700. *Organic Peroxides. Part VIII.* The Stereochemistry and Mechanism of the Preparation and Reduction of* 1-*Methyl*-1-*phenylpropyl Hydroperoxide.*

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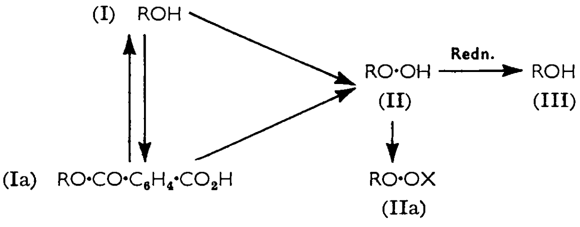
Treatment of optically active 2-phenylbutan-2-ol or its hydrogen phthalate with hydrogen peroxide gives the active hydroperoxide, which can be reduced back to the active alcohol. It is concluded that the reductions proceed with complete retention of configuration in the 1-methyl-1-phenylpropyl group, and therefore that the hydroperoxide is formed from the alcohol and from the hydrogen phthalate with predominating retention of configuration, by an S_Ni mechanism.

In Part VI [1] we reported a stereochemical study of the formation and reduction of 1-phenylethyl hydroperoxide. The availability of optically active 2-phenylbutan-2-ol and its hydrogen phthalate [2] has enabled us to carry out a similar study of 1-methyl-1-phenylpropyl hydroperoxide.

Results

We have shown previously [3] that hydrogen peroxide reacts with the alcohol (I) under acid conditions, and with the sodium salt of the hydrogen phthalate (Ia) giving the hydroperoxide (II); treatment of the hydroperoxide with xanthhydrol gives the 9-xanthenyl derivative (IIa). These reactions have now been repeated with the optically active compounds; the rotatory powers of the reactants and products are shown in the first two columns respectively of Tables 3, 4, and 2. Under neutral conditions the active alcohol was partially converted into the hydroperoxide which was isolated as its 9-xanthenyl derivative [3] (IIa); data on this reaction are included in Table 3.



R = Ph·CMeEt. X = 9-Xanthenyl.

Experiments with the [^{18}O]alcohol and hydrogen phthalate showed that the reaction of both with hydrogen peroxide proceeds by alkyl–oxygen fission (cf. Part V [4]).

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* Part VII, *J.*, 1956, 4669.

[1] Davies and Feld, *J.*, 1956, 665.

[2] Davies, Kenyon, and Salamé, *J.*, 1957, 3148.

[3] Davies, Foster, and White, *J.*, 1954, 2200.

[4] Bassey, Bunton, Davies, Lewis, and Llewellyn, *J.*, 1955, 2471.

The optically active hydroperoxide (II) was then reduced back to the alcohol (III) with sodium sulphite, hydrogen and platinum, zinc and acetic acid, and lithium aluminium hydride; the results are recorded in Table 1.

The Steric Course of the Reduction of the Hydroperoxide [(II) ⟶ (III)].—The sensibly constant ratio of α_{III}/α_{II} (Mean, $+0{\cdot}37$; Table 1) shows that the reductions of the hydroperoxide with the four reagents must all have the same stereochemical result. This implies that these reductions, like those of 1-phenylethyl hydroperoxide,[1] all proceed with configurational retention. Therefore 2-phenylbutan-2-ol and 1-methyl-1-phenylpropyl hydroperoxide of the same sign of rotation have corresponding configurations (cf. the 1-phenylethyl [1] and 1-methylhexyl [5] compounds), and if we assume that the maximum rotatory power of the alcohol is $\alpha_D = 18{\cdot}1°$,[2, 6] the optically pure hydroperoxide has α_D = *ca.* 49°.

TABLE 1. *Reduction of hydroperoxide* (II) *to alcohol* (III).

α_{II}	α_{III}	Reagent	α_{III}/α_{II}
$+0{\cdot}60°$	$+0{\cdot}21°$	Na_2SO_3	$+0{\cdot}35$
$+4{\cdot}05$	$+1{\cdot}55$	Zn–HOAc	$+0{\cdot}38$
$+4{\cdot}05$	$+1{\cdot}54$	$LiAlH_4$	$+0{\cdot}38$
$+4{\cdot}05$	$+1{\cdot}55$	H_2–Pt	$+0{\cdot}38$
		Mean:	$+0{\cdot}37$

TABLE 2. *Conversion of hydroperoxide into xanthenyl derivative* (IIa).

α_{II}	α_{IIa}	α_{II}/α_{IIa}
$+4{\cdot}05°$	$+3{\cdot}46°$	$+1{\cdot}17$
$+1{\cdot}81$	$+1{\cdot}3$	$+1{\cdot}4$
	Mean:	$+1{\cdot}3$

TABLE 3. *Conversion of alcohol into hydroperoxide*

	α_I	α_{II}	$[\alpha]_{IIa}$	α_{III}/α_I
Acid ...	$+6{\cdot}00°$	$+0{\cdot}61°$	—	$+3{\cdot}8\%$ [a]
	$+6{\cdot}24$	$+0{\cdot}26$	—	$+1{\cdot}5\%$ [a]
Neutral	$-11{\cdot}62$	—	$-1{\cdot}07°$	$+4{\cdot}4\%$ [b]

[a] Derived from $\alpha_{III}/\alpha_{II} \times \alpha_{II}/\alpha_I$.
[b] Derived from $[\alpha]_{IIa}/\alpha_I \times \alpha_{II}/[\alpha]_{IIa} \times \alpha_{III}/\alpha_{II}$. Values for α_{III}/α_{II} and $\alpha_{II}/[\alpha]_{IIa}$ are taken from Tables 1 and 2.

TABLE 4. *Conversion of hydrogen phthalate* (Ia) *into hydroperoxide* (II)

$[\alpha]_{Ia}$	α_{II}	α_{III}/α_I
$-43°$	$+4{\cdot}05°$	$+9{\cdot}1\%$ [c]
-15	$+1{\cdot}81$	$+11{\cdot}6\%$

[c] Derived from $\alpha_{II}/[\alpha]_{Ia} \times [\alpha]_{Ia}/\alpha_I \times \alpha_{III}/\alpha_{II}$. The value for α_{III}/α_{II} is taken from Table 1. $[\alpha]_{Ia}/\alpha_I = -2{\cdot}6$ (see below).

The Steric Course of the Formation of the Hydroperoxide from the Alcohol [(I) ⟶ (II)] *and the Hydrogen Phthalate* [(Ia) ⟶ (II)].—We accept therefore that the hydroperoxide (II) is reduced to the alcohol (III) with 100% retention of configuration, such that $\alpha_{III}/\alpha_{II} = +0{\cdot}37$. The value of $\alpha_{III}/\alpha_{II} \times \alpha_{II}/\alpha_I$ recorded for the reaction of the alcohol under acid conditions, in Table 3, therefore gives a measure of the configurational result of the reaction (I) ⟶ (II): under acid conditions the hydroperoxide is formed from the alcohol with at least $+3{\cdot}8$ to $+1{\cdot}5\%$ retention of purity of configuration. These values, and those derived below, are minimal because no allowance has been made for any racemisation of the reactant or product previous or subsequent to reaction, respectively.

It is safe to assume that the hydroperoxide (II) is converted into the 9-xanthenyl derivative (IIa) with complete retention of configuration in the 1-methyl-1-phenylpropyl group.[1, 3] The value of $\alpha_{II}/[\alpha]_{IIa}$ in Table 2 therefore represents in sign and magnitude the ratio of the rotatory powers of (II) and (IIa) of corresponding configuration. The expression $[\alpha]_{IIa}/\alpha_I \times \alpha_{II}/[\alpha]_{IIa} \times \alpha_{III}/\alpha_{II}$ (Table 3) therefore represents the configurational result of the reaction (I) ⟶ (II): under neutral conditions the hydroperoxide is formed from the alcohol with $+4{\cdot}4\%$ retention of purity of configuration.

To derive the corresponding result for the formation of the hydroperoxide from the hydrogen phthalate [(Ia) ⟶ (II)] we need to know the relation in sign and magnitude between the alcohol and the hydrogen phthalate, $[\alpha]_{Ia}/\alpha_I$. Zeiss [6] showed that the hydrogen phthalate ($[\alpha]_D$ $+11{\cdot}8°$) gave, with complete retention, the alcohol (α_D $-4{\cdot}53°$), whence $[\alpha]_{Ia}/\alpha_I = -2{\cdot}60$. Similarly Davies, Kenyon, and Salamé [2] found that the hydrogen phthalate ($[\alpha]_D^{20}$ $+48{\cdot}3°$) corresponds to the alcohol ($\alpha_D^{21{\cdot}5}$ $-18{\cdot}4°$), whence $[\alpha]_{Ia}/\alpha_I = -2{\cdot}62$. Inserting this value in the expression $\alpha_{II}/[\alpha]_{Ia} \times [\alpha]_{Ia}/\alpha_I \times \alpha_{III}/\alpha_{II}$ we derive from the value of α_{III}/α_I that the hydroperoxide is formed from the hydrogen phthalate with from $+9{\cdot}1$ to $+11{\cdot}6\%$ retention of configurational purity.

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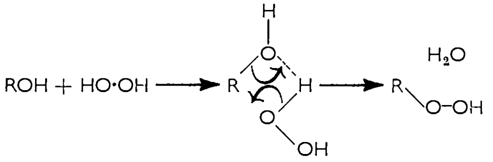
[5] Williams and Mosher, *J. Amer. Chem. Soc.*, 1954, **76**, 3495.
[6] Zeiss, *ibid.*, 1951, **73**, 2391.

DISCUSSION

Any mechanism for the formation of 1-methyl-1-phenylpropyl hydroperoxide from the alcohol or from the hydrogen phthalate must be compatible with the observations that both reactions proceed by alkyl–oxygen fission, and that both give predominating retention of configuration.

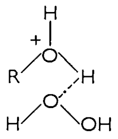
As there is no configuration-holding group in the 1-methyl-1-phenylpropyl structure, it would appear that both these reactions must proceed, at least in part, by an S_Ni mechanism.[7] This might reasonably be expected because the same structural factors in the reacting molecule appear to favour similarly the S_N1 and S_Ni mechanisms, and because the hydrogen peroxide molecule can form strong hydrogen bonds. Indeed we have postulated previously[3] a mechanism involving such hydrogen bond-assisted ionisation to account for the high reactivity of alcohols towards neutral hydrogen peroxide.

The alcohol would therefore appear to react by the mechanism shown in eqn. 1, in which the bond-breaking process is predominant.

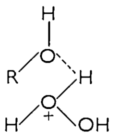


. . . . . . (1)

Under acid conditions the reaction is accelerated with little change in the net stereochemical effect. The reacting species may now be represented by structures (IV) or (V), or by a hybrid of these two structures.

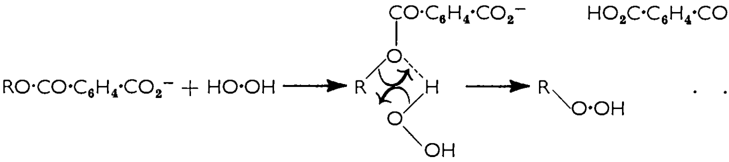


(IV)



(V)

There appears to be no clear precedent for a reaction of a carboxylic ester involving alkyl–oxygen fission by an S_Ni mechanism. The present example is illustrated in eqn. 2.



. . . . . (2)

In contrast, we found that 1 : 2 : 3 : 4-tetrahydro-1-naphthol and its hydrogen phthalate reacted with hydrogen peroxide with complete racemisation within the experimental error [8,*] and that 1-phenylethanol gave the hydroperoxide with predominating inversion of configuration (retention of configurational purity, −2·2 to −4·6%); its hydrogen phthalate did not react with hydrogen peroxide under our usual experimental conditions. We proposed an S_N1 mechanism for these reactions.

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[*] Ikeda[9] has since resolved the hydroperoxide by asymmetric adsorption on (+)-quartz, and found that it had a specific rotatory power of at least $[\alpha]_D^{20}$ 20° (apparently in benzene). If we assume that the rotatory power does not differ greatly between a chloroform and a benzene solution, and that we could have measured a rotation of 0·02°, then the optical purity of the hydroperoxide from the alcohol and the hydrogen phthalate was not greater than 5% and 1·25% respectively. Our attempts to repeat Ikeda's resolution have as yet been unsuccessful.

[7] Cowdrey, Hughes, Ingold, Masterman, and Scott, *J.*, 1937, 1252; Dostrovsky, Hughes, and Ingold, *J.*, 1946, 173.

[8] Davies, Foster, and White, *J.*, 1953, 1541.

[9] Ikeda, *Bull. Liberal Arts Coll., Wakayama Univ.*, 1954, **4**, 27; *Chem. Abs.*, 1955, **49**, 9583.

EXPERIMENTAL

Unless otherwise stated, all values of α_D of liquids were recorded on the undiluted specimens in 1 dm. tubes at temperatures between 18° and 22°.

The usual explosion precautions were taken during the preparation of the hydroperoxides; no trouble in fact was encountered.

The resolution of the alcohol through its hydrogen phthalate has already been described.[2]

The Hydroperoxide from the Active Alcohol.—(i) *Acid conditions.* (+)-2-Phenylbutan-2-ol (2·79 g.), α_D +6·00°, was stirred for 6·5 hr. with 90% hydrogen peroxide (3 c.c.) containing sulphuric acid (1 drop). Water (6 c.c.) was then added, and the product extracted with pentane. The extract was washed with aqueous potassium carbonate and dried (Na_2SO_4). Distillation gave the (+)-hydroperoxide (1·9 g.), b. p. 53°/*ca.* 0·001 mm., n_D^{25} 1·5201, α_D^{20} +0·61°.

In a second experiment the (+)-alcohol (2·96 g.), α_D^{21} +6·24°, gave the (+)-hydroperoxide (1·5 g.), b. p. 75°/0·04 mm., n_D^{25} 1·5194, α_D^{20} +0·26°.

(ii) *Neutral conditions.* The alcohol (0·99 g.) α_D −11·62°, and 90% hydrogen peroxide (2 c.c.) were shaken at room temperature; iodimetric analysis showed the product to contain 30% of the hydroperoxide after 6 hr. and 46% after 18 hr. The alcohol–hydroperoxide mixture (0·642 g.) was added to acetic acid (5 c.c.) containing xanthhydrol (0·485 g.). 1-Methyl-1-phenylpropyl 9-xanthenyl peroxide (0·65 g.), m. p. and mixed m. p. 82°, α_D^{20} −1·07° (*l*, 2; *c*, 12·59 in chloroform), separated within 30 min.; a further small amount was recovered when the mother liquors were poured into water.

The Hydroperoxide from the Active Hydrogen Phthalate.—(−)-1-Methyl-1-phenylpropyl hydrogen phthalate (4·13 g.), $[\alpha]_D^{19\cdot5}$ −43° (*l*, 1; *c*, 15·1 in ethanol), in 90% hydrogen peroxide (10 c.c.) containing sodium hydrogen carbonate (2·1 g.) was kept at 0—10° for 18 hr. The combined products from two such reactions yielded the (+)-hydroperoxide (3·17 g.), b. p. 60—61°/*ca.* 0·001 mm., which after redistillation had b. p. 56°/*ca.* 0·001 mm., n_D^{25} 1·5198, α_{6563}^{18} +3·19°, α_D^{18} +4·05°, α_{5463}^{18} +4·83° (Found: C, 72·9; H, 8·8. Calc. for $C_{10}H_{14}O_2$: C, 72·3; H, 8·4%).

The combined products from two similar preparations from the (−)-hydrogen phthalate (3·0 g.), α_D^{19} −15·0° (*l*, 1; *c*, 10·31 in ethanol) gave the (−)-hydroperoxide (1·66 g.), b. p. 64°/0·03 mm., n_D^{25} 1·5201, α_D^{19} +1·81°.

1-*Methyl*-1-*phenylpropyl* 9-*Xanthenyl Peroxide.*—The hydroperoxide (0·486 g.), α_D^{18} +4·05°, gave the crude peroxide which, after recrystallisation from aqueous ethanol, had (0·55 g.) m. p. 80—81°, $[\alpha]_D^{19}$ +3·40° (*l*, 1; *c*, 5·3 in chloroform).

Similarly a specimen of the hydroperoxide (0·4 g.), α_D^{19} +1·81°, gave the 9-xanthenyl derivative (0·59 g.; from ethanol), m. p. and mixed m. p. [with the (±)-compound] 82—82°, $[\alpha]_D^{19}$ +1·3° (*l*, 2; *c*, 5·8 in chloroform).

Reduction of the Hydroperoxide.—(i) *With sodium sulphite.* The hydroperoxide (1·60 g.), α_D^{19} +0·60°, was stirred with a solution of sodium sulphite heptahydrate (5·0 g.) in water (20 c.c.) at room temperature for 21 hr. A pentane extract gave the alcohol (1·15 g.), b. p. 75—80° (bath)/0·5 mm., n_D^{25} 1·5164, α_D^{18} +0·21° (Found: C, 80·0; H, 9·45. Calc. for $C_{10}H_{14}O$: C, 80·0; H, 9·4%).

(ii) *With zinc and acetic acid.* Zinc dust (2·0 g.) was added to a solution of the hydroperoxide (0·99 g.), α_D^{18} +4·05°, in acetic acid (5 c.c.). Water (1 c.c.) was then added dropwise with cooling. After 2 hr. the solution was diluted with water, neutralised with sodium hydrogen carbonate, and filtered from excess of zinc. An ethereal extract of the zinc and the filtrate gave the alcohol (0·70 g.), b. p. 75° (bath)/0·5 mm., n_D^{24} 1·5153, α_D^{18} +1·55°.

(iii) *With lithium aluminium hydride.* The hydroperoxide (0·65 g.), α_D^{18} +4·05°, was added dropwise to a stirred suspension of lithium aluminium hydride (0·17 g.) in ether (10 c.c.). The mixture was heated under reflux for 30 min., then treated with water and dilute sulphuric acid. The ethereal layer yielded the alcohol (0·35 g.), b. p. 80° (bath)/0·8 mm., $n_D^{24\cdot4}$ 1·5163, α_D^{19} +1·54°.

(iv) *With hydrogen and platinum.* Hydrogen was bubbled for 1·5 hr. through a solution of the hydroperoxide (0·96 g.), α_D^{18} +4·05°, in methanol (10 c.c.) containing reduced platinum oxide. The solution then gave a negative peroxide test; it was filtered and dried, yielding the alcohol (0·7 g.), b. p. 68°/0·4 mm., n_D^{25} 1·5162, α_D^{18} +1·55°.

The [^{18}O]*Alcohol and Its Hydrogen Phthalate.*—A solution of the alcohol (10 g.) in dioxan (70 c.c.), [^{18}O]water (0·87% enriched), and concentrated sulphuric acid (0·2 c.c.) was heated (steam bath) for 2 hr. Solid potassium carbonate was then added to neutralise the acid, and the bulk of the solvent removed by distillation. Pentane was added to the residue, the whole shaken with solid potassium carbonate, and the small aqueous layer removed. The pentane solution was dried (K_2CO_3) and distilled giving a first fraction of the olefin (*ca.* 5 c.c.), followed by the alcohol (*ca.* 5 c.c.), b. p. 80° (bath)/0·4 mm. (Found: [^{18}O], 0·621% enriched). Its infrared spectrum was indistinguishable from that of the original alcohol.

A mixture of the [^{18}O]alcohol (3·07 g.), triethylamine (3·03 g.), and phthalic anhydride (3·03 g.) was stirred at 100° (bath) for 9·5 hr. By the usual method the hydrogen phthalate was isolated (2·50 g.), m. p. 110—112°. The isotopic constitution of the oxygen atom attached to the alkyl group was assumed to be the same as that in the alcohol.

The Hydroperoxide from the [^{18}O]*Alcohol.*—A mixture of the [^{18}O]alcohol (2 c.c.), 85% hydrogen peroxide (3 c.c.), and concentrated sulphuric acid (2 drops) was stirred at room temperature for 6·5 hr. The hydroperoxide was extracted into pentane in the usual way; the extract was stirred twice with 45% sodium hydroxide solution, and the sodium salt of the hydroperoxide was filtered off. The salt was washed thoroughly with pentane, then the hydroperoxide was regenerated from aqueous solution with carbon dioxide. The hydroperoxide was extracted into pentane and the solvent removed. The hydroperoxide smelled of phenol; a fraction (0·49 g.) was therefore treated with xanthhydrol (0·585 g.) giving 1-methyl-1-phenylpropyl 9-xanthenyl peroxide, m. p. and mixed m. p. 83·5—84° (0·42 g.), which was isotopically normal.

The Hydroperoxide from the Hydrogen Phthalate of the [^{18}O]*Alcohol.*—The powdered [^{18}O]ester (2·50 g.) was added to a solution of sodium hydrogen carbonate (1·75 g.) in 85% hydrogen peroxide (10 c.c.) at 0°. The oil which separated was collected in pentane in the usual way, and the solvent removed at 50°/0·04 mm., giving the hydroperoxide which was isotopically normal.

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