

Initiated, *tert*-Butyl Hydroperoxide-loaded, Low-temperature Autoxidation of Alkenes: A Chemoselective Synthesis of Allylic Hydroperoxides, allowing Analysis of the Regioselectivity of Hydrogen Atom Abstraction from some Unsymmetrically Substituted Substrates¹

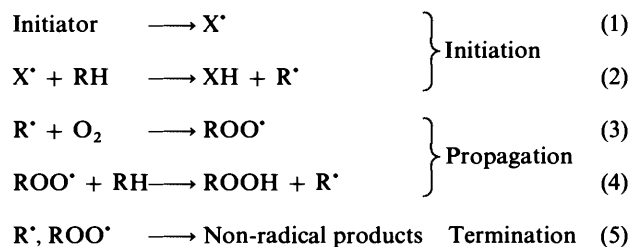
John L. Courtneidge* and Melanie Bush

Malaysian Rubber Producers' Research Association, Tun Abdul Razak Laboratory, Brickendonbury, Hertford SG13 8NL, UK

A method for the preparation of allylic hydroperoxides is introduced: the method involves the rapid, low-temperature, initiated autoxidation of an alkene (in these instances 1-methylcyclohexene and the isomeric 4-methyloct-4-enes) in the presence of *tert*-butyl hydroperoxide. The success of the method relies upon the selectivity of hydrogen atom abstraction from the substrate by the chain-carrying *tert*-butylperoxyl radicals, according to the preference for formation of the most stable intermediate allylic radicals, and the reduced rates of chain termination *via* these same radicals. The method gives a regioselectivity for attack broadly in agreement with predictions from Bolland's rules, and a sufficiently high chemoselectivity for allylic hydroperoxide formation that ready isolation of these products in good yield is achieved.

Autoxidation is rarely considered as a useful synthetic procedure: the great body of work that has been directed towards this widespread process has been more concerned with its destructive consequences than constructive considerations. As part of our work concerning the uses of Natural Rubber (NR),² we have become interested in the question of autoxidation.

The now-classical Scheme, eqns. (1)–(5), for alkene autoxidation was developed on the basis of kinetic analysis in the late 1940's and early 1950's by Bateman, Bolland and co-workers³ following the isolation by Criegee, Farmer and their co-workers⁴ of some simple allylic hydroperoxides formed during alkene autoxidation.



The elastomeric properties of NR derive from crosslinking and entanglement of the hydrocarbon chains and, during oxidative degradation, progressive scission of the chains results in the loss of these properties. Although our understanding of the events which occur during the autoxidation of many unsaturated substrates has undergone a revolution in refinement in recent years,⁵ the exact cause(s) of chain-scission during NR autoxidation remains a subject of some debate.⁶ To join this debate, we have instituted a programme of work designed to understand more deeply the (aut)oxidation chemistry of some NR-model compounds.

We initially wished to know the regiochemistry of the hydrogen-atom abstraction of an NR-model and, especially in view of both mechanistic considerations and the existing literature,⁷ we decided to study the chemistry of some trisubstituted alkenes. In considering the older data we realised that the plethora of products seen in most autoxidations is a result of both the decomposition of primary products needed to initiate reaction chains and the diversion of the chain-carrying

peroxyl radicals to termination steps and to other non-hydroperoxide generating reactions. In order to discover the selectivity *via* product analysis, we therefore needed a process by which the initial hydroperoxidic products could be rapidly generated and preserved against subsequent decomposition.

We reasoned that these drawbacks in simple autoxidation could be overcome in two ways. Firstly, inclusion of a labile initiator could start the chain reactions at low temperatures and, therefore, hopefully, avoid product decomposition. Secondly, inclusion of an excess of a *tertiary* hydroperoxide in the reaction medium might preserve the product peroxyl radicals as hydroperoxide rather than commit them to other pathways.

To our satisfaction, inclusion of *tert*-butyl hydroperoxide in di-*tert*-butyl peroxyoxalate-initiated autoxidations of 1-methylcyclohexene at 30, 40 and 50 °C and of the isomeric 4-methyloct-4-enes at 60 °C achieved this goal and has resulted in a synthetically useful procedure for the preparation of some allylic hydroperoxides.

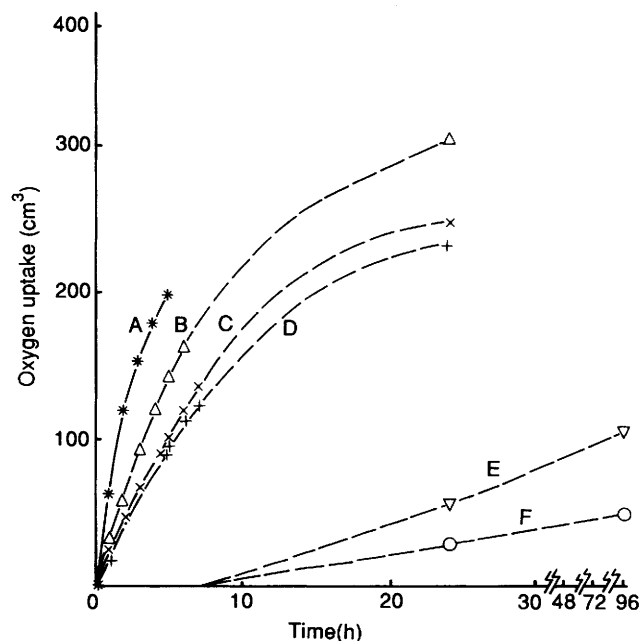
Results

(a) *tert*-Butyl Hydroperoxide-loaded Autoxidation.—Unstirred reaction mixtures containing the substrate of interest (0.1 mol dm⁻³), the chosen initiator (0.005 mol dm⁻³) and *tert*-butyl hydroperoxide (1.0 mol dm⁻³) in an appropriate solvent (total 250 cm³), were allowed to absorb oxygen at different temperatures. The rates of oxygen uptake at 30 °C for reaction of some cycloalkenes in benzene using di-*tert*-butyl peroxyoxalate (DTBPOX) as initiator are displayed in Figure 1, the data for a run conducted using a sample in which the *tert*-butyl hydroperoxide was omitted also being shown.

At the end of the oxidation runs, the reaction mixtures were prepared for analysis by ¹H NMR (400 MHz) spectrometry. Storage prior to analysis as concentrated oxidates or as frozen benzene solutions did not materially affect the analyses obtained (Table 1). In those runs for 1-methylcyclohexene conducted at 40 and 50 °C, analysis revealed the presence of trace amounts of the substrate-derived epoxide, 1-methyl-1,2-epoxycyclohexane, while allylic alcohols or other products, if present at all, were below the level of detection.

Reactions for the isomeric 4-methyloct-4-enes were likewise

conducted in *tert*-butyl hydroperoxide-loaded solutions, using either DTBPOX or commercial bis-4-*tert*-butylcyclohexyl peroxydicarbonate (BCHPC) as initiators. A somewhat more elevated temperature (60 °C) was required for the conversion of these substrates (little oxygen uptake was noted at 40 °C) while chemoselective conversion of the substrates into allylic hydroperoxides was again achieved. The product compositions (judged both before and after triphenylphosphine reduction) are collected in Table 2. The identities of the individual hydroperoxides was ensured by their individual isolation and reduction to allylic alcohols that had been prepared by reliable routes and fully characterized by spectroscopic and combustion analysis (see the following paper). In one instance, reaction



Data points	Presence/absence of <i>tert</i> -butyl hydroperoxide	Temp. (°C)	Initial oxygen uptake rate (cm ³ h ⁻¹)
A	1-MCH ✓	40	69.2
B	3-MCH ✓	30	30.7
C	1-MCH ✓	30	22.8
D	1-MCH ✓	30	22.5
E	MCH ✓	30	3.4
F	1-MCH ×	30	1.7

Fig. 1 Oxygen uptake profiles from *tert*-butyl hydroperoxide-loaded and -unloaded, DTBPOX-initiated alkene autoxidations *a* 1-MCH = 1-methylcyclohexene, 3-MCH = 3-methylcyclohexene and MCH = methylenecyclohexane

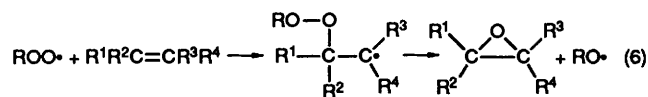
using BCHPC as initiator was conducted using 2,2,4-trimethylpentane as reaction solvent (a solution of *tert*-butyl hydroperoxide in this solvent is commercially available). A low level of solvent autoxidation was, however, noted and the resulting contaminant (2,4,4-trimethylpentan-2-yl hydroperoxide) caused some problems in product purification.

(b) *Allylic Hydroperoxide Equilibration Studies*.—In order to decide whether *tert*-butyl hydroperoxide-loaded autoxidation involved suppression of hydroperoxide rearrangement, some experiments designed to induce such rearrangement in the presence or in the absence of *tert*-butyl hydroperoxide were performed: the mixture of isomers obtained by singlet oxygenation of 1-methylcyclohexene (purified by Kugelrohr distillation) was used as substrate. In order to mimic the 1-methylcyclohexene autoxidations (where final total allylic hydroperoxide concentrations were *ca.* 0.03 mol dm⁻³) benzene solutions (containing either no or 1.0 mol dm⁻³ *tert*-butyl hydroperoxide) were prepared which contained di-*tert*-butyl peroxyoxalate (0.005 mol dm³) and the mixed allylic hydroperoxides (total 0.015 mol dm⁻³).

Samples of these mixtures were maintained for 21 h at appropriate temperatures under oxygen atmospheres before rotary evaporation (bath 25–38 °C; *p* 60 mmHg) prior to highfield ¹H NMR spectrometric examination. The collected data are displayed in Table 3.

Discussion

The primary aim of this investigation was to determine the regioselectivity of hydrogen atom abstraction from some trialkylalkenes. We chose to conduct our analysis at the level of the first-formed product of autoxidation, the allylic hydroperoxides. The autoxidation scheme outlined earlier, eqns. (1)–(5), is a simplification of the reactions which occur during substrate conversion. Firstly, in autoinitiated autoxidation at comparatively elevated temperatures, product hydroperoxide is lost by the decomposition necessary to initiate new chains. Furthermore, peroxy radicals are diverted from hydroperoxide formation by self-reaction in termination steps, eqn. (5), and by addition reactions, eqn. (6). The latter reaction can, for



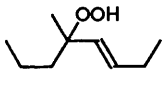
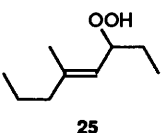
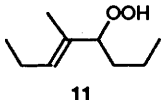
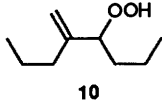
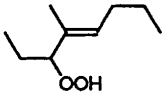
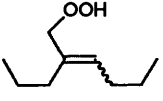
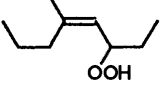
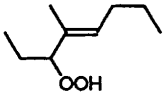
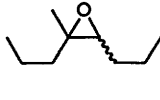
certain substrates become an almost exclusive pathway. In styrene autoxidation, for example, repetitive addition results in the formation of alternating peroxide co-polymer, while for highly alkylated alkenes, epoxide formations becomes increasingly important (the partitioning of these competing reactions has been presented schematically by Brill⁸). We therefore

Table 1 Products (%) from DTBPOX initiated, Bu^tOOH loaded autoxidation of 1-methylcyclohexene in benzene

T/°C	t/h	Conversion (%)	Sample storage ^a					
30	24	40	A	36	37	24	1.5	1.5
40	5	30	A	33	40	25	1	1
			B	31	37	26	3	3
50	4	30	A	31	40	26	1.5	1.5
			B	33	39	24	2	2

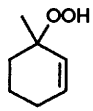
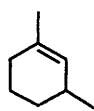
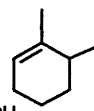
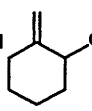
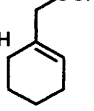
^a A = oxidate stored as frozen benzene solution prior to NMR analysis; B = concentrated oxidate stored in deep freeze prior to NMR analysis

Table 2 Product distributions (%) from *tert*-butyl hydroperoxide-loaded autoxidations of 4-methyloct-4-enes^a

									
	9	25	11	10	21	23/50	24	21	23/50
1 <i>cis</i> -Alkene (0.04 mol dm ⁻³), Bu'OOH (1 mol dm ⁻³) DTBPOX (1 mmol dm ⁻³) in benzene, 60 °C	19	35	17	3	4	5	3	4	14
2 As run 1, but BCHPC (1 mmol dm ⁻³) as initiator: analysis as peroxides	16	32	16	6	6	7	6	6	11
2 Analysis after Ph ₃ P treatment	17	32	16	4	8	6	7	7	11
3 As run 2, but <i>trans</i> -alkene: analysis as peroxides	16	33	17	6	11	7	2	7	8
3 Analysis after Ph ₃ P treatment	16	34	17	6	13	6	Trace	6	9
4 As run 2 but analysis of distilled products ^b	20	22	15	4	4	8	1	4	15 ^c

^a Structural numbering taken from following paper. ^b α , β -Unsaturated carbonyls ca. 8%. ^c *cis*:*trans* ca. 2:1 from ¹³C NMR spectrum.

Table 3 Free radical-mediated equilibrations (in mol %) of *tert*-butyl hydroperoxide -loaded and -unloaded 1-methylcyclohexene ene hydroperoxides^a

					
Starting distilled peroxides	39	3	12	45	1
40 °C/added Bu'OOH	28	15	10	44	3
40 °C/no Bu'OOH	11	34	9	35	10
60 °C/added Bu'OOH	15	35	9	43	8
60 °C/no Bu'OOH	10	35	12	30	14
Neat alkene autoxidation 60 °C ^b	34	29	34	2	1
Loaded autoxidation 50 °C ^c	32	39	24	2	2

^a 0.015 mol dm⁻³ mixed allylic hydroperoxides, 1.0 or 0.0 mol dm⁻³ Bu'OOH, 0.005 mol dm⁻³ DTBPOX in benzene. ^b Ref. 1a. ^c From Table 1.

needed to develop a procedure by which substrate-derived peroxy radicals could be rapidly formed at low temperatures and, once formed, could, more or less irreversibly, be trapped as hydroperoxides.

The requirement for a low-temperature initiator suggested use of di-*tert*-butyl peroxyoxalate,⁹ whilst for peroxy radical

trapping, we considered that the inclusion of an added hydroperoxide in the autoxidation medium might be effective. This proposition would rely on the ready formation of the equilibrium shown in eqn. (7): the viability of this had been



demonstrated by Howard and Ingold,¹⁰ who, in kinetic studies, added *tert*-butyl hydroperoxide where they wished to be certain of the identity of the chain-carrying species.

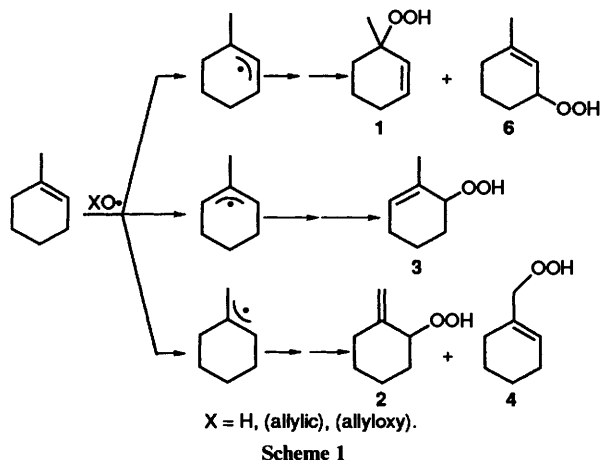
The choice of *tert*-butyl hydroperoxide as the carrier hydroperoxide occasions two other benefits. Firstly, its volatility allows fairly easy removal at the end of the oxidation reaction, while secondly, and of substantial advantage, the *tert*-butylperoxyl radicals derived therefrom undergo self-reaction at rates significantly lower than those of (substrate-derived) *secondary* and/or *primary* peroxyl radicals.¹¹ The accelerative effect of the carrier hydroperoxide is apparent in the data shown in Figure 1. Although a small level of carrier hydroperoxide decomposition might be initiating some chains, this rate enhancement is most likely a consequence of an overall increase in propagation chain length.

Finally, we needed to select suitable substrates. For acyclic substrates, generation of allylic radicals, eqn. (4), occurs at an entropic penalty (see the discussion by Walling and Thaler¹²). Thus a cycloalkene appeared the substrate of choice and, partly in view of prior studies, 1-methylcyclohexene was taken for the initial studies.

Pritzkow and co-workers,¹³ in an extensive study of cycloalkene autoxidation have summarised the early work by Criegee,^{4a} by Farmer^{4b} and their co-workers, wherein more or less pure samples of allylic hydroperoxides had been isolated by careful separation of the complex product mixtures from 1-methylcyclohexene autoxidations. We can confirm the product diversity found in the uninitiated, neat autoxidation of this alkene,¹⁴ and recent work¹⁴ by Russian scientists support those findings.

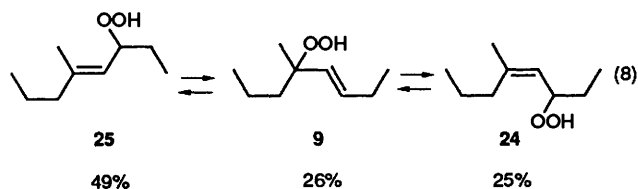
Application of the *tert*-butyl hydroperoxide-loaded autoxidation procedure, in contrast, permitted rapid and clean conversion of this substrate to allylic hydroperoxides (Table 1 and Figure 1). The data obtained were reasonably reproducible with respect to variation in the manner of sample analysis and the regiochemistry of the reaction was relatively invariant over the range of reaction temperatures employed.

The selectivity of hydrogen atom abstraction accords fairly well with that calculated by an additivity scheme (Bolland's Rule):¹⁵ the experimentally determined hydrogen atom ratio of [(CH₂ *trans* to Me): (CH₂ *gem* to Me): (Me)] being [3:1:ca. 0.1]. Abstraction at the methylene *trans* to the methyl group gives what is probably the most stable allylic radical (1,1,3-trialkylated) and reaction at this position is sterically least congested (Scheme 1). Thus, the isoallylic pair of hydroperoxide isomers **1** and **6*** is predominantly formed.



* Structural numbers relate to the structural diagrams given in the following paper.

Loaded oxidations at the higher temperatures noted in Table 1 resulted in the formation of trace amounts of epoxide and this reaction was seen to be a significant contributor at the higher temperatures encountered in autoinitiated neat-hydrocarbon autoxidations.^{1a} For both 4-methyloct-4-enes, the data presented in Table 2 again show that abstraction (at 6-H₂) to give the hyperconjugatively most stabilised radicals is preferred while, in both instances, abstraction from the methyl groups is more favoured than is the case for 1-methylcyclohexene. This latter finding is probably most reasonably ascribed to the entropic effect discussed earlier, where accelerated abstraction from the allylic methylene positions in 1-methylcyclohexene accounts for its apparently enhanced rate of autoxidation and where loss of rotational freedom suppresses abstraction from its methyl group. Inspection of the product distribution from the reactions of the acyclic substrates suggests the apparent anomaly of geometrical isomerization of the double bond during the production of the preferred *secondary* allylic hydroperoxide. This isomerization is, however, not the result of isomerization of the substrate alkene or, we believe, of intermediate allylic radicals, but is probably the result of facile rearrangement of allylic peroxyl radicals within the reaction media: independent studies¹⁶ indicate that the *tertiary* hydroperoxide can be readily converted into a mixture of three hydroperoxides under free radical conditions [equation (8): AIBN, deuteriochloroform, 60 °C].



Inspection of the data in Table 2 shows a small but, perhaps systematic, variation in the pattern of reactivity of the different allylic sites in the substrates chosen. The averaged data (excluding the data for Run 4 where some product decomposition can be inferred) are presented in Figure 2 on a *per*-hydrogen atom basis.

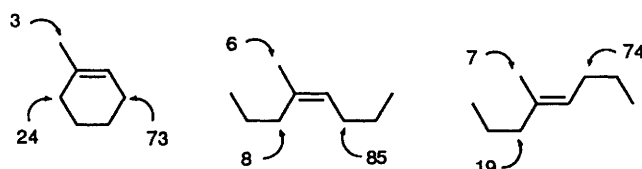


Fig. 2 Per hydrogen atom abstraction ratios for some trisubstituted alkenes in *tert*-butylhydroperoxide-loaded autoxidations

It is instructive to compare the data for these intermolecular abstraction ratios with ratios from ene singlet oxygenations (Figure 3: again on a *per*-hydrogen basis†) where the best

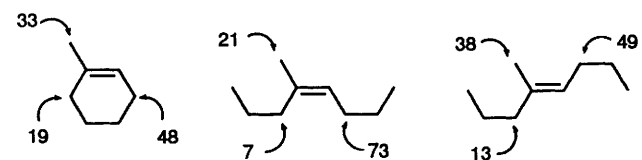


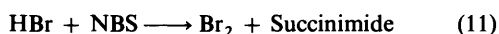
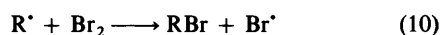
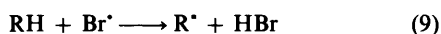
Fig. 3 Per hydrogen atom abstraction ratios for some trisubstituted alkenes in photo-assisted singlet oxygenations (see text for references).

† Abstraction ratios for the 4-methyloct-4-enes are taken from work of Chaineaux and Tanielian, quoted by Golub;¹⁷ our data for reaction of the *cis*-isomer give a slightly different ratio of 80:16:3.

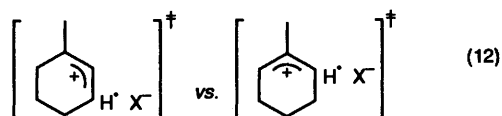
present mechanistic picture is one of *intramolecular* abstraction in a peroxide-type intermediate.

The generalised selectivity for preferential reaction in the latter case at the most highly substituted side of the double bond is emphasised by these data. This generalization had been rationalized¹⁸ on the basis of rotational barriers to abstraction, and calculations on such barriers¹⁹ in the parent alkenes (though *not* in the postulated peroxide intermediates) had been brought forward to support this contention. Though scepticism has recently been cast upon this interpretation,²⁰ it is tempting to speculate that such barriers might also fine tune the ease of abstraction in the *intermolecular* reaction encountered in autoxidation: the similarity in hydroperoxy O–H and allylic C–H bond strengths suggest these to be almost thermonutral reaction steps and as such the Curtin–Hammett principle might again be invoked.

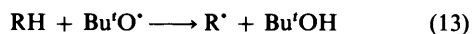
The selectivity in the hydrogen atom abstraction step in these autoxidation studies might briefly be compared with other reactions in which 1-methylcyclohexene undergoes hydrogen atom abstraction. Allylic bromination by NBS is considered²¹ to be a process, whereby a bromine atom/molecule chain reaction is instituted [eqns. (9)–(11)]:



In the reaction of 1-methylcyclohexene, abstraction at the methylene positions again seems preferred while reaction at the methyl group seems essentially non-existent. The reported product ratio (see data in the following paper) indicates that selectivity in the NBS reaction is less than in autoxidation (abstraction ratio *ca* 1:1). This might be a result of the relative electrophilicities of the attacking radicals: a simple transition state analysis which might assist in these considerations is depicted in eqn. (12) and indicates that the oxygen-centred peroxy radicals are showing greater sensitivity to the polar-stabilisation effect than do bromine atoms.



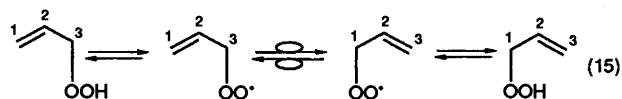
Allylic chlorination by *tert*-butyl hypochlorite appears to proceed by substrate-dependent mechanisms. For mono- and di-alkyl alkenes, Walling and Thaler¹² have indicated that a free radical-mediated reaction occurs [eqns. (13) and (14)]:



For tetra-alkylated alkenes, however, polar mechanisms appear to operate in the apparent absence²² or in the presence of acidic catalysts,²³ and quite stereospecific halogenations can be achieved. As far as we are aware, the mechanistic details concerning the reactions of this reagent with simple trialkylated alkenes have not been defined. Our data for the reaction of 1-methylcyclohexene (see the accompanying paper) accord most closely with a reaction in which a polar process predominates.

Finally we address the question concerning the suppression, or otherwise, of free-radical mediated rearrangement(s) of those hydroperoxides detected in the *tert*-butyl hydroperoxide-loaded autoxidations.

Judged at face value, the fact that, in both the autoinitiated and hydroperoxide-loaded reactions the pairs of isoallylic hydroperoxides are formed in roughly equal amounts in each pair might suggest that dioxygen molecule attachment to the first-formed allylic radicals, being a radical-radical reaction, is rather insensitive to the pattern of substitution around the target allylic radical. However, autoinitiated reactions occur in reaction media in which peroxy radical rearrangements might reasonably be expected to occur, eqn. (15), and the loaded reactions are deliberately designed to run under free-radical containing conditions where, again, rearrangements are possible.



Such rearrangements can be driven almost exclusively to one product or to equilibrating mixtures,²⁴ depending on the pattern of substitution around the allyl moiety, and, in order to discover the equilibrium position for the 1-methylcyclohexene cases, we examined the mixtures produced when solutions containing the ene-hydroperoxides from this alkene were allowed to react over 24 h, under initiated conditions, in the presence or absence of *tert*-butyl hydroperoxide. The resultant data are accumulated in Table 3 (under the conditions chosen, little diversion to other products was seen).

Scrutiny of these data suggests that *tert*-butyl hydroperoxide loading is fairly effective in retarding the equilibration of the *primary/secondary* hydroperoxide isomer pair at ambient temperatures over the time of the loaded autoxidation experiment, but that this control is probably less efficient in the case of the *tertiary/secondary* pair. On balance, then, the data in Table 3 suggest that the allylic radical/oxygen molecule reaction (which is known to be fast) is, in terms of attachment, essentially without discrimination for either end of the accepting allylic radical and, furthermore, that under the loaded conditions, especially at the lowest practical working temperatures, equilibration of the product peroxides is not necessarily complete.

Conclusion.—The proposition that low-temperature, initiated autoxidation of alkenes in the presence of *tert*-butyl hydroperoxide might be a chemoselective route to allylic hydroperoxides has been demonstrated. The method allows the regiochemistry of hydrogen atom abstraction from unsymmetrically substituted alkenes to be measured and a rationale for this regiochemistry on the basis of the stability of the intermediate allylic radicals (perhaps modestly influenced by rotational barriers to their formation) has been advanced. At the lowest practical operating temperatures (*ca.* ambient) the product hydroperoxides seem to bear some relationship to the ratio of initial reaction of the intermediate allylic radicals with oxygen molecules, whilst at only modestly elevated temperatures equilibration of the allylic hydroperoxides *via* allylic peroxy radicals readily occurs.

Experimental

HAZARD NOTE.—Workers new to the manipulation of organic peroxides should read appropriate literature prior to work (texts by Davies,²⁵ Swern and others²⁶ contain useful material). A few relevant points are: (i) avoid contamination with strong acids, metals and their salts, and peroxidizable solvents (especially ethers); (ii) work where possible at ambient

and sub-ambient temperatures and on the minimum practicable scale; and (iii) use substrates and reaction mixtures that contain the minimum levels of 'active oxygen'. Sensible use of safety screens is essential.

General Methods

(a) *Spectroscopic*.—NMR spectra were recorded in deuteriochloroform (with included tetramethylsilane), using a Perkin-Elmer R32 spectrometer (for ^1H NMR spectra at 90 MHz), a Varian VXR-400 spectrometer (for ^1H NMR spectra at 400 MHz, and ^{13}C spectra at 100 MHz) or a General Electric QE300 spectrometer (for ^1H NMR spectra at 300 MHz and ^{13}C NMR spectra at 75 MHz). Chemical shifts are quoted as values in δ p.p.m. downfield from the internal standard; J and w values are in Hz. ^{13}C NMR spectral assignments were aided by acquisition of APT spectra.

(b) *Experimental*.—Oxidation studies were performed using apparatus connected to water-filled gas burettes filled with oxygen. The singlet oxygenations were carried out in a Pyrex, immersion-well reactor in which light from a vertically-mounted high-pressure sodium lamp (Thorn SON-T 400W at 85–95% power output) was filtered through a jacket containing running cold water and passed through a stirred solution of the photolysate under a static oxygen atmosphere.

Kugelrohr distillations were performed using a Büchi GKR-50 apparatus. In those instances where hydroperoxides were being distilled, the apparatus was placed behind a good safety screen and *very careful* attention to temperature control was exercised. The crude hydroperoxides always contained the antioxidant BHT which might be affording protection against free-radical induced (explosive) decomposition: this antioxidant was involatile under the distillation conditions described. Whether or not the BHT was protective in action, this procedure should be approached *with due care* and we recommend that comparable preparations should not be conducted on larger scales than those indicated.

TLC was carried out using aluminium-backed silica gel sheets (Merck 5554) employing dichloromethane as eluant, except where noted. After examination under a short-wave UV lamp (allylic hydroperoxides rarely quenched the fluorescence), the plates were sprayed with either vanillin in concentrated sulfuric acid or phosphomolybdic acid in ethanol (10 or 20 wt%): colour reactions were observed at ambient temperatures or during heating on a hot plate (fume-cupboard). Peroxides were located with the very sensitive ADADH spray (Fluka) described by Buzlanova *et al.*²⁷ The spray solution seems indefinitely stable and gives characteristic pink and brown spots with hydroperoxides at room temperature.

Liquid flash chromatography was carried out using 230–400 mesh silica gel (Merck, Grade 60) using dichloromethane as eluent, which eluent was collected in fractions of *ca.* 25 cm³. Very light sample loadings were found advantageous as, occasionally, was use of a jacketed column operating at *ca.* –10 °C.

(c) *Materials*.—Di-*tert*-butyl peroxyoxalate was prepared on two occasions by the method of Bartlett *et al.*⁹ on the scale described. On the second occasion we experienced a sharp **EXPLOSION** while shaking the solvent-wetted, recrystallized product from one glass vessel to another. This is an extremely friction sensitive material²⁸ and we strongly recommend that it be prepared and handled using good safety screens and personal protection.

Dry *tert*-butyl hydroperoxide was prepared from the commercial material (70% hydroperoxide, 30% water) in the following manner²⁹ Interlox and Aldrich materials are 70%

solutions of the hydroperoxide in water. To Interlox material (350 g) was added saturated brine (100 cm³): after shaking, two layers quickly separated. The lower layer was run off (165 cm³, $\frac{2}{3}$ of the water in the original hydroperoxide). The remaining upper layer was diluted with an equal volume of dichloromethane (300 cm³) and to this solution was added sufficient anhydrous magnesium sulfate to give a discrete white lower aqueous layer. The decanted top layer was dried with fresh anhydrous magnesium sulfate sufficient to give mobile desiccant layers.

(NOTE: a very small sample of the *undiluted*, partly dried, hydroperoxide was treated with magnesium sulfate: a *RISE IN TEMPERATURE* from 22 to 27 °C was noted: *UNDER NO CIRCUMSTANCES* should the *undiluted* material be treated with the desiccant.)

The dry solution was concentrated (**TAKE CARE**) using a rotary evaporator at room temperature and the residue was distilled (**SAFETY SHIELD!**) using a bath *absolutely* no hotter than 70 °C (b.p. 28 °C/8 mm Hg). The purified material was stored in a refrigerator (a freezer might have been better: m.p. 4.2 °C). This material, even at this temperature, undergoes significant deterioration: samples dissolved in benzene over a period of a few weeks gave increasingly cloudy mixtures.

(Z)-4-Methyloct-4-ene. This was prepared from oct-4-yne using the zirconocene dichloride-catalysed addition of trimethylaluminium according to the method described for dec-5-yne by Negishi *et al.*:³⁰ reactions in hot 1,2-dichloroethane (50–70 °C) using neat trimethylaluminium were found most effective. Considerable care should be exercised in the quenching step since copious volumes of methane are released: quenching at low temperature in the manner described for related reactions³¹ might be considered for large-scale reactions. Small-scale reactions (76 mmol alkyne) gave fair yields of distilled alkene (99+ % *cis*; 48% yield; b.p. 134 °C) but, perhaps because of the problems with quenching, larger scale reactions (0.27 mol) resulted in poorer yields. Spectroscopic data are given in the accompanying paper.^{1b}

(E)-4-Methyloct-4-ene. This was prepared by analogy to the method used by Negishi *et al.* for (E)-5-methyldec-5-ene,³⁰ using zirconocene dichloride-catalysed methylaluminiumation of pent-1-yne followed by an iodine quench, to provide (E)-1-iodo-2-methylpent-1-ene (0.27 mol scale; b.p. 65 °C, 12 mmHg; 46% yield) as a rather unstable colourless liquid, characterised by iodine analysis (Found: 58.8 ± 0.8%. Calc.: 60.41%) and by spectroscopy [δ_{H} (400 MHz) δ 5.854 (m, 1 H, 1-H), 2.176 (dt, 2 H, J 1.2, 7.6, 3-H₂), 1.815 (d, 3 H, J 0.8, 2-Me), 1.457 (*ca.* sextet, 2 H, 4-H₂) and 0.875 (t, 3 H, $J_{4,5}$ 7.2, 5-Me); δ_{C} (100 MHz) 147.94 (C-2), 74.51 (C-1), 41.58 (C-3), 20.84 (C-4), 13.51 (C-5) and 23.73 (Me)].

Preparation of the corresponding vinylolithium using metallic lithium under a variety of conditions was unsuccessful: the transmetallation procedure of Seebach³² was eventually found straightforward. Thus, a solid CO₂-cooled, nitrogen-protected and magnetically stirred solution of the vinyl iodide (15.75 g, 0.075 mol) in anhydrous tetrahydrofuran (Aldrich; 75 cm³) was treated with a solution of *tert*-butyllithium in pentane (1.7 mol dm⁻³; 88 cm³, 0.15 mol). The initially pale yellow solution was, in a moderately exothermic reaction (T_{int} to –45 °C), converted into one that was at first colourless and then, by the very end of the addition, to a cloudy, bright yellow mixture. After 1 h, the still cold mixture was treated with 1-iodopropane (molecular sieves dried and nitrogen flushed, 7.3 cm³, 0.075 mol). Unlike an earlier small-scale reaction using diethyl ether as solvent, this addition resulted in a vigorously exothermic reaction (T_{int} –78 to –20 °C) to give a heterogenous mixture that was left to warm to room temperature overnight. The next morning, the mixture was quenched by addition of a little water (the absence of effervescence indicated that complete transmetallation had

occurred). Water washing ($2 \times 200 \text{ cm}^3$), drying (MgSO_4), addition of a little BHT and distillation under nitrogen (4 in. glass helices-packed column) gave, after solvents and a forerun containing a mixture of 1-iodopropane and product had been removed, a clean sample of *trans*-4-methyloct-4-ene (b.p. 125–130 °C; 27% total yield of alkene). Spectroscopic analysis indicated a *trans* alkene content of 97.5+%.

(d) *Initiated Autoxidation of Alkenes in tert-Butyl Hydroperoxide-loaded Solutions.*—The reaction apparatus consisted of a two-necked, 1 dm³ round-bottomed flask immersed in water bath equipped with a Grant FH 15V circulating thermostat. The oxidations were carried out in a dimly illuminated room or with rudimentary shading and the reaction mixtures were unstirred. In the oxygen-flushed flask was placed a solution (250 cm³) comprising benzene, *tert*-butyl hydroperoxide (1.0 mol dm⁻³; 25.0 cm³, 0.25 mol), the substrate alkene (0.1 mol dm⁻³; 25 mmol) and the initiator (*CARE!*) di-*tert*-butyl peroxyoxalate (0.005 mol dm⁻³; 0.29 g, *ca* 10 mol% initiating *tert*-butoxyl radicals). After suitable times, portions were removed and manipulated for analysis (see text). Commonly, at the completion of the oxidation, the bright yellow product solutions were stored in the deep freeze until required.

Thus, for example, a sample of (*Z*)-4-methyloct-4-ene treated on this scale at 60 °C for 1 day absorbed *ca.* 0.5 equiv. of oxygen to give, after removal of volatiles at ambient temperature (by rotary evaporation and then at the oil pump) a crude product which was purified by repetitive flash chromatography. The initial separation (150 g silica gel, dichloromethane eluant) gave two groups of hydroperoxidic fractions: the former group, upon concentration (0.49 g; $R_{f,DCM} = 0.35\text{--}0.22$) represented a 62% isolated yield of converted alkene as products, the latter (0.43 g) was composed of allylic hydroperoxides (**9**, **24** and **25**)* somewhat contaminated with *tert*-butyl hydroperoxide ($R_{f,DCM} = 0.13$; diffuse spot). The former group was rechromatographed in the same manner, but with an initial column temperature of -31 °C, rising to ambient. This gave a trace of α,β -saturated ketone **43** ($R_{f,DCM} = 0.35$; ¹H NMR spectrum as authentic material), then *exo*-methylene hydroperoxide **10** (90 mg, 0.57 mmol, 11% of converted alkene) containing trace amounts of both primary allylic hydroperoxides **23** and **50**. This was followed by an unresolved mixture of hydroperoxides ($R_{f,DCM} = 0.29\text{--}0.28$), followed a discrete mixture of three hydroperoxides **9**, **24** and **25**. The final inseparable mixture ($R_{f,DCM} = 0.26$, 400 mg, 2.5 mmol, isolated) represented a recovery of 50% of the converted alkene.

A comparable reaction, but using 2,2,4-trimethylpentane as solvent and BCHPC as initiator gave, after 1 day, *ca.* 78% conversion (by oxygen uptake). After addition of BHT (*ca.* 0.1 g) the mixture was concentrated by rotary evaporation (ambient temp.; *p*/15 mmHg) to give a colourless liquid (7.41 g) which was subjected to Kugelrohr distillation (*TAKE CARE!*). Operating at *p*/0.02 mmHg, a volatile fraction (5.23 g; condensed in a solid CO₂-cooled trap) was shown by ¹H NMR spectroscopy, to contain unisomerised *cis*-alkene (3.2 mmol, 32% recovered), along with solvents and traces of hydroperoxide scission products. Raising the oven temperature (with care) eventually to 60 °C gave a colourless distillate (1.16 g) which condensed in the ice-cooled receiving bulbs. The alkene-derived product distribution for this distillate determined by ¹H NMR (400 MHz) is given in Table 3 as Run 4, the additional components being BHT and the solvent-derived hydroperoxide [identified by comparison with an independently prepared specimen:³³ 2,4,4-trimethylpentan-2-yl hydroperoxide:

δ_H (300 MHz) 7.41 (br s, 1 H, OOH), 1.596 (s, 2 H, ³CH₂), 1.305 (s, 6 H, 2-Me₂) and 1.017 (s, 9 H, 4-Me₃); δ_C (75 MHz) 84.07 (C-2), 50.36 (C-3), 31.26 (4-Me₃), 31.01 (C-4) and 25.86 (2-Me₂); $R_{f,DCM} = 0.32$. The spectral integral for this distillate and its isolated weight indicates that it contained 64% alkene as product. Chromatographic separation of the materials contained in the pot suggest that it contained mostly initiator-derived alcohols ($R_{f,DCM}$: *cis* = 0.19 and *trans* = 0.11) along, seemingly, with similarly derived dialkyl peroxides ($R_{f,DCM} = 0.79$).

(e) *Hydroperoxide Rearrangements under Free Radical-initiating Conditions.*—A sample of the mixed hydroperoxides from the singlet-oxygenation of 1-methylcyclohexene was purified by Kugelrohr distillation (oven 45–65 °C, *p*/0.04 mmHg) recovery equivalent to 83% starting alkene as hydroperoxide (for further details, see the accompanying paper).

Two benzene solutions (each 125 cm³) were prepared. The first contained the mixed peroxides (0.015 mol dm⁻³) and di-*tert*-butyl peroxyoxalate (0.005 mol dm⁻³). The second contained these reagents along with *tert*-butyl hydroperoxide (1.0 mol dm⁻³). Samples (50 cm³) of each solution were maintained in lightly stoppered flasks (250 cm³ capacity) under oxygen atmospheres for 21 h at the temperatures noted in Table 3 before being manipulated as described in the section on loaded autoxidation (*vide supra*).

Acknowledgements

We are grateful to the staff of the Analytical Group, MRPRA for analytical services. Especial thanks are due to Mr. P. S. Farley of the Chemistry Group, MRPRA for carefully recording highfield NMR spectra using the VXR-400 spectrometer located in the Chemistry Department at University College, London and finally we are grateful to the Director and Board of MRPRA for permission to publish this work.

References

- (a) Preliminary communication: J. L. Courtneidge and M. Bush, *J. Chem. Soc., Chem. Commun.*, 1989, 1227; (b) for supporting synthetic studies, see J. L. Courtneidge, M. Bush and L-S. Loh, following paper.
- (a) *The Chemistry and Physics of Rubber-like Substances*, ed. L. Bateman, McLaren and Sons, London, 1963; (b) *Natural Rubber Science and Technology*, A. D. Roberts, ed. Oxford University Press, Oxford, 1988.
- (a) J. L. Bolland, *Q. Rev.*, 1949, 3, 1; (b) L. Bateman, *Q. Rev.*, 1954, 8, 147.
- (a) R. Criegee, H. Pilz and H. Flygare, *Chem. Ber.*, 1939, 72, 1799; (b) E. H. Farmer and A. Sundralingam, *J. Chem. Soc.*, 1942, 121.
- (a) T. Mill and D. G. Hendry, in *Comprehensive Chemical Kinetics*, eds. C. H. Bamford and C. F. H. Tipper, vol. 16, *Liquid Phase Oxidation*, ch. 1, Elsevier, Amsterdam, 1980; (b) *Autoxidation of Unsaturated Lipids*, ed. H. W.-S. Chan, Academic Press, London, 1987; (c) N. A. Porter, *Acc. Chem. Res.*, 1988, 19, 262.
- A. J. Boon, *J. Nat. Rubber Res.*, 1988, 3, 90.
- See the discussion in R. V. Kucher and V. I. Timokin, *Nefikimiya*, 1986, 26, 736 (*J. Petrol. Chem. USSR*, 1986, 26, 205).
- (a) W. F. Brill, Preprints of the Symposium on Selective Oxidation Processes, *A. C. S. Div. Petrol. Chem.*, Chicago 1964. D-73; (b) *Adv. Chem. Ser.*, 1965, 51, 70.
- P. D. Bartlett, E. P. Benzing and R. E. Pincock, *J. Am. Chem. Soc.*, 1960, 82, 1762.
- See ref. 5a and J. A. Howard in *Advances in Free Radical Chemistry*, vol. IV, ed. G. H. Williams, ch. 2, Logos Press, London, 1972.
- See ref. 5a, part 4.4.
- C. Walling and W. Thaler, *J. Am. Chem. Soc.*, 1961, 83, 3877.
- (a) Product studies: K. Blau, V. Müller, W. Pritzkow, W. Schmidt-Renner and Z. Sedshaw, *J. Prakt. Chem.*, 1980, 322, 915; (b) Kinetics: E. Lawson, W. Pritzkow and V. Voerckel, *J. Prakt. Chem.*, 1983, 325, 543.

* Structural numbers relate to the structural diagrams given in the following paper.

- 14 (a) M. R. Musaev and A. S. Safarov, *Dokl. Akad. Nauk Az. SSR*, 1978, **34**, 45; (b) M. R. Musaev, Kh. M. Alimardanov and A. A. Medzhidor, *Azerb. Khim. Zh.*, 1980, 40; (c) M. R. Musaev, A. S. Safarov, G. A. Azizova and F. A. Alimirzoev, *Azerb. Khim. Zh.*, 1981, 94; (d) R. M. Azhikova and A. M. Syroezhko, *Zh. Prikl. Khim. (Leningrad)*, 1985, **58**, 2304.
- 15 J. L. Bolland, *Trans. Faraday Soc.*, 1950, **46**, 358 and also see ref. 26.
- 16 J. L. Courtneidge and P. S. Farley, unpublished results.
- 17 M. A. Golub, *Pure Appl. Chem.*, 1980, **52**, 305.
- 18 K. H. Schulte-Elte and V. Rautenstrauch, *J. Am. Chem. Soc.*, 1980, **102**, 1938 and references cited therein.
- 19 K. N. Houk, J. C. Williams, Jr., P. A. Mitchell and K. Yamaguchi, *J. Am. Chem. Soc.*, 1981, **103**, 949.
- 20 M. Orfanopoulos, M. Stratakis and Y. Elmes, *J. Am. Chem. Soc.*, 1991, **113**, 3180.
- 21 See P. Kaushal and B. P. Roberts, *J. Chem. Soc., Perkin Trans. 2*, 1989, 1559 and references therein.
- 22 E. W. Meijer, R. M. Kellogg and H. Wynberg, *J. Org. Chem.*, 1982, **47**, 2005.
- 23 (a) L. W. Hertel and L. A. Paquette, *J. Am. Chem. Soc.*, 1979, **101**, 7620; (b) W. Sato, N. Ikeda and H. Yamamoto, *Chem. Lett.*, 1982, 141; (c) L. Novak, L. Poppe, C. Szantay and E. Szabo, *Synthesis*, 1985, 939.
- 24 H.-S. Dang, A. G. Davies, I. G. E. Davison and C. H. Schiesser, *J. Org. Chem.*, 1990, **55**, 1432.
- 25 A. G. Dzviets *Organic Peroxides*, Butterworths, London, 1961.
- 26 *Organic Peroxides*, D. Swern, vols. I-III, Wiley-Interscience, New York, 1971.
- 27 (a) M. M. Buzlanova, V. F. Stepanovskaya and V. L. Antonovskii, *J. Anal. Chem. USSR (Eng. Transl.)*, 1966, **21**, 1324; (b) M. M. Buzlanova, V. F. Stepanovskaya, A. F. Nesterov and V. L. Antonovskii, *J. Anal. Chem. USSR (Engl. Transl.)*, 1966, **21**, 454.
- 28 A. G. Davies, University College London, personal communication.
- 29 Adapted from A. J. Bloodworth and J. L. Courtneidge, *J. Chem. Soc., Perkin Trans. 1*, 1981, 3258.
- 30 D. E. Van Horn and E.-i. Negishi, *J. Am. Chem. Soc.*, 1978, **100**, 2252.
- 31 W. Nagata, M. Yoshioka and M. Murakami, *Org. Synth.*, 1972, **52**, 96.
- 32 D. Seebach and H. Neumann, *Chem. Ber.*, 1974, **107**, 847.
- 33 (a) J. Hoffman, *Org. Synth.*, 1960, **40**, 76; (b) C. Walling and A. A. Zavitsas, *J. Am. Chem. Soc.*, 1963, **85**, 2084.

Paper 2/01111E

Received 2nd March 1992

Accepted 10th March 1992