The autoxidation of aliphatic esters. Part 2.[1] The autoxidation of neopentyl esters †

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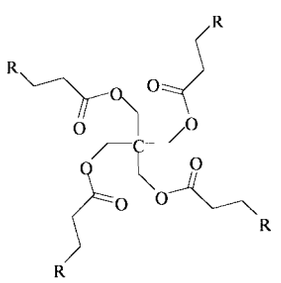
The autoxidation of six esters, neopentyl butanoate, 2,2-dimethylpropanoate, 3,3-dimethylbutanoate, 2,2-dimethylbutanoate, 2-methylbutanoate and 1,1-[$^2H_2$]-neopentyl butanoate, has been studied at 438 K. The reaction products were determined for each system and key reactions leading to the formation and further reactions of the primary products have been identified.

Primary products include a range of hydroperoxides which lead to the formation of keto- and hydroxy-esters. Large amounts of neopentanol and the parent carboxylic acid are formed from each ester. It is shown that these are principally oxidation, and not hydrolysis, products.

The relative rates of autoxidation of the first five esters mirror the relative rates of attack that occur on reaction with alkoxyl radicals; the sites of attack are on both the alkyl and acyl groups, with the α-alkyl hydrogen atoms on the ester showing particular vulnerability compared to the acyl hydrogen atoms. The analysis of products from the deuterated ester supports this conclusion.

Introduction

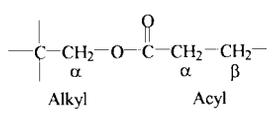
With modern engines being designed to operate at high temperatures, there is an increasing demand to improve the thermo-oxidative stability of lubricants. There are several synthetic base fluids which are being increasingly used. Among these are the polyol esters which have good viscometric, biodegradability and lubricity properties; furthermore they are relatively involatile and also have good thermal, oxidative and hydrolytic stabilities.[2] The polyol esters account for nearly one-fifth of the synthetic lubricants now produced and the pentaerythrityl esters are amongst the most important of this class of ester (Scheme 1).[3]



Scheme 1 Pentaerythrityl ester.

To understand how to improve further their resistance to autoxidation, it is clear that a thorough fundamental understanding of the oxidation of the polyol esters is needed. However, this is yet to be achieved and there is even controversy about the autoxidation of simple esters where published studies disagree about such crucial evidence as the point of initial attack.[4]

In the previous paper in this series, it was shown that the initial attack of alkoxyl radicals on some simple neopentyl carboxylate esters occurs both on the acyl and alkyl groups (Scheme 2).[1] For example, with neopentyl butanoate, there is

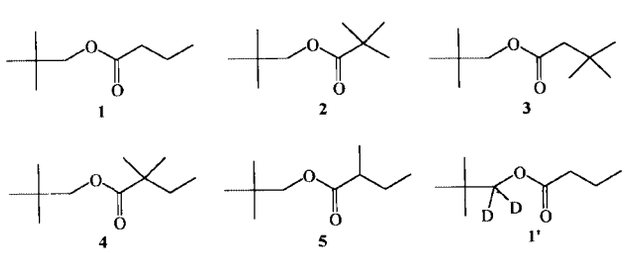


Scheme 2 Notation to identify C–H bonds in ester.

clear evidence that initial attack is at the α-alkyl, α-acyl and β-acyl positions as well as at the primary C–H bonds. That all these positions are attacked by alkoxyl radicals is supported, independently, by EPR studies of Gilbert and coworkers.[5]

Alkoxyl radicals play a very important part in the autoxidation of esters, albeit subsequent to the formation of the initial peroxyl radicals. Thus, using these data and by studying the autoxidation of some simple esters, it should be possible to determine more clearly the initial point(s) of attack in the early stages of reaction.

This paper is concerned with the latter experiments, namely the autoxidation of six esters (**1**–**5** and **1′**). Neopentyl esters were chosen for the study as the neopentyl group models the alkyl core of the pentaerythrityl esters, having no hydrogen atoms on the β-carbon and two secondary hydrogens on the α-carbon. The acids which were chosen for the acyl moiety allowed for comparison of various α-, β- and γ-C–H sites on oxidation.



Considering the acyl portion of the esters, **1** has *sec*-hydrogen atoms at the α- and β-positions; **2** has no *sec*-hydrogen atoms; **3** has only *sec*-hydrogen atoms at the α-position; **4** has only

† Tables A–H, containing data on the autoxidation of compounds **1**–**5** and **1′**, are available as supplementary data. For direct electronic access see http://www.rsc.org/suppdata/p2/b0/b004589f/.

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Table 1 The autoxidation of neopentyl butanoate (**1**), 2,2-dimethylpropanoate (**2**), 3,3-dimethylbutanoate (**3**), 2,2-dimethylbutanoate (**4**), 2-methylbutanoate (**5**) and 1,1-[$^2H_2$]-butanoate (**1′**): 1.5 cm^3, ester; 5 bar, oxygen; 438 K

	Yields/10^{-2} mol dm^{-3}											
Substrate	**1**		**2**		**3**		**4**		**5**		**1′**	
Reaction time/min	60		240		180		150		60		60	
Δ[Substrate][a]	10.1		10.9		11.8		17.6		27.7		[d]	
Products	A[b]	B[c]	A[b]	B[c]	A[b]	B[c]	A[b]	B[c]	A[b]	B[c]	A[b]	B[c]
Carbon monoxide	[d]	[d]	1.73	[d]	2.33	[d]	[d]	[d]	5.00	[d]	[d]	[d]
Carbon dioxide	0.09	[d]	0.26	[d]	0.64	[d]	1.10	[d]	2.09	[d]	0.77	[d]
Formaldehyde	0.04	[d]	0.06	[d]	0.05	[d]	0.02	[d]	0.01	[d]	—[e]	—
Acetone	0.37	0.38	1.77	1.66	2.89	2.70	3.46	3.29	4.90	4.47	2.08	2.01
Butanone	—	—	—	—	—	—	0.38	0.42	8.25	8.21	—	—
3-Methylbutan-2-one	—	—	—	—	—	—	1.03	1.04	—	—	—	—
tert-Butyl hydroperoxide	0.08	—	0.09	—	0.12	—	—	—	0.12	—	—	—
2-Methylpropan-2-ol	0.15	0.24	0.78	0.84	1.69	1.77	—	—	1.84	2.22	0.47	0.48
tert-Butyl formate	0.06	0.06	0.15	0.14	0.27	0.26	—	—	—	—	0.04	0.04
Neopentanol	0.53	0.52	0.26	0.26	0.76	0.76	—	—	3.37	3.34	1.89	1.94
Neopentyl formate	0.02	0.02	—	—	0.28	0.28	—	—	0.19	0.19	0.14	0.14
Neopentyl acetate	—	—	—	—	—	—	—	—	—	—	0.10	0.10
2,2-Dimethylpropanal	—	0.18	—	—	—	0.08	—	0.15	0.17	1.69	0.23	0.24
2,2-Dimethylpropanoic acid	0.02	0.03	2.87	3.10	0.38	0.38	0.57	0.63	1.71	1.82	0.03	0.03
Acetic acid	—	—	—	—	—	—	1.91	1.99	4.44	5.16	0.83	1.01
Propanoic acid	0.03	0.02	—	—	—	—	—	—	—	—	0.37	0.39
Butanoic acid	0.24	0.30	—	—	—	—	—	—	[d]	[d]	1.27	1.37
2-Methylbutanoic acid	—	—	—	—	—	—	—	—	5.15	5.31	—	—
3,3-Dimethylbutanoic acid	—	—	—	—	3.92	4.13	—	—	—	—	—	—
2,2-Dimethylbutanoic acid	—	—	—	—	—	—	3.71	3.86	—	—	—	—
e	0.12	0.29	0.13	0.17	0.10	0.14	—	—	3.44	4.04	0.50	0.55
f	0.25	0.09	—	—	0.33	0.31	—	—	3.61	3.61	0.77	0.77
h	0.28	0.53	—	—	0.18	0.21	0.25	0.29	—	—	1.70	1.80
i	[d]	—	—	—	—	—	0.83	0.80	—	—	0.22	0.21
l	—	—	—	—	0.32	0.35	—	—	—	—	0.20	0.23
n	0.04	0.08	—	—	0.08	0.15	0.49	0.67	—	—	0.52	0.53
r	0.01	0.03	0.03	0.07	0.07	0.11	0.15	0.20	—	—	0.11	0.13
t	0.06	0.10	0.16	0.22	0.27	0.34	0.28	0.43	0.37	0.44	0.36	0.41
Peroxides[f]	0.87	—	0.47	—	0.82	—	1.14	—	1.13	—	0.16	—

[a] Conversion of the substrate: $[Substrate]_0$ = 5.30 mol dm^{-3} (**1**), (**1′**); 4.59 mol dm^{-3} (**2**); 4.20 mol dm^{-3} (**3**), (**4**); 5.39 mol dm^{-3} (**5**). [b] Yield before triphenylphosphine reduction. [c] Yield after triphenylphosphine reduction. [d] Not determined. [e] Not found. [f] Total yield of hydroperoxides, peracids and hydrogen peroxide.

sec-hydrogen atoms at the β-position; and **5** has a *tert*-hydrogen at the α-position and *sec*-hydrogens at the β-position. Thus differences in reactivities towards autoxidation can be used to pinpoint initial positions of attack.

From the distributions of the molecular products from the autoxidation of these esters and their dependence on time, mechanisms of the reactions are proposed, and to test specific crucial aspects of these mechanisms, other experiments have been carried out. For example, the autoxidation of 1,1-[$^2H_2$]-neopentyl butanoate (**1′**) has been examined to elucidate further the reactions at the α-carbon of the alkyl group.

Results

(a) The autoxidation of the neopentyl esters

The autoxidation of six esters, neopentyl butanoate (**1**), 2,2-dimethylpropanoate (**2**), 3,3-dimethylbutanoate (**3**), 2,2-dimethylbutanoate (**4**), neopentyl 2-methylbutanoate (**5**) and 1,1-[$^2H_2$]-neopentyl butanoate (**1′**), has been studied at 438 K in the same steel autoclave. In a separate series of experiments, it was shown that the rate of reaction and the product distribution are little changed in a glass (Pyrex) vessel.

Table 1 gives examples of results obtained from the six esters. A more comprehensive set of results can be found in the supplementary data (Tables A–E). The results show product analyses prior to and following treatment with triphenylphosphine which enables the concentrations of hydroperoxides to be determined. The total *minimum* yield of hydroperoxides from each ester is given by the sum of the increases in the yields of the alcohols and that of 2,2-dimethylpropanal following triphenylphosphine treatment. Comparison of these yields and the total yield of hydroperoxides, peracids and hydrogen peroxide from the autoxidation of the neopentyl esters (measured by iodometric titration) (Table 2) indicates that the hydroperoxides are the dominant type of peroxide in these reactions and therefore peracids and hydrogen peroxide must be minor components. Furthermore, it is likely that even in the later stages of the autoxidation, the hydroperoxides are still the principal peroxides formed.

In the early stages of reaction, other main liquid phase products are the parent carboxylic acid and acetone. Neopentanol is also a major product formed in the initial stages of the autoxidation of **1**, **4** and **5** whereas with **2** it is insignificant and with **3** there is more 2-methylpropan-2-ol than neopentanol (Table 1). Another major product only detected with **5** is acetic acid.

Longer reaction times lead to the build-up of hydroxy- and keto-esters and to their oxidation/degradation products for all the esters.

Trace quantities of low molecular weight alkanes (methane, ethane, propane and 2-methylpropane) and alkenes (ethene, propene and 2-methylpropene) are also formed.

(b) Other experiments

(i) Test for hydrolysis of neopentyl butanoate (1). The ester was heated in the autoclave at 438 K with and without added

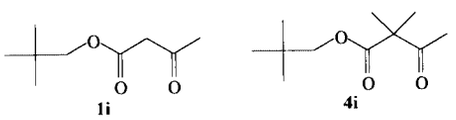
Table 2 The autoxidation of neopentyl esters: yields of hydroperoxides and total yields of hydroperoxides, peracids and hydrogen peroxide: 1.5 cm^3, ester; 5 bar, oxygen; 438 K

		Yields/10^{-2} mol dm^{-3}							
Neopentyl ester	Time/min	60	75	90	120	150	180	210	240
Butanoate (**1**)	Hydroperoxides[a]	0.79	1.62	2.35	1.10	—	—	—	—
	Total peroxides[b]	0.87	2.06	2.60	1.41	—	—	—	—
2,2-Dimethylpropanoate (**2**)	Hydroperoxides[a]	—	—	—	0.18	—	0.26	—	0.19
	Total peroxides[b]	—	—	—	0.24	—	0.31	—	0.47
3,3-Dimethylbutanoate (**3**)	Hydroperoxides[a]	—	—	—	0.53	0.52	0.48	0.44	—
	Total peroxides[b]	—	—	—	0.65	0.77	0.82	0.69	—
2,2-Dimethylbutanoate (**4**)	Hydroperoxides[a]	—	—	0.48	0.69	0.83	1.00	—	—
	Total peroxides[b]	—	—	1.06	1.04	1.14	1.36	—	—

[a] Determined by the triphenylphosphine method. [b] Determined by iodometric titration.

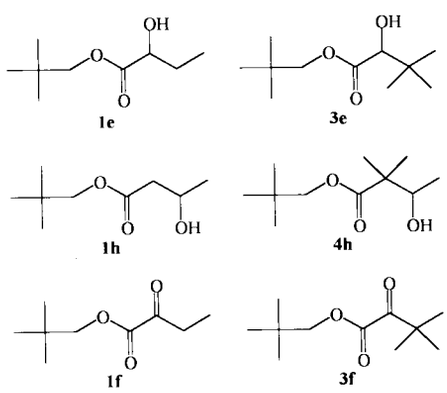
water and formic acid (to simulate the acidic conditions during the autoxidation of the ester) under nitrogen for an hour. The amounts added were equal to those formed from the esters under the same conditions. Products from hydrolysis of the ester could not be detected.

(ii) Decomposition of ester derivatives at elevated temperatures. Neopentyl 3-oxobutanoate (**1i**) and neopentyl 2,2-dimethyl-3-oxobutanoate (**4i**) were heated in the reactor under nitrogen for 1 h at 438 K with and without water and an acid (again to simulate conditions during autoxidation of the esters). The former substrate yielded acetone and neopentanol in high yields, together with carbon dioxide, whereas the latter was stable under these conditions.



1i **4i**

Similar experiments were carried out with neopentyl 2-hydroxybutanoates (**1e** and **3e**), neopentyl 3-hydroxybutanoates (**1h** and **4h**) and neopentyl 2-oxobutanoates (**1f** and **3f**). All these compounds were stable to hydrolysis and thermal decomposition, under the conditions used in the autoxidation of the esters.



1e **3e** **1h** **4h** **1f** **3f**

Discussion

(a) Introduction

The aim of this study was to monitor the *initial* stages of the autoxidation of the neopentyl ester substrates. The acyl moieties, butanoyl (**1**), 2,2-dimethylpropanoyl (**2**), 3,3-dimethylbutanoyl (**3**), 2,2-dimethylbutanoyl (**4**) and 2-methylbutanoyl (**5**), were chosen to investigate the influence of selectively blocking the oxidative attack at the α- (**2** and **4**) and β- (**3**) acyl positions and of directing the attack to the α-acyl position (**5**). A library of authentic oxidation products was prepared and a simple GC protocol was developed to analyse the products, including the hydroperoxide intermediates (see Experimental). The results from these analyses allow us to suggest mechanisms for the autoxidations and to draw conclusions about the initial sites of oxidative attack.

In general, the results suggest that the mechanism of autoxidation of the neopentyl esters bears a strong resemblance to that of alkanes and that the fates of the radical intermediates and molecular products are similar for the two classes of compound. For example, hydroperoxides are formed early in the reaction, and high yields of oxygenated products corresponding to carbonyl compounds and acids, formed during the oxidation of alkanes, were also observed.

The autoxidation of neopentyl butanoate (**1**) will be discussed first and then compared with the reactions of the other esters studied, **2**–**5** and **1′**. The key reactions leading to the formation of the ester hydroperoxides are discussed, followed by their reactions, in particular their decomposition to alkoxyl radicals. Product analyses show that there are several such species formed early in the reaction and these are examined in turn. Amongst the most important products are the hydroxy- and keto-esters and their reactions are discussed subsequently.

(b) The oxidation of neopentyl butanoate (1)

(i) Formation and reactions of esterperoxyl radicals. The high yields of hydroperoxides detected early in the reaction (supplementary data, Table G) indicate that, by analogy with the oxidation of alkanes, ester and esterperoxyl radicals are chain carriers in the early stages of the reaction and the main reactions can be described by Reactions (1)–(4). Five isomeric

$$RH + O_2 \longrightarrow R^{\bullet} + HO_2^{\bullet} \quad (1)$$

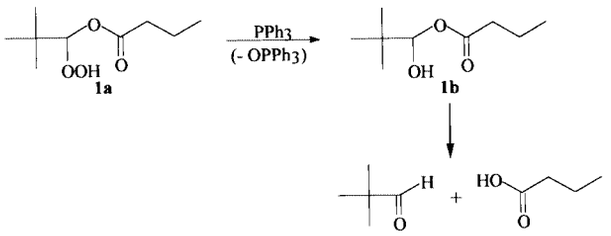
$$R^{\bullet} + O_2 \longrightarrow RO_2^{\bullet} \quad (2)$$

$$RO_2^{\bullet} + RH \longrightarrow RO_2H + R^{\bullet} \quad (3)$$

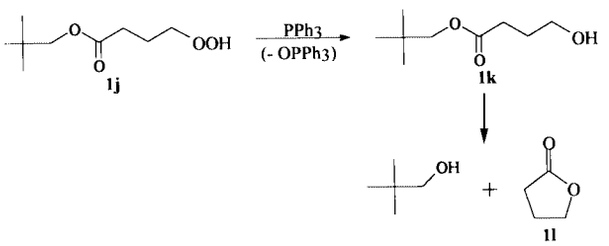
$$2RO_2^{\bullet} \longrightarrow \text{Molecular products} \quad (4)$$

hydroperoxides are formed early in the reaction revealing that the oxidation involves all types of C–H bonds in the ester (Table 1). Thus the oxidation of **1** gives three secondary, (**1a**, **1d** and **1g**) and two primary (**1j** and **1q**) hydroperoxides which after reduction with triphenylphosphine lead to an increase in the yields of 2,2-dimethylpropanal (Scheme 3), hydroxyesters **1e**, **1h** and **1r** and the γ-lactone **1l** (Scheme 4), respectively.

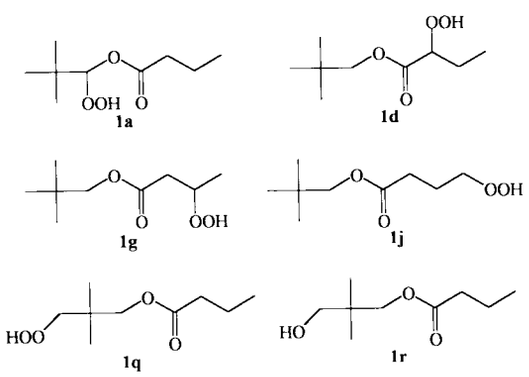
Apart from hydrogen atom abstraction to form hydroperoxides, esterperoxyl radicals can also combine to give tetroxides [Reaction (5)] which, as in hydrocarbon autoxidation, will react further to give the corresponding alcohols and carbonyl compounds [Reaction (6)] or alkoxyl radicals [Reaction (7)]. Presumably the relative rates of the two decomposition reactions of the tetroxide[6] will depend on the structure of R and the



Scheme 3 The products formed on reaction of the hydroperoxide, **1a**, with triphenylphosphine.



Scheme 4 The products formed on reaction of the hydroperoxide, **1j**, with triphenylphosphine.



$$2RO_2^{\bullet} \rightleftharpoons [RO_4R] \quad (5)$$

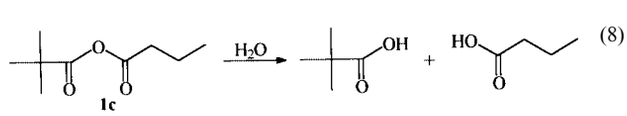
$$RO_4R \longrightarrow ROH + R'R''CO + O_2 \quad (6)$$

$$RO_4R \longrightarrow 2RO^{\bullet} + O_2 \quad (7)$$

temperature. A large array of products is possible, even in the earliest stages, given that there are five different esterperoxyl radicals in the system, and these can self- and cross-react.

Examples of products from these reactions include the alcohols **1b**, **1e**, **1h**, **1k** and **1r**. **1b** and **1k** are not observed since the former decomposes readily to 2,2-dimethylpropanal and butanoic acid (Scheme 3) and the latter rapidly cyclises to the γ-lactone **1l** (Scheme 4) under the reaction conditions.

The alcohols, formed early in the reaction, are matched by carbonyl compounds. For example, the observed ketones **1f** and **1i** correspond to the alcohols **1e** and **1h** respectively, and the anhydride **1c** which decomposes to 2,2-dimethylpropanoic and butanoic acids corresponds to **1b** [Reaction (8)].



The carbonyl products corresponding to **1k** and **1r** are aldehydes. Their fate is being investigated.

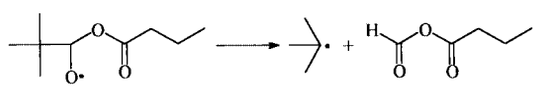
(ii) Reactions of alkoxyl radicals. Alkoxyl radicals are produced by a variety of reactions including those summarised by Reaction (7) and by the decomposition of hydroperoxides. They can abstract hydrogen atoms from the ester substrate [Reaction (9)] or from hydroperoxides [Reaction (10)] to form the same

$$R'O^{\bullet} + RH \longrightarrow R'HO + R^{\bullet} \quad (9)$$

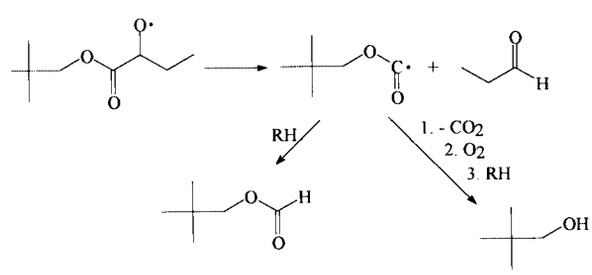
$$R'O^{\bullet} + R''O_2H \longrightarrow R'OH + R''O_2^{\bullet} \quad (10)$$

alcohols, the latter reaction becoming relatively more important as the reaction proceeds. In competition with these reactions, the alkoxyl radicals also undergo β-scission.[7]

Three types of secondary alkoxyl radicals are intermediates in the autoxidation of neopentyl butanoate. The α-alkylalkoxyl radical preferentially[8] undergoes carbon–carbon bond cleavage to produce the *tert*-butyl radical and a mixed anhydride by Reaction (11). The anhydride is hydrolysed by water or reacts with alcohols to give an ester and a carboxylic acid and would provide an alternative route to neopentyl formate to that discussed later.

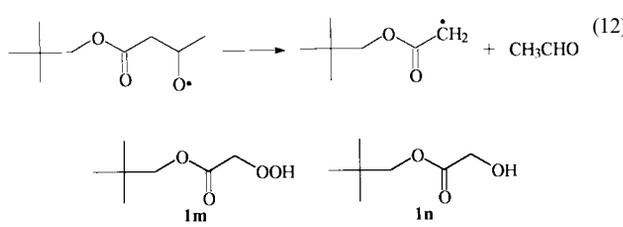


The major route for fragmentation of the α-acylalkoxyl radical will be to form the neopentoxycarbonyl fragment and propanal (Scheme 5) and that for the β-acylalkoxyl radical



Scheme 5 The formation of neopentanol from the fragmentation of the α-acyloxyl radical of **1**.

(based on the pattern of behaviour of simpler alkoxyl radicals[7]) is to react to form the resonance stabilised neopentyloxycarbonylmethyl radical [Reaction (12)]. The formation of this radical would lead to the hydroperoxide **1m** and alcohol **1n**, which are indeed observed.



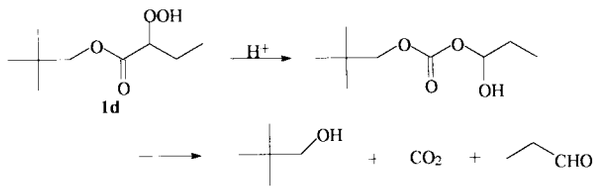
(iii) Reactions of ester hydroperoxides. The hydroperoxides under the reaction conditions are thermally decomposed by both homolytic and heterolytic cleavage of the O–O bond. Radical pathways give alkoxyl radicals which react as described above.

A major non-radical decomposition pathway involves elimination of water, primary and secondary hydroperoxides yielding aldehydes and ketones respectively. Also, by analogy with the established mechanisms for the reactions of 2- and 3-hydroperoxyketones in the autoxidation of ketones,[9,10] the 2-hydroperoxyester (**1d**) would be expected to rearrange and decompose as shown in Scheme 6 to give the observed products, carbon dioxide and propanal (Table 1). The 3-hydroperoxyester, **1g**, would give neopentanol, acetone and carbon dioxide (Scheme 7), all of which are observed products from the autoxidation of **1**.

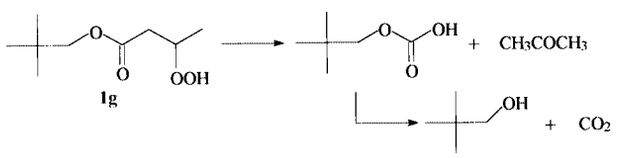
A further important reaction of hydroperoxides, discussed above, involves hydrogen atom abstraction by alkoxyl radicals [Reaction (10)].

Table 3 Yields of **1e** and **1f** (mol $dm^{-3} \times 10^{-4}$) from the autoxidation of neopentyl butanoate (**1**): 1.5 cm^3, ester; 5 bar, oxygen; 438 K

	60 min	75 min	90 min	120 min
1e	0.12	0.41	0.63	0.96
1f	0.09	0.47	0.88	1.50



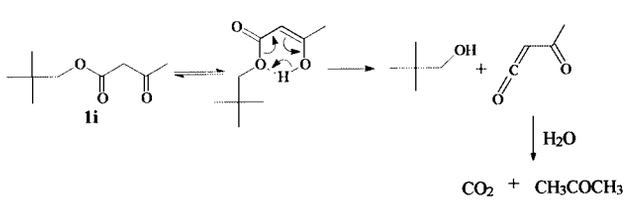
Scheme 6 The non-radical decomposition of 2-hydroperoxy ester, **1d**.



Scheme 7 The non-radical decomposition of 3-hydroperoxy ester, **1g**.

(iv) Thermal stability of hydroxy- and keto-esters and the decomposition of neopentyl 3-oxobutanoate (1i). The hydroxy- and keto-esters, formed in the reactions described above, are significant products from the autoxidation of neopentyl butanoate. For example, the yields of the hydroxy- and keto-esters (**1e** and **1f**), formed by reactions at the α-acyl position, are comparable, with the ketone being favoured in the later stages of the reaction (Table 3).

It is not possible to look in such a detailed way at other pairs of hydroxy- and keto-esters as they undergo further reactions rapidly under the conditions of the experiments, as described above. However, the very low yield of **1i**, compared with the alcohol, **1h**, is worth exploring further. Neopentyl 3-oxobutanoate (**1i**) on heating in the absence of oxygen decomposes to neopentanol, carbon dioxide and acetone, suggesting that the decarboxylation occurs directly from **1i**, probably *via* its enol tautomer,[11] rather than by hydrolysis followed by decarboxylation of the 3-keto acid (Scheme 8). Consequently in the



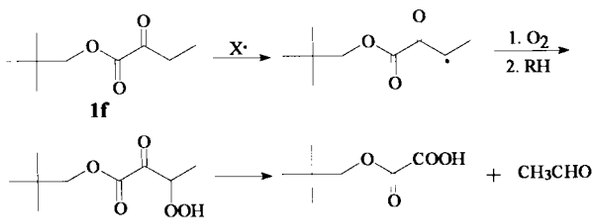
Scheme 8 The thermolysis of the β-keto ester, **1i**.

autoxidation of **1**, the low yield of **1i** arises from the latter's decomposition to give neopentanol and acetone in equal amounts. Further support for this conclusion comes from the oxidation of ester **4** (see below).

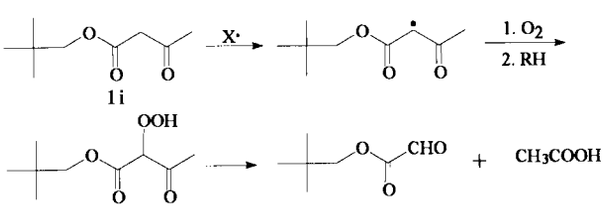
The observed thermal stability of the 2- and 3-hydroxy derivatives of **1** shows that it is unlikely that these products decompose further in the autoxidation without the involvement of oxygen (the latter is discussed in the next section).

(v) Autoxidation of hydroxy- and keto-esters. Studies on the autoxidation of simple alcohols and ketones indicate that oxidation involves cleavage of the α-C–H bonds.[9] This occurs more readily than the autoxidation of a typical C–H bond in alkanes because the bond dissociation energies (BDE) of the former are lower [BDE (kJ mol^{-1}): H–$CH(CH_3)OH$ = 401,[12] H–$CH(CH_3)COCH_3$ = 386[13] and H–$CH(CH_3)_2$ = 409].[14] Aliphatic esters have also been shown to be more stable to radical oxidation than ketones in a recent EPR study using *tert*-butoxyl radicals.[15] Thus, it is likely that keto- and hydroxy-ester products will be oxidised faster than the substrate esters. Furthermore, it is likely that the hydroxy-esters are oxidised in a similar way to alcohols. Scheme 9 illustrates one such mechanism based on the oxidation of alcohols above 373 K.

Schemes 10 and 11, which are based on the established autoxidation mechanism of ketones at temperatures >373 K [9,10] show how the 2- and 3-keto-esters may be autoxidised, where X is an oxygenated radical such as hydroxyl or alkoxyl.



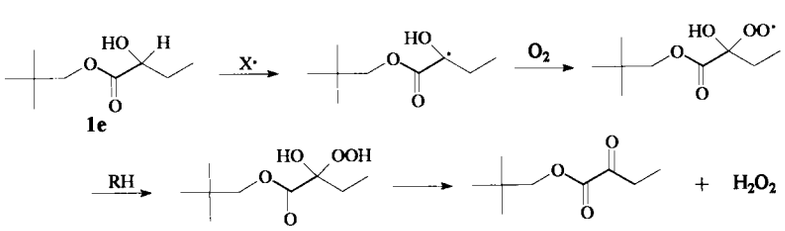
Scheme 10 The proposed mechanism for the autoxidation of neopentyl 2-oxobutanoate, **1f**.



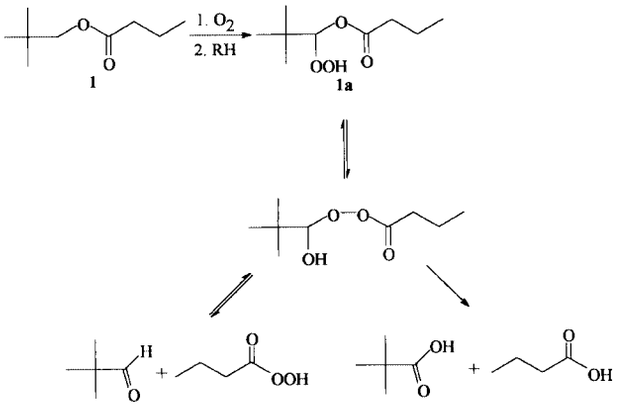
Scheme 11 The proposed mechanism for the autoxidation of neopentyl 3-oxobutanoate, **1i**.

(vi) Formation of neopentanol and butanoic acid. A potential route to butanoic acid and neopentanol, two major products in the autoxidation of neopentyl butanoate, is by hydrolysis of **1**. To test this hypothesis, water and formic acid were added to **1** in amounts equal to the yield from neopentanol from the autoxidation of **1**. Under nitrogen, no hydrolysis was detectable with added water or with water and formic acid from which it is apparent that the alcohol and acid must arise from an oxidative rather than a hydrolytic pathway.

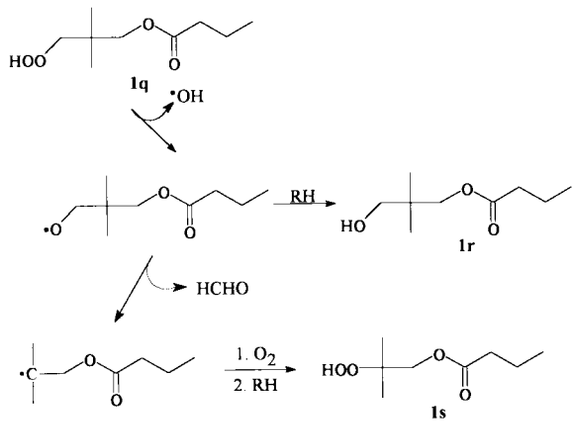
Oxidation of the α-carbon of the alkyl group, suggested previously by Novozhilova *et al.* to explain the formation of acetic acid in the autoxidation of pentyl acetate,[16,17] is a likely route to butanoic acid. Their mechanism (applied to ester **1** in Scheme 12) has also been used to account for the formation of carboxylic acids from the autoxidation of pentaerythrityl esters.[18,19]



Scheme 9 The proposed mechanism for the autoxidation of neopentyl 2-hydroxybutanoate, **1e**.



Scheme 12 An oxidative mechanism for the formation of butanoic acid from neopentyl butanoate, **1**.

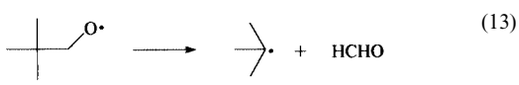


Scheme 13 Decomposition mechanism of 3-hydroperoxy-2,2-dimethylpropyl butanoate, **1q**.

An alternative route to butanoic acid that has been discussed above and also involves α-alkyl oxidation is the decomposition of the α-hydroxyalkyl ester **1b** (Scheme 3), the latter being formed from the corresponding alkoxyl or peroxyl radical.

There are also autoxidation routes leading to neopentanol. Non-radical pathways from the α- and β-hydroperoxy esters can, as discussed above, result in the formation of the alcohol (for example, Schemes 6 and 7). Other non-radical routes to neopentanol, discussed above, are the lactonisation of neopentyl 4-hydroxybutanoate (**1k**) (Scheme 4) and the decomposition of neopentyl 3-oxobutanoate (**1i**) (Scheme 8). However, radical pathways to neopentanol are also possible. Itoh *et al.*[20] reported that methanol and ethanol are major products from the autoxidation of methyl and ethyl 2-methylpropanoate, respectively. Based on their mechanism, neopentanol would arise from fragmentation of the ester α-acyloxyl radical to give the alkoxycarbonyl radical which in turn decarboxylates to the neopentyl radical. This is subsequently oxidised *via* the neopentoxyl radical to neopentanol (Scheme 5). In agreement with this mechanism, the alkoxycarbonyl radical, which is long lived enough to abstract a hydrogen atom, would give the observed product, neopentyl formate.

However, Itoh's mechanism, which involves hydrogen abstraction by the neopentoxyl radical, is unlikely to be a major route to neopentanol since the dominant pathway for this radical will be the very rapid fragmentation to the *tert*-butyl radical and formaldehyde [Reaction (13)].[21]



(13)

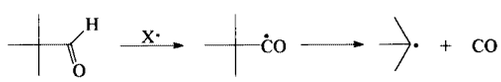
(vii) Reactions arising from oxidation of primary C–H bonds. The discussion so far has been concerned principally with the oxidation of the ester **1** *via* initial attack at the three different CH_2 centres. Although primary C–H bonds are significantly less reactive than secondary C–H bonds, neopentyl butanoate nevertheless contains twice as many primary as secondary hydrogens and products from their reactions are observed in these autoxidations.

As has been described, hydroperoxide **1j** is formed and the concentration of lactone, **1l**, which is produced from the corresponding alcohol, **1k**, builds up during the reaction (supplementary data, Table A). The hydroperoxide **1q** is also formed as is the corresponding alcohol, **1r**.

Further reactions of the hydroperoxide **1q** lead to the removal of one carbon atom from the tertiary centre, to form, eventually, the hydroperoxide **1s** (Scheme 13). **1s**, in turn, will react to form the corresponding alcohol **1t**.

(viii) Formation of acetone and 2-methylpropan-2-ol. A major source of acetone and 2-methylpropan-2-ol, which are formed in high yields throughout the autoxidation of **1**, is oxidation of the *tert*-butyl radical,[22] which, in turn, can only come from the neopentyl group.

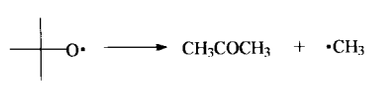
There are three potential routes to the *tert*-butyl radical. One is by radical oxidation and decarbonylation of 2,2-dimethylpropanal (Scheme 14).[23] The others have been discussed above



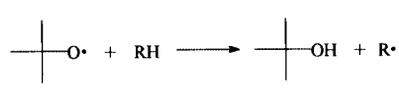
Scheme 14 Formation of *tert*-butyl radicals from 2,2-dimethylpropanal.

and involve fragmentation of (a) the α-alkylalkoxyl ester radical (from α-alkyl oxidation) [Reaction (11)] which competes with hydrogen atom abstraction [Reactions (9) and (10)] and (b) the neopentoxyl radical [Reaction (13)].

The *tert*-butyl radicals are oxidised very rapidly, *via tert*-butylperoxyl, to *tert*-butoxyl radicals, which under the conditions of the experiments, both fragment and abstract hydrogen atoms from hydroperoxides and the ester substrate [Reactions (14) and (15)].



(14)



(15)

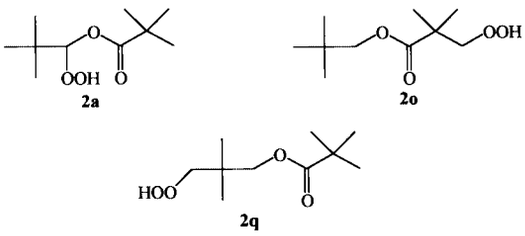
Two further sources of acetone, discussed above, which do not involve the *tert*-butyl radical, are the non-radical thermolyses of the β-acylhydroperoxide **1g** and the β-ketoester **1i** (Schemes 7 and 8).

(c) The oxidation of neopentyl 2,2-dimethylpropanoate (2), 3,3-dimethylbutanoate (3) and 2,2-dimethylbutanoate (4)

Esters **2**, **3** and **4** were chosen to keep the alkyl group constant, and allow the acyl moieties to be altered to show how the blocking of oxidative attack at the α- (**2**, **4**) and β- (**3**) positions affects the autoxidations of esters.

In general, similar products were obtained to those from neopentyl butanoate (**1**), with oxidative attacks occurring at all the C–H positions. For example, **2** yields the three hydroperoxides **2a**, **2o** and **2q** (supplementary data, Table G). Similar results were obtained for the other esters, **3** and **4** (supplementary data, Table G). Further, as for the butanoate **1**, the corresponding alcohols and ketones are observed (Table 1) and the corresponding aldehyde from primary attack is not.

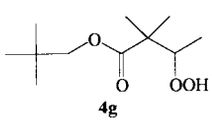
The absence of aldehydes in the product mixtures, we believe, arises from their susceptibility to oxidation under the conditions of the experiments.[24]



Taking as a crude measure of autoxidation rate, the rate of consumption of the ester, the order of reactivity of esters **1**–**4** is **1** > **4** > **3** > **2** (supplementary data, Table H). There are two results here that are of considerable importance. First, in spite of blocking all the secondary sites on the acyl moiety, the rate of oxidation of **2** is only reduced by a factor of between 2–4 compared to esters **3** and **4**, suggesting that the α-alkyl site is very important as a point of attack and/or significant reaction occurs at the primary C–H bonds. The second is that blocking the β-acyl secondary carbon (as in **3**) has a greater effect on the rate of oxidation than blocking the α-acyl secondary positions. That the β-position seems more prone to oxidative attack than the α-position has also been seen in a separate study where alkoxyl radicals were allowed to react with these esters.[1]

It is noteworthy that despite the selective blocking of reaction at the α- and β-acyl positions in **2**, **3** and **4**, all four esters (**1**–**4**) give similar products. Thus, not unexpectedly, each substrate gives the parent acid by oxidation at the α-alkyl position (Scheme 12). Interestingly, however, blocking either the α- or β-acyl position does not prevent acyl group oxidations leading to neopentanol, in agreement with the multiple routes to this product discussed above (for example, Schemes 5–8). On closer examination, it is clear that the yield of neopentanol from ester **2** is particularly low. This is not surprising since the α-acyl position is blocked and the only routes are *via* oxidation of the less reactive β-acyl primary C–H bonds (Schemes 7 and 8).

Two of the key products in the autoxidation of **1** are the hydroperoxy esters **1d** and **1g**. Based on the work of Jensen *et al.*[25] we propose that **1g** decomposes to give neopentanol, acetone and carbon dioxide (Scheme 7). Blocking the β-acyl position unfortunately does not block the formation of these products since they can arise from several other routes. Support for Jensen's mechanism, however, comes from the oxidation of **4** which, by reaction *via* **4g**, gives large concentrations of 3-methylbutan-2-one.

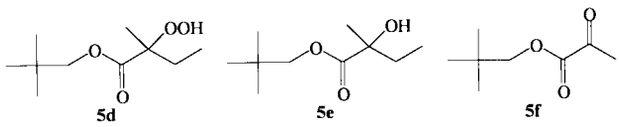


β-Ketoesters corresponding to **1i** cannot be obtained from esters **2** and **3**, but, from **4**, **4i** is formed, indeed in much higher yields than **1i**. This is because **4i**, having no C–H bonds between the two carbonyl groups, is unable to enolise, and consequently is stable to thermal decarboxylation[26] (Scheme 8). Thus **4i** dominates over **4h** whereas **1h** dominates over **1i**.

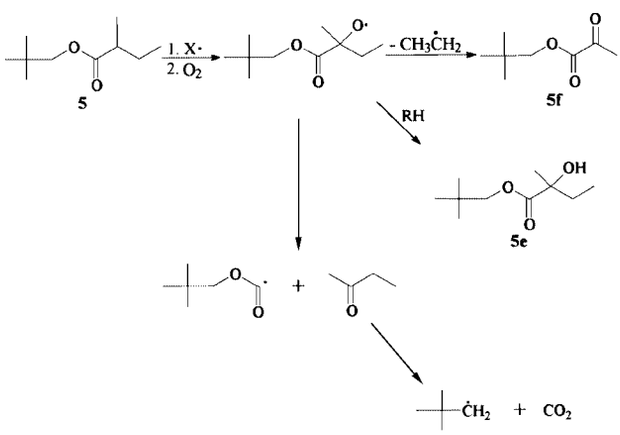
The relative stabilities of **1i** and **4i** were confirmed by heating authentic samples of each in the absence of oxygen with or without added water and a carboxylic acid, where the former decomposed, whereas **4i** was stable.

(d) The autoxidation of neopentyl 2-methylbutanoate (5)

Neopentyl 2-methylbutanoate (**5**), which has a tertiary α-acyl C–H bond, was chosen as a substrate with the aim of increasing the selectivity of the autoxidation for the α-acyl position. Indeed, the autoxidation of this substrate was significantly faster than that of **1**, giving approximately the same yield of products at 438 K in 60 min observed with **1** after 90 min (supplementary data, Table E). Product analyses show, as expected, that the major products are **5d**, **5e** and **5f** from attack at the tertiary α-C–H position. Nevertheless, attack at the α-alkyl site is still very important as gauged by the high yield of 2-methylbutanoic acid. This again is a finding borne out on looking at specific alkoxyl radical reactions on, for example, **1** and **3** compared with **5**.[4]



Assuming that all the parent acid arises from oxidation of the alkyl group, it is possible to compare the relative rates of product formation from **1** and **5** relative to that of the parent acid (Table 4). The most significant differences are seen in the increased relative rate of formation, from **5**, of carbon dioxide, 2-hydroxyester (**5e**), 2-keto-ester (**5f**), acetic acid, 2,2-dimethylpropanal (after PPh_3 treatment) and 2,2-dimethylpropanoic acid. An increased rate of formation of carbon dioxide, **5e** and **5f** would be expected from increased selectivity of the reaction for the tertiary α-acyl C–H bond giving the α-acylalkoxyl radical (Scheme 15).



Scheme 15 Products arising from the oxidation of the α-acyl position of neopentyl 2-methylbutanoate.

(e) Autoxidation of 1,1-[$^2H_2$]-neopentyl butanoate (1′)

As a mechanistic check on the autoxidation of the neopentyl esters, the autoxidation of the dideuterated analogue of **1**, 1,1-[$^2H_2$]-neopentyl butanoate (**1′**) was investigated.

Similar products were obtained, following autoxidation of the two esters (supplementary data, Table F). Neopentanol, which is produced by oxidative attack on the α-acyl and β-acyl positions and not the α-alkyl position and whose yield should not therefore be significantly influenced by deuteration of the α-alkyl position, was taken as the standard against which to compare the yields of products from **1** and **1′** (Table 5). The relative yield of butanoic acid is significantly decreased by the introduction of the C–D bonds at the α-alkyl position indicating that, as argued in this paper, it arises by initial oxidative attack at this position.

Furthermore, the decreases in relative yields of 2,2-dimethylpropanal and 2,2-dimethylpropanoic acid are as large as that of butanoic acid confirming that they, too, are predominantly produced by oxidation of the α-alkyl position. The relative yields of acetone and 2-methylpropan-2-ol are also decreased by the deuteration, supporting the route to these compounds *via* the *tert*-butyl radical arising from α-alkyl oxidation and oxidative decarbonylation of 2,2-dimethylpropanal, discussed

Table 4 Comparison of yields of products, relative to butanoic acid and 2-methylbutanoic acid, from the autoxidation of neopentyl butanoate (**1**) and neopentyl 2-methylbutanoate (**5**), respectively: 1.5 cm^3, ester; 5 bar, oxygen; 438 K

	Relative yields					
Substrate	**1**		**5**			
Reaction time/min	90		60		Ratio changes[a]	
Products	A[b]	B[c]	A[b]	B[c]	A[b]	B[c]
Carbon monoxide	0.58	[d]	0.77	[d]	+0.33	—
Carbon dioxide	0.18	[d]	0.43	[d]	+1.39	—
Formaldehyde	0.01	[d]	0.00	[d]	−1.00	—
Acetone	0.81	0.73	0.95	0.84	+0.17	+0.15
Butanone	[d]	[d]	1.60	1.50	—	—
tert-Butyl hydroperoxide	0.07	0.00	0.02	0.00	−0.71	—
2-Methylpropan-2-ol	0.42	0.46	0.36	0.42	−0.14	−0.09
tert-Butyl formate	0.07	0.07	0.00	0.00	−1.00	−1.00
Neopentanol	0.54	0.51	0.65	0.63	+0.20	+0.24
Neopentyl formate	0.05	0.05	0.02	0.04	−0.60	−0.20
2,2-Dimethylpropanal	0.00	0.13	0.23	0.32	—	+1.46
2,2-Dimethylpropanoic acid	0.15	0.15	0.33	0.34	+1.20	+1.27
Acetic acid	0.37	0.35	0.86	0.97	+1.32	+1.77
Butanoic acid	1.00	1.00	[e]	[e]	[f]	[f]
2-Methylbutanoic acid	[e]	[e]	1.00	1.00	[f]	[f]
e	0.12	0.17	0.67	0.76	+4.58	+3.47
f	0.21	0.16	0.70	0.68	+2.33	+3.25
t	0.09	0.13	0.07	0.08	−0.22	−0.39

[a] [(Relative yield from the autoxidation of **5**) − (Relative yield from the autoxidation of **1**)]/(Relative yield from the autoxidation of **1**). [b] Yield before triphenylphosphine reduction. [c] Yield after triphenylphosphine reduction. [d] Not determined. [e] Not applicable. [f] Reactions of **1** and **5** standardised to the yields of butanoic acid and 2-methylbutanoic acid, respectively.

Table 5 Comparison of yields of products, relative to neopentanol, from the autoxidation of neopentyl butanoate (**1**) and 1,1-[$^2H_2$]-neopentyl butanoate (**1′**): 1.5 cm^3, ester; 5 bar, oxygen; 438 K

	Relative yield					
Substrate	**1**		**1′**			
Reaction time/min	90		60		Ratio changes[a]	
Products	A[b]	B[c]	A[b]	B[c]	A[b]	B[c]
Carbon dioxide	0.32	[d]	0.25	[d]	−0.22	—
Acetone	1.85	1.77	1.10	1.10	−0.41	−0.38
2-Methylpropan-2-ol	0.87	0.87	0.25	0.25	−0.71	−0.71
tert-Butyl formate	0.09	0.09	0.02	0.02	−0.78	−0.78
Neopentanol	1.00	1.00	1.00	1.00	0.00	0.00
Neopentyl formate	0.08	0.08	0.07	0.07	−0.13	−0.13
Neopentyl acetate	0.04	0.05	0.05	0.05	+0.25	0.00
2,2-Dimethylpropanal	0.30	0.32	0.12	0.13	−0.60	−0.59
2,2-Dimethylpropanoic acid	0.14	0.15	0.02	0.02	−0.86	−0.87
Acetic acid	0.47	0.44	0.44	0.53	−0.06	+0.20
Propanoic acid	0.25	0.23	0.20	0.21	−0.20	−0.09
Butanoic acid	1.77	1.81	0.67	0.72	−0.62	−0.60
1e	0.31	0.31	0.26	0.29	−0.16	−0.07
1f	0.42	0.42	0.41	0.41	−0.02	−0.02
1h	0.73	0.75	0.90	0.95	+0.23	+0.27
1i	0.00	0.00	0.12	0.11	—	—
1l	0.16	0.15	0.11	0.12	−0.31	−0.20
1n	0.22	0.22	0.28	0.28	+0.27	+0.27
1r	0.03	0.04	0.06	0.07	+1.00	+0.75
1t	0.17	0.17	0.19	0.22	+0.12	+0.29

[a] [(Relative yield from the autoxidation of **1′**) − (Relative yield from the autoxidation of **1**)]/(Relative yield from the autoxidation of **1**). [b] Yield before triphenylphosphine reduction. [c] Yield after triphenylphosphine reduction. [d] Not determined.

above (Scheme 14). Interestingly, the effect of deuteration is more pronounced on the yield of 2-methylpropan-2-ol than that of acetone. This is in agreement with suggestions above that acetone is also formed by β-acyl oxidation pathways that do not generate the *tert*-butyl radical (Schemes 7 and 8). The relative concentration of *tert*-butyl formate is decreased significantly on deuteration, suggesting that it may be formed *via* 2-methylpropan-2-ol. Similar reactions have been observed during the oxidation of 1,1,1-tris(propylcarboxymethyl)propane.[24]

Experimental

Methods

Apparatus. A stainless steel autoclave (inside volume 4.87 cm^3), with a Teflon seal and a magnetic stirrer, was constructed with a high pressure valve attached to the autoclave through 1.6 mm od stainless steel tubing.[4] The same autoclave was used throughout the study.

For the reaction, the autoclave containing 1.5 cm^3 of an ester

was connected to a pressure line and the reaction vessel and contents purged with oxygen for 30 min and then pressurised. After closing the high pressure valve, the autoclave was disconnected from the line and placed in an aluminium block. The block was heated and the temperature monitored.

After the reaction, the autoclave was removed from the heating block, cooled and re-connected to the pressure line and the high pressure valve was opened to release the pressure to the line. Analysis was by GC and the identity of the products confirmed using authentic compounds by GC retention times and by GC-MS.

Instrumentation. GC analysis was carried out on Pye Unicam gas chromatographs (PU4500 and GCD), fitted with a temperature programming facility and flame ionisation (FID) and thermal conductivity (TCD) detectors. Data collection was carried out with a Trio Trivector integrator. Two capillary columns were used. One was GSQ (30 m length, 0.53 mm id), another was Carbowax 20 M (30 m length, 0.25 mm id, 0.25 μm film thickness). A packed column of Carbosieve SII (3 m length, 3 mm id) was also used. EI- and CI-GC mass spectra were obtained with a mass spectrometer (VG Autospec S Series A027) linked to a gas chromatograph (Hewlett Packard 5890 Series 2). The spectra were analysed using a VAX3100 Workstation.

^{1}H and ^{13}C NMR spectra were obtained using JEOL 270 and Bruker MSL 300 spectrometers. Tetramethylsilane was used as the internal standard.

Peroxide and formaldehyde analyses. Formaldehyde was determined by the Nash method.[27]

The total yields of peroxides (hydroperoxides, peracids and hydrogen peroxide) were estimated by two iodometric procedures, one by titration (the Hercules procedure)[28] and the other by colorimetry.[29] However, it is not possible to determine the concentrations of specific hydroperoxides by these methods or by gas chromatography. Although GC analysis can be used to analyse some hydroperoxides, in the present study the ester hydroperoxides were thermally unstable, decomposing during chromatography to ketones and to a lesser extent to alcohols. To overcome this problem, the product mixtures were reduced with triphenylphosphine and the minimum yields of hydroperoxides were obtained by comparing GC analyses before and after this treatment.

With the α-alkylhydroperoxide, treatment with triphenylphosphine gives the corresponding α-hydroxyester which is thermally unstable and decomposes to 2,2-dimethylpropanal and a carboxylic acid (Scheme 3).

Materials

All materials were commercially available and used as purchased unless otherwise stated.

Esters

The ester substrates **1**–**5** were synthesised by heating the carboxylic acid with neopentanol in toluene in the presence of sulfuric acid, as described previously.[1] (Method A) Similarly, we have also described the preparation of 1,1-[$^{2}H_2$]-neopentyl butanoate (**1′**) from 1,1-[$^{2}H_2$]-neopentanol and butanoic acid.[1]

Authentic samples of the majority of the product esters were prepared by this method or by using Method B, by adding the acid chloride (0.075 mol) to a stirred solution containing the respective alcohol (0.068 mol), pyridine (0.070 mol) and diethyl ether (150 cm^3). Water was added after refluxing for 1 h and the ether phase was separated and washed with 10% aqueous sulfuric acid followed by 10% aqueous solution of sodium carbonate. Diethyl ether was removed under vacuum.

The products from both procedures were purified by flash chromatography using silica gel followed by distillation.

Neopentyl formate. Method A, yield 34.9%; bp 106–108 °C (lit.[30] 112 °C); δ_H ($CDCl_3$) 0.96 (9H, s), 3.87 (2H, d, J = 0.9 Hz), 8.11 (1H, t, J = 0.9 Hz); MS(EI), *m*/*z* 73(30), 57(100), 55(40), 41(35), 2(29).

Neopentyl acetate. Method B; yield 66.4%; bp 124–126 °C (lit.[31] 126 °C); δ_H ($CDCl_3$) 0.94 (9H, s), 2.07 (3H, s), 3.77 (2H, s); MS(EI), *m*/*z* 75(22), 57(81), 56(17), 43(100), 41(22).

Neopentyl propanoate. Method B, yield 66.4%; bp 142–144 °C (lit.[31] 147–148 °C); δ_H ($CDCl_3$) 0.94 (9H, s), 1.16 (3H, t, J = 7.56 Hz), 2.36 (2H, q, J = 7.57 Hz), 3.78 (2H, s); MS(EI), *m*/*z* 89(21), 57(100), 43(12), 41(17), 29(34).

2,2-Dimethyl-3-hydroxypropyl butanoate (1r). Method A (the amount of 2,2-dimethylpropane-1,3-diol used was twice that of the acid); yield 20.0%; bp 74–78 °C 0.8 mmHg; δ_H ($CDCl_3$) 0.92 (6H, s), 0.96 (3H, t, J = 7.4 Hz), 1.67 (2H, m, 2.33 (2H, t, J = 7.4 Hz), 2.86 (1H, s), 3.31 (2H, s), 3.93 (2H, s); MS(EI), *m*/*z* 89(60), 71(100), 56(97), 43(60), 41(26); MS(CI), *m*/*z* 192 (24, MNH_4^+), 175 (100, MH^+).

2,2-Dimethyl-3-hydroxypropyl 2,2-dimethylpropanoate (2r). Method A (the amount of 2,2-dimethylpropane-1,3-diol used was twice that of the acid); yield 54.8%; bp 66–67 °C 0.7 mmHg (lit.[32] 129–131 °C 2.0 mmHg); δ_H ($CDCl_3$) 0.93 (6H, s), 1.22 (9H, s), 2.65 (1H, s), 3.29 (2H, s), 3.92 (2H, s); MS(EI), *m*/*z* 103(42), 57(100), 56(41), 45(18), 41(30); MS(CI), *m*/*z* 206 (13, MNH_4^+), 189 (100, MH^+).

2,2-Dimethyl-3-hydroxypropyl 3,3-dimethylbutanoate (3r). Method A (the amount of 2,2-dimethylpropane-1,3-diol used was twice that of the acid); yield 30.9%; bp 75–76 °C 0.5 mmHg; δ_H ($CDCl_3$) 0.93 (6H, s), 1.04 (9H, s), 2.23 (2H, s), 2.76 (1H, s), 3.32 (2H, s), 3.91 (2H, s); MS(EI), *m*/*z* 117(75), 99(61), 57(100), 56(73), 41(30).

2,2-Dimethyl-3-hydroxypropyl 2,2-dimethylbutanoate (4r). Method A (the amount of 2,2-dimethylpropane-1,3-diol used was twice that of the acid); yield 41.4%; bp 73–76 °C 0.5 mmHg; δ_H ($CDCl_3$) 0.85 (3H, t, J = 7.5 Hz), 0.93 (6H, s), 1.17 (6H, s), 1.58 (2H, q, J = 7.5 Hz), 2.74 (1H, s), 3.30 (2H, s), 3.92 (2H, s); MS(EI), *m*/*z* 117(69), 71(100), 56(39), 43(41), 41(20); MS(CI), *m*/*z* 220 (7, MNH_4^+), 203 (100, MH^+).

2-Hydroxy-2-methylpropyl butanoate (1t). Method A (the amount of the acid used was twice that of 2-methylpropane-1,2-diol); yield 34.0%; δ_H ($CDCl_3$) 0.97 (3H, t, J = 7.4 Hz), 1.25 (6H, s), 1.68 (2H, m, J = 7.4 Hz), 2.35 (2H, t, J = 7.4 Hz), 2.65 (1H, s), 3.96 (2H, s); MS(EI), *m*/*z* 87(20), 71(64), 59(100), 43(69), 41(26).

2-Hydroxy-2-methylpropyl 2,2-dimethylpropanoate (2t). Method A (the amount of the acid used was twice that of 2-methylpropane-1,2-diol); yield 17.3%; δ_H ($CDCl_3$) 1.24 (9H, s), 1.25 (6H, s), 2.23 (1H, s), 3.95 (2H, s); MS(EI), *m*/*z* 101(30), 85(17), 59(85), 57(100), 41(27); MS(CI), *m*/*z* 206 (11, MNH_4^+), 189 (100, MH^+).

2-Hydroxy-2-methylpropyl 3,3-dimethylbutanoate (3t). Method A (the amount of the acid used was twice that of 2-methylpropane-1,2-diol); yield 16%; δ_H ($CDCl_3$) 1.05 (9H, s), 1.26 (6H, s), 2.27 (2H, s), 3.95 (2H, s); MS(EI), *m*/*z* 99(64), 59(96), 57(100), 55(51), 43(51); MS(CI), *m*/*z* 220 (10, MNH_4^+), 203 (100, MH^+).

2-Hydroxy-2-methylpropyl 2,2-dimethylbutanoate (4t). Method A (the amount of the acid used was twice that of 2-methylpropane-1,2-diol); yield 6.4%; δ_H ($CDCl_3$) 0.86 (3H, d, J = 7.5 Hz), 1.20 (6H, s), 1.26 (6H, s), 1.60 (2H, q, J = 7.5 Hz),

2.24 (1H, s), 3.95 (2H, s); MS(EI), *m*/*z* 115(29), 71(100), 70(21), 59(68), 43(53).

Neopentyl hydroxyacetate (1n). Method A (the amount of the acid used was twice that of the alcohol); yield 55.0%; bp 40 °C 2.5 mmHg; δ_H ($CDCl_3$) 0.95 (9H, s), 2.66 (1H, s), 3.90 (2H, s), 4.19 (2H, s); MS(EI), *m*/*z* 73(44), 71(52), 57(100), 43(63), 41(47); MS(CI), *m*/*z* 164 (100, MNH_4^+), 147 (4, MH^+).

Neopentyl 2-oxobutanoate (1f). Method A; yield 46.2%; bp 42–44 °C 1.2 mmHg; δ_H ($CDCl_3$) 0.99 (9H, s), 1.14 (3H, d, J = 7.2 Hz), 2.86 (2H, q, J = 7.2 Hz), 3.95 (2H, s); MS(EI), *m*/*z* 71(44), 57(66), 55(12), 43(66), 41(21); MS(CI), *m*/*z* 190 (MNH_4^+).

2-Hydroxyalkanoates

Neopentyl 2-hydroxybutanoate (1e). Compound **1e** was prepared by reduction of neopentyl 2-oxobutanoate (**1f**) by the method of Kamitori *et al.*[33] Yield 19.2%; bp 46 °C 0.6 mmHg; δ_H ($CDCl_3$) 0.96 (9H, s), 0.98 (3H, t, J = 7.5 Hz), 1.71 (1H, dm, J = 14.0, 7.1 Hz), 1.87 (1H, dqd, J = 14.0, 7.5, 4.5 Hz), 2.63 (1H, s), 3.84 (1H, d, J = 10.6 Hz), 3.93 (1H, d, J = 10.6 Hz), 4.19 (1H, dd, J = 4.4, 6.6 Hz); MS(EI), *m*/*z* 71(60), 59(100), 57(52) 43(72), 41(37); MS(CI), *m*/*z* 192 (100, MNH_4^+), 175 (10, MH^+).

The other neopentyl 2-hydroxyalkanoates were prepared by the following procedure.[34,35] A solution of *N*-2-propylcyclohexylamine (0.023 cm^3) in anhydrous tetrahydrofuran (40 cm^3) was placed in a dry flask equipped with a magnetic stirrer after flushing with argon. Butyllithium in hexane (9 cm^3; 2.5 mol dm^{-3}) was added at 0 °C under argon. The mixture was stirred and after 15 min was cooled to −78 °C and the neopentyl ester (0.020 mol) was added dropwise over a period of 5 min and the stirring was continued for a further 30 min. The solution temperature was allowed to rise to 0 °C, and dry oxygen was then bubbled through it for 1 h before it was treated with 1 M hydrochloric acid until the starch–iodide test showed the absence of peroxides. Extraction with ethyl acetate, drying ($MgSO_4$) and removal of the solvent yielded the 2-hydroxyalkanoate. The esters were purified by vacuum distillation.

Neopentyl 2-hydroxy-2-methylpropanoate (2n). Synthesized from neopentyl 2-methylpropanoate; yield 44.0%; bp 37–40 °C 1.5 mmHg; δ_H ($CDCl_3$) 0.93 (9H, s), 1.46 (6H, s), 3.09 (1H, s), 3.87 (2H, s); MS(EI), *m*/*z* 71(11), 59(100), 57(16), 43(23), 41(15); MS(CI), *m*/*z* 192 (100, MNH_4^+), 175 (64, MH^+).

Neopentyl 2-hydroxy-2-methylbutanoate (4e). Synthesized from neopentyl 2-methylbutanoate; yield 33.7%; bp 46–48 °C 1.3 mmHg; δ_H ($CDCl_3$) 0.89 (3H, t, J = 7.4 Hz), 0.96 (9H, s), 1.42 (3H, s), 1.70 (1H, dq, J = 13.8, 7.4 Hz), 1.80 (1H, dq, J = 13.8, 7.4 Hz), 3.13 (1H, s), 3.83 (1H, d, J = 10.5 Hz), 3.89 (1H, d, J = 10.5 Hz); MS(EI), *m*/*z* 73(100), 71(17), 56(12), 55(16), 43(20); MS(CI), *m*/*z* 206 (80, MNH_4^+), 189 (100, MH^+).

Neopentyl 3,3-dimethyl-2-hydroxybutanoate (3e). Synthesized from neopentyl 3,3-dimethylbutanoate; yield 57.2%; bp 63–65 °C 2.0 mmHg; δ_H ($CDCl_3$) 0.97 (9H, s), 0.99 (9H, s), 3.00 (1H, s), 3.84 (1H, s), 3.83 (1H, d, J = 10.6 Hz), 3.91 (1H, d, J = 10.6 Hz); MS(EI), *m*/*z* 87(66), 71(100), 57(62), 43(47), 41(39); MS(CI), *m*/*z* 220 (100, MNH_4^+), 203 (86, MH^+).

3-Hydroxyalkanoates

The neopentyl 3-hydroxybutanoates were prepared by the Reformatskii reaction using 2-bromoalkanoates[36] which were obtained using Method B[37] followed by purification by vacuum distillation.

Neopentyl bromoacetate. Yield 90.7%; bp 41–42 °C 1.5–1.8 mmHg; δ_H ($CDCl_3$) 0.97 (9H, s), 3.77 (2H, s), 3.87 (2H, s); MS(EI), *m*/*z* 121(14), 57(100), 56(20), 55(16), 41(22).

Neopentyl 2-bromo-2-methylpropanoate. Yield 87.4%; bp 41–42 °C 0.7–0.9 mmHg; δ_H ($CDCl_3$) 0.99 (9H, s), 1.95 (6H, s), 3.86 (2H, s); MS(EI), *m*/*z* 181(26), 71(71), 70(26), 57(100), 43(52), 41(46).

Zinc powder (0.084 mol), activated by the method of Vaughan, Bernstein and Lorber,[38] was added to tetrahydrofuran (50 cm^3), stirred and heated to reflux before a solution of the neopentyl 2-bromoalkanoate (0.072 mol) and acetaldehyde or acetone (0.047 mol) in tetrahydrofuran (50 cm^3) was added over 30 min and the mixture was stirred and refluxed for a further hour. The cooled solution was poured into 1 M hydrochloric acid (200 cm^3), the excess of zinc was removed by filtration and the crude products were extracted into ethyl acetate. The organic layer was washed twice with aqueous $NaHCO_3$ and water, and dried ($MgSO_4$). Removal of the solvent under vacuum gave the crude ester which was purified by column chromatography followed by distillation under reduced pressure.

Neopentyl 3-hydroxybutanoate (1h). Synthesized from neopentyl bromoacetate and acetaldehyde; yield 25.7%; bp 66–68 °C 2.2 mmHg; δ_H ($CDCl_3$) 0.95 (9H, s), 1.24 (3H, d, J = 6.3 Hz), 2.47 (1H, dd, J = 16.1, 7.8 Hz), 2.52 (1H, dd, J = 16.1, 4.5 Hz), 3.22 (1H, s), 3.81 (2H, s), 4.21 (1H, qdd, J = 6.3, 4.5, 7.8 Hz); MS(EI), *m*/*z* 87(83), 71(79), 57(44), 45(42), 43(100); MS(CI), *m*/*z* 192 (40, MNH_4^+), 175 (100, MH^+).

Neopentyl 3-hydroxy-3-methylbutanoate (3h). Synthesized from neopentyl bromoacetate and acetone: yield 52.8%; bp 49–50 °C 0.6 mmHg; δ_H ($CDCl_3$) 0.95 (9H, s), 1.30 (6H, s), 2.53 (2H, s), 3.60 (1H, s), 3.83 (2H, s); MS(EI), *m*/*z* 103(46), 101(40), 71(100), 59(94), 43(84); MS(CI), *m*/*z* 206 (7, MNH_4^+), 189 (100, MH^+).

Neopentyl 2,2-dimethyl-3-hydroxybutanoate (4h). Synthesized from neopentyl 2-bromo-2-methylpropanoate and acetaldehyde; yield 34.2%; bp 62 °C 0.6 mmHg; δ_H ($CDCl_3$) 0.96 (9H, s), 1.15 (3H, d, J = 6.5 Hz), 1.20 (6H, s), 2.82 (1H, s), 3.78 (1H, d, J = 10.6 Hz), 3.81 (1H, d, J = 10.6 Hz), 3.89 (1H, q, J = 6.5 Hz); MS(EI), *m*/*z* 115(30), 88(100), 87(42), 70(35), 43(47); MS(CI), *m*/*z* 203 (MH^+).

Neopentyl 3,3-dimethyl-2-oxobutanoate (3f). Neopentyl 3,3-dimethyl-2-hydroxybutanoate (0.015 mol) in dichloromethane (5 cm^3) was added to a stirred suspension of pyridinium chlorochromate[39] (0.022 mol) in anhydrous dichloromethane (30 cm^3). After 200 h, the black residue was washed thoroughly with anhydrous diethyl ether and the combined organic solutions were passed through a short pad of silica gel and the solvent was removed under reduced pressure. The oxobutanoic acid ester was purified by vacuum distillation; yield 31.7%; bp 48–50 °C 0.5 mmHg; δ_H ($CDCl_3$) 0.99 (9H, s), 1.27 (9H, s), 3.95 (2H, s); MS(EI), *m*/*z* 85(15), 71(18), 57(100), 43(27), 41(35); MS(CI), *m*/*z* 218 (MNH_4^+).

3-Oxoalkanoates

The neopentyl 3-oxobutanoates were prepared in the same manner as the neopentyl 3-hydroxybutanoates using acetonitrile instead of the carbonyl compound,[40] and were purified by flash column chromatography followed by distillation under reduced pressure.

Neopentyl 3-oxobutanoate (1i). Yield 22.2%; bp 52–54 °C 0.6 mmHg (lit.[41] 100–116 °C 45 mmHg); δ_H ($CDCl_3$) 0.95 (9H, s), 2.29 (3H, s), 3.48 (2H, s), 3.85 (2H, s); MS(EI), *m*/*z* 117(25), 85(38), 57(66), 43(100), 41(31); MS(CI), *m*/*z* 190 (100, MNH_4^+), 173 (47, MH^+).

Neopentyl 2,2-dimethyl-3-oxobutanoate (4i). Yield 44.0%; bp 56 °C 0.9 mmHg; δ_H ($CDCl_3$) 0.94 (9H, s), 1.39 (6H, s), 2.18 (3H, s), 3.81 (2H, s); MS(EI), *m*/*z* 88(75), 71(39), 57(32), 43(100); MS(CI), *m*/*z* 218 (9, MNH_4^+), 201 (100, MH^+).

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