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THE CHEMISTRY OF SMALL RING COMPOUNDS—XX

CIDNP EFFECTS IN THE OXIDATION OF 2,2-DIMETHYLCYCLOPROPANONE METHYL HEMIACETAL

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Abstract—Mild oxidation of 2,2-dimethylcyclopropanone methyl hemiacetal (**1**) with oxygen, t-butylhydroperoxide or di t-butylperoxalate leads to hydrogen abstraction from the OH group of **1**. The cyclopropyl ring probably breaks simultaneously to give ring-opened tertiary radical **3a** and primary radical **3b**. In $CDCl_3$, CIDNP effects are observed in the saturated disproportionation product of **3a** and also in products resulting from disproportionation and combination of **3a** with solvent derived $\dot{C}Cl_3$ and $\dot{C}DCl_2$ radicals. The large difference in *g*-values between individual radical components in each of these latter pairs explains the observed emissions.

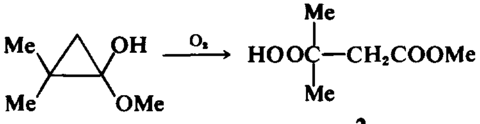
In benzene, solvent does not interfere and CIDNP effects mainly arise from radical pairs, consisting of identical components, *e.g.* two radicals **3a** or at least of components with practically equal *g*-values. Thus disproportionation leads to absorption-emission (multiplets effects) for the unsaturated esters **5** and **6** and the isovalerate **8**.

INTRODUCTION

While studying the methanol adducts of substituted cyclopropanones,[1] we noticed that the hemiacetal of 2,2-dimethylcyclopropanone[2] (**1**) showed peculiar NMR behaviour, when freshly dissolved in $CDCl_3$, the spectrum sometimes showing a strong negative peak (*i.e.* emission) at $\delta = 7{\cdot}28$ ppm, the position where $CHCl_3$ normally absorbs. This negative signal often persisted for ten minutes before gradually disappearing. There were often additional weak emission signals of shorter life time and these were especially noticable when solutions were shaken with air or oxygen. It was also observed that these emissions required a brief induction period. Considering that especially alkyl substituted cyclopropanols[3,5] are readily oxidised by oxygen, it became apparent that hemiacetal **1** consumes a trace of oxygen during the induction period and that the oxidation product initiates a series of reactions, which are responsible for the appearance of emission signals in the NMR spectra. The nature of these reactions is elucidated in the present paper.

Initiators

When an excess of oxygen is passed through a solution of 2,2-dimethylcyclopropanone methylhemiacetal **1** at room temperature, the main product is hydroperoxide **2**.[4]



1 **2**

A similar hydroperoxy ester has been isolated by DePuy *et al.*[5] for the ringsubstituted tetramethyl derivative. In this connection it should be noted that the unsubstituted hemiacetal reacts very sluggishly with oxygen.

When a small amount of the hydroperoxyester **2** is added to a solution of hemiacetal **1** in $CDCl_3$ at room temperature, the NMR spectrum displays negative peaks almost instantaneously. The same effect can be achieved with t-butylhydroperoxide. These results suggest that the observed CIDNP effects,[6] mentioned in the introduction, are caused by hydroperoxide **2** (from **1** and traces of oxygen) and that these effects can generally be initiated by any hydroperoxide or other source of alkoxyradicals. In this respect, we have found di-t-butylperoxalate (TBPO) at 60° to be the most convenient source of t-butoxy radicals,[7] leading to relatively strong and reproducable effects. A detailed study of the reaction of TBPO with the hemiacetal in different solvents has therefore been undertaken.

Radical reactions of hemiacetal 1 *with TBPO in* $CDCl_3$

The labile hydrogen of the hydroxyl group is easily abstracted by the t-butoxy radical during the

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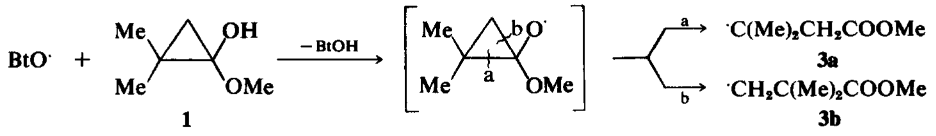
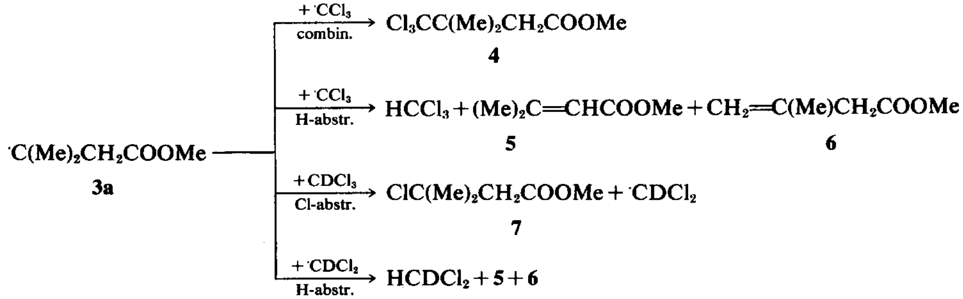
*Part of the forthcoming thesis of B. H. Bakker.

†From whom reprints may be obtained.



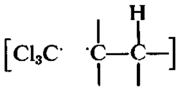
oxidation of hemiacetal **1** with one equivalent of TBPO at 56°. The cyclopropyloxy radical appears to be extremely unstable. Even at very low temperatures (−150°), it forms the isomeric ring-opened radicals **3a** and **3b** (ratio 10:1). These can be trapped in reactions of **1** with t-nitrosobutane,[8] which acts as an oxidant as well as a radical scavenger, thus forming a relatively stable nitroxide, characterized by ESR. The ring-opened radicals **3a** and **3b** give rise to direct or indirect formation of methyl 3-hydroxy-3-methylbutyrate (5%, probably from the originally present hydroperoxide **2**), methyl isovalerate **8** (37%), methyl pivaloate **9** (13%), together with methyl 3-chloro-3-methylbutanoate **7** (15%) and methyl 3-trichloromethyl-3-methylbutanoate **4** (5%). The chlorine-containing compounds are logically explained in the following way.

$$\text{t-BuO}^{\cdot} + CDCl_3 \rightarrow \text{t-BuOD} + {}^{\cdot}CCl_3$$



SCHEME 1

When an NMR spectrum of the mixture in $CDCl_3$ is taken immediately after the reaction has started, transient emission peaks are observed of trichloroester **4** and of the unsaturated esters methyl 3-methyl-2-butenoate **5** and methyl 3-methyl-3-butenoate **6**, even though these unsaturated esters are formed in very low yield (< 1%), hardly detectable by GLC after the reaction is complete. The NMR effects can last up to 5 min (Table 1 and Fig 1). An especially strong emission is found at $\delta = 7{\cdot}28$ ppm for $CHCl_3$ and more curiously a weaker emission at $\delta = 5{\cdot}3$ ppm, the position where normally CH_2Cl_2 absorbs. However, the emission cannot be due to CH_2Cl_2 itself because there is a splitting into three lines with equal intensities and a splitting constant of about 1 Hz (Fig 1). This strongly suggests the presence of $CHDCl_2$,[10] the proton splitting being caused by coupling with deuterium ($I = 1$). These CIDNP effects can be explained by disproportionation and by combination reactions of free radical encounters of the ring-opened tertiary radical **3a** with $^{\cdot}CCl_3$ or $^{\cdot}CDCl_2$ radicals respectively. Singlet-triplet mixing in the radical pairs,[11] caused by a combination of the different electron Zeeman interactions and by nuclear hyperfine interactions, gives rise to net emission or enhanced absorption for the combination and disproportionation products. The chlorinated radicals in these radical pairs possess a higher *g*-value[12] than the alkyl* radical **3a**. Using the rules[13] of Kaptein for net effects, all products obtained from these pairs give emissions for the magnetically active protons with positive hyperfine coupling constants.† Even after all hemiacetal **1** has been consumed (but not all TBPO) CIDNP effects persist. This is caused by further reaction of TBPO with products such as the unsaturated esters **5** and especially **6**, as shown in a blanc experiment (see experimental). This is also consistent with the low yield in which these products are ultimately formed when generated from hemiacetal **1**. During these "blanc" reactions (in $CDCl_3$) the only appreciable CIDNP effects observed are those of $CHCl_3$. The long-lived $CHCl_3$ emission (up to about 30 min) must be explained by assuming hydrogen abstraction in radical pairs, such as



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*The *g*-values of the ring-opened alkyl radicals **3a** and **3b** are not reported in the literature. We assume that these are comparable with the *g*-values of the methyl and ethyl radicals[9] ($g \approx 2{\cdot}0025$).

†Ne = $\mu \epsilon \Delta g A$ = + + − + (Emission).

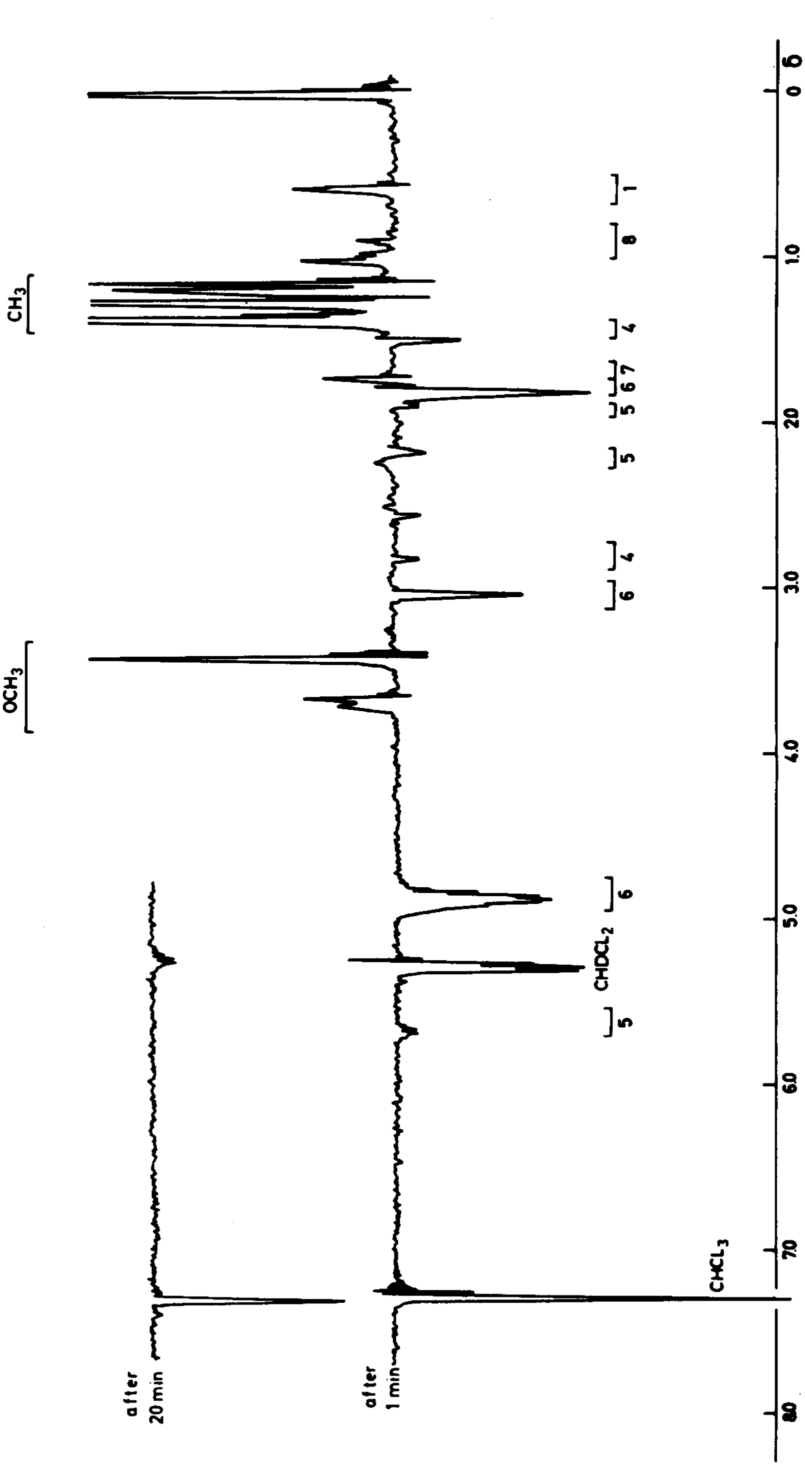

Fig 1 Spectrum of a mixture of 30 μl of 1 and 32 mg of TBPO in 0·5 ml of $CDCl_3$ at 56° (sweeptime 250 s.). Assignment: $Cl_3CC(CH_3)_2CH_2COOCH_3$ (4); $(CH_3)_2C{=}CHCOOCH_3$ (5); $CH_2{=}C(CH_3)CH_2COOCH_3$ (6); $ClC(CH_3)_2CH_2COOCH_3$ (7); $HC(CH_3)_2CH_2COOCH_3$ (8).

Table 1. CIDNP effects, chemical shifts and coupling constant of the esters **4**, **5**, **6** and **8** obtained in the reaction of hemiacetal **1** with TBPO in $CDCl_3$ and in C_6D_6 at 56° and 65°C resp.

Product	δ (ppm) in $CDCl_3$	δ (ppm) in C_6D_6	Proton Assignment	Coupling Constant (Hz)
$Cl_3CC(Me)_2CH_2COOMe$ (**4**)	1·45 E	—	C—CH_3	—
—	2·80 E	—	CH_2CO	—
$(Me)_2C{=}CHCOOMe$ (**5**)	1·85 E	1·51 A/E	C—CH_3 (H_a)	
—	2·16 E	2·12 A/E	C—CH_3 (H_b)	$J_{bc} = J_{ac} - 1{\cdot}4^{a,b}$
—	5·70 E	5·60 A/E	=CH (H_c)	
$CH_2{=}C(Me)CH_2COOMe$ (**6**)	1·81 E	1·67 A/E	C—CH_3 (H_a)	$J_{ac} = J_{bd} - 1{\cdot}5^{b,c}$
—	3·02 E	2·80 A/E	CH_2CO (H_b)	$J_{ad} = J_{bc} - 1{\cdot}3^{b,c}$
—	4·87 E	4·73[c] 4·77 } A/E	$=C(H_c)(H_d)$	$J_{cd} + 2{\cdot}0^{c}$
$HC(Me)_2CH_2COOMe$ (**8**)	0·95 A/E	0·85 A/E	C—CH_3 (H_a)	$J_{ab} = J_{bc}\ 7^{c}$
—		(2·09)[c] (A/E)	CH (H_b)	
—		2·18 (A/E)	CH_2CO (H_c)	
$CHCl_3$	7·28 E	—	CH	—
$CHDCl_2$	5·3 E	—	CH	$J_{HD} = 1{\cdot}0$

The hfs constants of the radical $(Me)_2\dot{C}CH_2COOMe$ (**3a**) are assumed to be equal to those of the t-pentyl radical[9] (22·7 G (6H) and 18·0 G (2H)).

[a] J. V. Hatton and R. E. Richards, *Mol. Phys.* 5, 153 (1962); L. M. Jackman and R. H. Wiley, *J. Chem. Soc.* 2881 (1960).

[b] R. R. Fraser and D. E. McGreer, *Can. J. Chem.* 39, 505 (1961).

[c] The coupling constants and chemical shifts were determined by comparison with simulated spectra using a Varian 620-i computer. The SIMEQ program was developed by Dr. C. W. F. Kort of this laboratory.

The saturated esters **8** and **9** cannot be formed by a thermal isomerisation of the (deuterated) hemiacetal **1**, since this process is relatively slow under the mild reaction conditions.

Furthermore it is found that only a small part of these esters are formed from radicals **3a** and **3b** by uptake of hydrogen from the solvent or from hemiacetal **1**, because the deuterium incorporation in these esters is low, when $CDCl_3$ or deuterated (OD) hemiacetal is used (experimental).

In other words the ring-opened radicals **3a** and **3b** abstract *hydrogen* (not deuterium) from some suitable (radical) source. A short-lived A/E multiplet effect* observed for the methyl protons of the isovalerate **8** at δ = 0·95 ppm supports this as outlined in Scheme 2 for the disproportionation between pairs of ring-opened radicals **3a** + **3a** or **3a** + **3b**.

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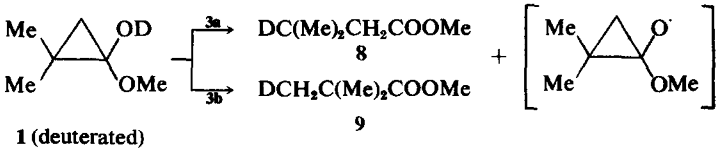
*Using Kaptein's rule[13] $Me = \mu\epsilon A_i A_j J_{ij} \sigma_{ij}$, an A/E effect can be predicted Me = + + + + + −.



$$2\,\dot{C}(Me)_2CH_2COOMe \xrightarrow{\text{disprop.}} (Me)_2C{=}CHCOOMe \text{ or } H_2C{=}C(Me)CH_2COOMe + HC(Me)_2CH_2COOMe$$

3a → **5** or **6** + **8**

$$\dot{C}(Me)_2CH_2COOMe + \dot{C}H_2C(Me)_2COOMe \xrightarrow{\text{disprop.}} \mathbf{5} \text{ or } \mathbf{6} + (Me)_3CCOOMe$$

3a + **3b** → **5** or **6** + **9**

SCHEME 2

Both components in the pair are now essentially alkyl radicals with equal or nearly equal g-values.* The observed absorption/emission (A/E) multiplet effect in the isovalerate **8** (*cf.* Table 1) is in full agreement with current theories[6,14] for disproportionation products from such radical pairs. In principle we should expect similar multiplet effects for the accompanying unsaturated esters **5** and **6**. However, we see emission only (*cf.* Table 1 under $CDCl_3$). This apparent anomaly is explained by two reactions in Scheme 1 i.e. the disproportionation between radical **3a** and $^{\cdot}CCl_3$ or $^{\cdot}CDCl_2$ radicals (with much higher g-values than alkyl radicals) leading to relatively strong emission, which overshadows the much weaker A/E effect, caused by reaction between two alkyl radicals.

It should be noted that radical **3b** is not a hydrogen donor but only an acceptor, and therefore disproportionation between two **3b** radicals is not feasible.

Radical reactions of 1 *with TBPO in hexadeuterobenzene*

In benzene there is no solvent-derived radical that interferes in the reactions. The reaction of hemiacetal **1** (in C_6D_6) with TBPO at 65° gives the isomeric isovalerate **8** (35%) and pivaloate **9** (24%), methyl 3-hydroxy-3-methylbutyrate (5%), the unsaturated esters **5** (3%) and **6** (11%), but also the isomeric $\alpha,\alpha,\beta',\beta'$- and $\beta,\beta,\beta',\beta'$-tetramethyladipate (**10** and **11**; 7% each), formed directly by combination of the radicals **3a** and **3b**.

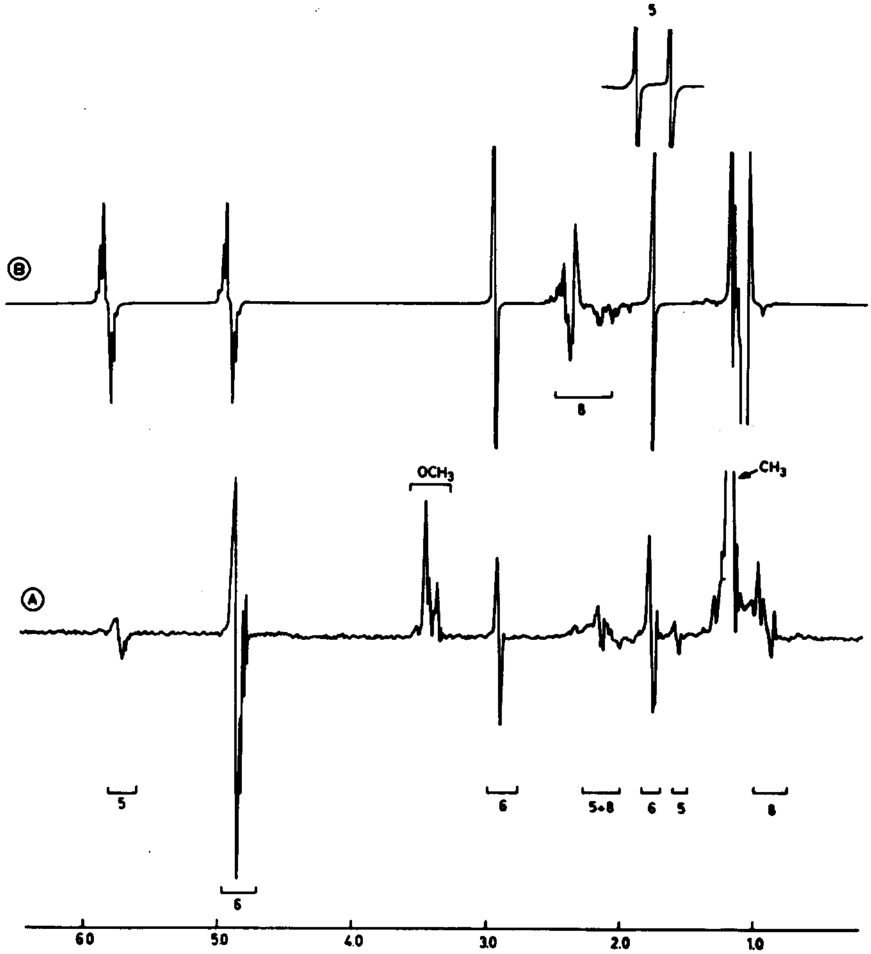


Fig. 2. (a) Spectrum of a mixture of 30 μl of **1** and 29 mg of TBPO in 0·5 ml of C_6D_6 at 65° (sweeptime 250 s.). Assignment: $(CH_3)_2C{=}CHCOOCH_3$ (**5**); $CH_2{=}C(CH_3)CH_2COOCH_3$ (**6**); $HC(CH_3)_2CH_2COOCH_3$ (**8**). (b) Calculated spectra of the products **5**, **6** and **8** by using the chemical shifts and coupling constants given in Table 1.

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*The g-values of the ring-opened alkyl radicals **3a** and **3b** are not reported in the literature. We assume that these are comparable with the g-values of the methyl and ethyl radicals[9] ($g \approx 2{\cdot}0025$).

$$3a + 3b \rightarrow \mathrm{MeOOCC(Me)_2CH_2C(Me)_2CH_2COOMe}$$

10

$$3a + 3a \rightarrow \mathrm{MeOOCCH_2C(Me)_2C(Me)_2CH_2COOMe}$$

11

The thermal isomerisation is very slow under these conditions. A radical-catalysed isomerisation was shown to be also unimportant in benzene by using deuterated hemiacetal **1** (with OD). The D-content was 2 mole % for **8** and 10 mole % for **9**. In benzene solution the disproportionation and combination of the ring-opened radicals are important processes. If an NMR spectrum is taken during the reaction (Fig 2A), A/E multiplet effects for the unsaturated esters **5** and **6** and for the isovalerate **8** are observed. These CIDNP effects[14] are in strong contrast with the emissions in $CDCl_3$ (*cf.* previous section) and are attributed to a disproportionation of free radicals, by encounters between alkyl radicals with about equal *g*-values i.e. the radicals **3a** and **3b**.

From the combination products, the adipates **10** and **11** we could in principle expect multiplet effects, but these are not observed in our particular case because all of the NMR absorptions are singlets.

By applying the theory[11, 14] of Kaptein, Oosterhoff and Closs and using the NMR and the ESR data (Table 1), we have an excellent agreement between the calculated and observed spectra of the products **5**, **6** and **8** (Fig 2).

It can be shown that a considerable fraction of the unsaturated ester $CH_2{=}C(Me)CH_2COOMe$ (**6**) reacts further with TBPO under the reaction conditions presumably because of two particularly reactive allylic hydrogens (experimental). Even with this in mind, the much higher yield of the saturated esters **8** and **9** (total 59%) from hemiacetal **1** and TBPO as compared with that of the unsaturated esters **5** and **6** (total 14%) cannot be explained exclusively by pure disproportionation reactions. We must therefore conclude that a large proportion of the saturated products is formed by hydrogen abstraction by ring-opened radicals from a suitable substrate containing allylic hydrogen, e.g. the unsaturated esters **5** and **6**.

Apparently hydrogen abstraction from the ring-opened radical **3a** by the bulky t-butoxy radical, which probably has a higher *g*-value[15] than alkyl radicals, does not take place, since no emission signals of the unsaturated ester protons of **5** and **6** are observed. It is interesting to note, that in benzene this reaction does occur between the t-butoxy radical and the tetramethyl β-propionate radical, obtained from tetramethylcyclopropanone hemiacetal and TBPO.[16]

The NMR spectra of the mixtures clearly show that a variety of radical processes is involved in the oxidation of the hemiacetal **1** with TBPO in $CDCl_3$ and C_6D_6. It is highly probable that the oxidations with t-butylhydroperoxyde or with air (*via* the initially formed hydroperoxide) takes a similar course.

EXPERIMENTAL

The NMR spectra were recorded on a Varian A-60D spectrometer. An Aerograph gaschromatograph, type 202, with linear temperature programmer was used for preparative and quantitative purposes. The mass spectra were taken on an AEI MS-902 instrument.

Starting materials. Dimethylcyclopropanone methylhemiacetal **1** was prepared from dimethylketene, CH_2N_2 and MeOH.[2] The hydroxyl proton of the hemiacetal was exchanged (only for some experiments) by deuterium with an excess of MeOD in hexane.

Di-t-butylperoxalate (TBPO) was obtained from t-butylhydroperoxide and oxalylchloride.[7]

Reaction of **1** *with TBPO.* In a typical experiment 500 mg of **1** and 520 mg of TBPO in 7 ml $CHCl_3$ were heated under N_2 for 1 h at 56°. The products were separated by VPC using a 5 m preparative silicon SE-30 column and quantitatively determined by means of 5 m analytical diethylene glycol- and SE-30 columns. Methyl 3-trichloromethyl-3-methylbutanoate **4** (5%), methyl 3-chloro-3-methylbutanoate **7** (15%), methyl isovalerate **8** (37%), methyl pivaloate **9** (13%) and methyl 3-hydroxy-3-methylbutyrate (5%) were identified by their IR and NMR spectra and by comparison with authentic samples (with the exception of **4**). (Calc. for $C_7H_{11}Cl_3O_2$ (**4**): C, 36·00; H, 4·75; Cl, 45·55. Found: C, 36·1; H, 4·7; Cl, 45·3%.)

The deuterium content of esters **8** and **9** (8% and 24% respectively from the reaction in $CDCl_3$) was determined by mass spectrometry, from the parent ion ratio of the deuterated- and non-deuterated esters. Starting with hemiacetal **1** (with OD) in $CHCl_3$, 16% deuterium was incorporated in **9** and none in **8**.

A similar procedure in benzene gave methyl 3-methyl-2-butenoate **5**,[2] (3%), methyl 3-methyl-3-butenoate **6** (11%),[2] methyl isovalerate **8** (35%), methyl pivaloate **9** (24%), dimethyl α,α,β′,β′-tetramethyladipate **10** (7%),[2] dimethyl β,β,β′,β′-tetramethyladipate **11** (7%) and methyl 3-hydroxy-3-methylbutanoate (5%); structures being confirmed by IR and NMR. Ester **11** was identical with the product, obtained from the electrochemical reductive dimerisation of methyl β-methylcrotonate.[17] The NMR spectrum of **11** showed three singlets at $\delta = 3{\cdot}67$ (OMe), 2·26 (CH_2) and 0·96 ppm (Me) with relative peak areas of 3:2:6. (Calc. for $C_{12}H_{22}O_4$: C, 62·58; H, 9·63. Found: C, 62·5; H, 9·7%.)

Reaction of unsaturated esters **5** *and* **6** *with TBPO (blanc exp.).* A solution of 54 mg of TBPO and 46 mg of the unsaturated ester **6** in 0·5 ml of $CHCl_3$ was heated for 15 min at 70°. GLC analysis showed (mesitylene as standard) that more than 90% of the ester had disappeared. In a similar experiment, unsaturated ester **5** was shown to be far more stable; only 20% disappeared in the same time. Stability differences could also be demonstrated by NMR, by adding an extra amount of **5** and **6** (10 μl of each) to hemiacetal **1** (50 μl) and TBPO (60 mg) in $CDCl_3$ (0·5 ml) at 56°. After 20 min **6** had disappeared almost completely, while **5** seemed hardly affected. When $CDCl_3$ was replaced by C_6D_6, again **5** was shown to be stable (at 65°), while **6** had reacted to about 50%.

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REFERENCES

[1] S. E. Schaafsma, *Thesis* Amsterdam (1968),

[2] S. E. Schaafsma, E. J. F. Molenaar, H. Steinberg and Th. J. de Boer, *Rec. Trav. Chim.* **86**, 1301 (1967).

[3] D. B. Priddy and W. Reusch, *Tetrahedron Letters* 2637 (1970).

[4] To be published with B. H. Bakker.

[5] D. H. Gibson and C. H. DePuy, *Tetrahedron Letters* 2203 (1969).

[6a] H. Fisher and J. Bargon, *Acc. Chem. Res.* **2**, 110 (1969); [b] H. R. Ward, *Ibid.* **5**, 18 (1972); [c] R. G. Lawler, *Ibid.* **5**, 25 (1972).

[7] P. D. Bartlett, E. P. Benzing and R. E. Pincock, *J. Am. Chem. Soc.* **82**, 1762 (1960).

[8] Unpublished results of P. K. Maarsen.

[9] R. F. Fessenden and R. H. Schuler, *J. Chem. Phys.* **39**, 2147 (1963).

[10] H. S. Gutowski, M. Karplus and D. M. Grant, *Ibid.* **31**, 1282 (1959).

[11a] G. L. Closs and A. D. Trifunac, *J. Am. Chem. Soc.* **92**, 2183 (1970); [b] R. Kaptein, *Thesis* Leiden (1971); [c] H. Fisher, *Z. Naturforsch.* **25a**, 1957 (1970); [d] F. Gerhart, *Tetrahedron Letters* 5061 (1969).

[12] A. Hudson and H. A. Hussain, *Mol. Phys.* **16**, 199 (1969); M. Lehnig and H. Fischer, *Z. Naturforsch.* **25a**, 1963 (1970).

[13] R. Kaptein, *Chem. Comm.* 732 (1971).

[14a] G. L. Closs, *J. Am. Chem. Soc.* **91**, 4552 (1969); [b] R. Kaptein and L. J. Oosterhoff, *Chem. Phys. Letters* **4**, 195, 214 (1969); [c] H. Fischer, *Ibid.* **4**, 611 (1970).

[15] A. Tkac, K. Vesely and L. Omelka, *J. Phys. Chem.* **75**, 2575 (1971).

[16] To be published.

[17] M. M. Baizer and J. D. Anderson, *J. Electrochem. Soc.* **111**, 223 (1964).