give the *trans*,*trans*-conjugated dienes.[7]

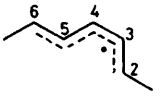
The formation of significant amounts of *trans*,*trans*-conjugated hydroperoxides from the *cis*,*cis*-diene indicates, as with hex-*cis*-3-ene, that the radical loses its defined stereochemistry. Rearrangement of the radical could occur by rotation about one of the carbon-carbon bonds to relieve the interactions between non-bonded atoms which sterically inhibit a planar, completely delocalised radical (*cf.* Scheme 2). Such isomerisation might be expected to be more facile in the diene series as delocalisation and the resulting resonance energy is not completely destroyed in the transition state, but decreased from that of a five-carbon system to that of a three-carbon system. With allylic carbonium ions, spectroscopic evidence indicates that the barrier to rotation decreases as the length of the conjugated system increases.[8]

Recently Porter *et al.*[1g,h] suggested that in the autoxidation of linoleic acid the dienyl peroxy-radicals, rather than the dienyl radicals themselves, play a crucial role in determining the stereochemistry of the final products. Under conditions in which autoxidation was kinetically controlled (less than 2% conversion, in the presence of a free radical initiator), the *trans*,*cis* to *trans*,*trans* ratios of hydroperoxides were not only dependent on temperature but also on the concentration of linoleic acid. Although isomerisation of the hydroperoxides was not detected under the greater degree of conversion dealt with in the present work with model dienes, the lower *trans*,*cis* to *trans*,*trans* ratios observed with hepta-*cis*-2,*cis*-5-diene (Tables 4 and 5) than those reported by Porter *et al.* with linoleic acid indicates that the stereochemistry of our products may also be influenced by thermodynamic effects. However, the peroxy-radical rearrangement mechanism of Porter *et al.* does not provide a complete explanation of the hydroperoxide isomers produced by autoxidation of the *cis*,*trans*- and *trans*,*trans*-isomers of hepta-2,5-diene.

Autoxidation of both *cis*,*trans*- and *trans*,*trans*-isomers of hepta-2,5-diene produced mainly *trans*,*trans*-conjugated hydroperoxides (Table 4). The isomer distribution among the products can be explained by considering the different planar conformations of the dienyl radicals. In the *trans*,*trans*-diene series, non-bonded interaction is at a minimum in radical (X) and at a maximum in (XII). Attack of oxygen at either end of radical (X)



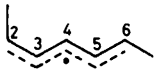
(X)



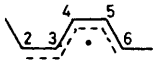
(XI)

(XII)

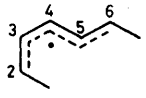
results in the *trans*,*trans*-diene hydroperoxide. Oxygen attack at C-6 of radical (XI) again gives the *trans*,*trans*-diene hydroperoxide, whilst attack at C-2 leads to the *cis*-3,*trans*-5-isomer, with the *cis*-double bond nearest the hydroperoxide group, which was also detected. The same *cis*,*trans*-isomer would be formed by reaction with oxygen on either end of radical (XII). The much higher proportion of *trans*,*trans*-isomers indicates that the extended radical (X) is the principal intermediate, and, perhaps, that (XI) is more reactive at C-6 than at C-2. Starting with the most extended and favourable diene radical (X), the corresponding peroxy-radicals expected would, by Porter's mechanism,[1g] produce only the *trans*-3,*trans*-5- and *trans*-3,*cis*-5-diene hydroperoxides. The absence of the *trans*-3,*cis*-5-diene hydroperoxide (Table 4) supports a mechanism involving both dienyl radicals (X) and (XI) rather than rearrangement of the peroxy-radicals from (X).



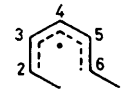
(XIII)



(XIV)



(XV)



(XVI)

With the *cis*,*trans*-diene, four delocalised planar radicals may be considered in which C-2 and C-6 are not

equivalent. The most extended and favourable radical (XIII) will give the *trans,trans*-isomer if the attack occurs at C-2 and the 2-hydroperoxy-*trans*-3,*cis*-5-diene if attacked at C-6. Radical (XIV) will produce the *trans,trans*-isomer by oxygen attack at C-2 and the *cis,cis*-isomer by attack at C-6. Increased steric interactions in radicals (XV) and (XVI) makes the formation of these radicals much less favourable. However, the formation of 3—5% of 2-hydroperoxy-*cis*-3,*trans*-5-diene can only be explained by invoking the intermediacy of one at least of these radicals. Similarly, the *cis,cis*-isomer detected to the extent of 3% in the autoxidation at 25 °C can be assumed to arise by oxygen attack on C-6 in either one or both of the radicals (XIV) and (XVI). Turning again to Porter's mechanism,[1g] the peroxy-radicals produced from the most extended and favourable diene radical (XIII) would lead to the *trans*-3,*trans*-5- and *trans*-3,*cis*-5-diene hydroperoxides. The formation of small amounts of *cis*-3,*trans*-5- and *cis*-3,*cis*-5-diene hydroperoxides (Table 4) is most readily explained by a mechanism involving dienyl radicals such as (XIV), (XV), or (XVI).

EXPERIMENTAL

Unsaturated substrates and hydroxy-products were prepared by unequivocal methods. Distillation yields are given in parentheses for each isolated compound; characterizations were based on standard spectroscopic methods (i.r., u.v., and ^{1}H n.m.r.).

Preparation of Monoenes.—Hex-*cis*-3-ene and hex-*trans*-3-ene were synthesised by stereospecific reduction of hex-3-yne (43%) which was prepared [9] from disodium acetylide and ethyl bromide. Catalytic hydrogenation with Lindlar's catalyst [10] in ethanol produced the *cis*-product (76%). Reduction with lithium aluminium hydride in diglyme–tetrahydrofuran [11] gave the *trans*-product (90%) in 96% purity [by g.l.c. on an $AgNO_3$–polyethylene glycol (PEG) column; impurities, 2% hex-3-yne and 2% hex-*cis*-3-ene].

Hex-1-ene (72%) was made by Lindlar hydrogenation of hex-1-yne (32%) which was prepared from sodium acetylide and n-butyl bromide. A mixture of *cis*- and *trans*-hex-2-ene (37%), prepared by the method of Schmitt and Boord,[12] was readily separated by preparative g.l.c. (30% $AgNO_3$–PEG; 30 °C).

Preparation of Dienes.—Hepta-2,5-diene was synthesised by reduction of hepta-2,5-diyne which was prepared [9] by condensation of propynylmagnesium bromide and 1-bromo-but-2-yne [13] with cuprous chloride as catalyst (54%). Reduction of hepta-2,5-diyne with Lindlar catalyst did not proceed smoothly (10—20%) and better results were obtained in ethanol with 0.5% palladium-on-calcium carbonate catalyst (without lead acetate as poison); hydrogenation was stopped after the theoretical uptake of hydrogren (57%). Hepta-*cis*-2,*trans*-5-diene (77%) was made by Lindlar reduction of hept-*trans*-2-en-5-yne, which was synthesised by condensing propynylmagnesium bromide with crotonyl bromide in the presence of a cuprous chloride catalyst (47%).

Reduction of hepta-2,5-diyne with sodium in liquid ammonia to prepare the *trans,trans*-diene did not prove satisfactory and led to conjugated products. Better results were obtained by thermal isomerisation (100 °C for 18 h) of hepta-*cis*-2,*trans*-5-diene, in the presence of selenium as catalyst,[14] into a mixture of nonconjugated isomers which was analysed by g.l.c. ($AgNO_3$–PEG; 25 °C). It consisted of the *trans,trans*-isomer (60%), the *cis,cis*-isomer (3%), starting material (30%), and other isomers (7%). The *trans,trans*-isomer was separated by preparative g.l.c. (18%).

Preparation of Hexenols.—Hex-3-en-2-ol was obtained by reduction of hex-3-yn-2-ol, prepared from but-1-ynylmagnesium bromide and acetaldehyde (62%). Catalytic Lindlar hydrogenation gave the *cis*-isomer (78%), and reduction with sodium in liquid ammonia yielded the *trans*-isomer (68%).

Hex-*trans*-4-en-3-ol was prepared from ethylmagnesium bromide and crotonaldehyde (70%). Hex-*cis*-4-en-3-ol was made (88%) by catalytic Lindlar hydrogenation of hex-4-yn-3-ol, prepared from prop-1-ynylmagnesium bromide and propionaldehyde (44%).

Hex-*cis*-2-en-1-ol was derived from hex-2-yn-1-ol by Lindlar hydrogenation (90%), and the corresponding hex-*trans*-2-en-1-ol by reduction with lithium aluminium hydride (86%). Hex-2-yn-1-ol was prepared (90%) by alkylation of prop-2-yn-1-ol protected as the tetrahydropyranyl ether.[15] Finally, hex-1-en-3-ol was prepared (52%) from n-propylmagnesium bromide and acrolein.

Preparation of Heptadienols.—Hept-*cis*-5-en-3-yn-2-ol (71%) and hept-*trans*-5-en-3-yn-2-ol (64%) were prepared from the corresponding pent-2-en-4-ynylmagnesium bromides and acetaldehyde. The *cis*-isomer in ethyl acetate was then catalytically hydrogenated with Lindlar catalyst to give hepta-*cis*-3,*cis*-5-dien-2-ol (84%), and reduced in diethyl ether with lithium aluminium hydride to give hepta-*trans*-3,*cis*-5-dien-2-ol (63%). The *trans*-isomer was catalytically hydrogenated with Lindlar catalyst to produce hepta-*cis*-3,*trans*-5-dien-2-ol (87%). Hepta-*trans*-3,*trans*-5-dien-2-ol was made by treating hexa-*trans*-2, *trans*-4-dienal with methylmagnesium iodide (73%).

Preparation of Heptanols.—Heptan-2-ol was prepared by treating pentylmagnesium bromide with acetaldehyde (26%). Similarly, heptan-3-ol was made from butylmagnesium bromide and propionaldehyde (45%), and heptan-4-ol from propylmagnesium bromide and butyraldehyde (60%).

Gas-liquid Chromatography.—Either a Pye-Argon chromatograph or an Aerograph A-90-3P chromatograph was used for analyses of reaction products. The latter instrument was also used for preparative g.l.c. Isomeric hexenols were separated on two 5-ft columns: (*a*) 30% of a 25% solution of $AgNO_3$ in PEG 300, and (*b*) 30% PEG 300, both operated isothermally at 75 °C. Isomeric heptadienols were partially separated with a 5-ft column operated at 75 °C and containing 30% of a 50% solution of trinitrofluorenone in PEG 300 with sufficient resolution to permit quantitative analysis. Analysis was completed with the $AgNO_3$–PEG column. Analyses of authentic mixtures of hexenols and heptadienols agreed with the known compositions to within ±1%. Products in reduced autoxidised mixtures were identified on the basis of retention times and mixed g.l.c. with the authentic pure isomers. Hexenes and heptadiene isomers were separated with a 14-ft $AgNO_3$–PEG column. This column was suitable for both analysis of the starting material and for isolation of hepta-*trans*-2,*trans*-5-diene by preparative g.l.c. Isomeric heptanols were separated with a 5-ft column containing 20% Carbowax 20M, operated at 100 °C.

Autoxidations.—The olefins were stirred under oxygen in a 5-ml round-bottomed flask attached to a reflux condenser and a gas burette. Samples were withdrawn from a side-arm sealed with a septum cap. Samples taken at 5 to 10% oxidation were reduced by adding triphenylphosphine, concentrated by evaporating the olefin under a stream of nitrogen, and analysed by g.l.c. Direct g.l.c. analysis of samples withdrawn from the autoxidised mixtures showed retention of stereochemistry in the unoxidised olefins. Control experiments showed no isomerisation of allylic alcohols when subjected to the same conditions of autoxidation as the olefin substrates both under oxygen and under nitrogen. Similarly, autoxidised olefins were maintained under the same autoxidation conditions in the presence of octanol as an internal standard. Analysis of reduced samples by g.l.c. showed no change in stereochemistry (Table 3).

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