[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY, DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CHICAGO]

REACTIONS OF ATOMS AND FREE RADICALS IN SOLUTION. XXXVI. FORMATION OF OPTICALLY ACTIVE ESTERS IN THE DECOMPOSITION OF OPTICALLY ACTIVE DIACYL PEROXIDES IN SOLUTION

M. S. KHARASCH, JEROME KUDERNA,[1] AND W. NUDENBERG

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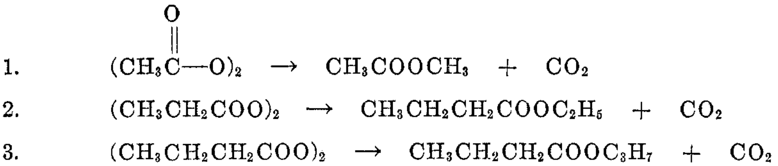
When aliphatic diacyl peroxides are decomposed thermally in organic solvents, esters are formed along with those compounds produced by the attack of the free radicals on the solvent molecules. The yield of ester depends somewhat on experimental conditions and increases appreciably with the length of the alkyl chain in the peroxide.



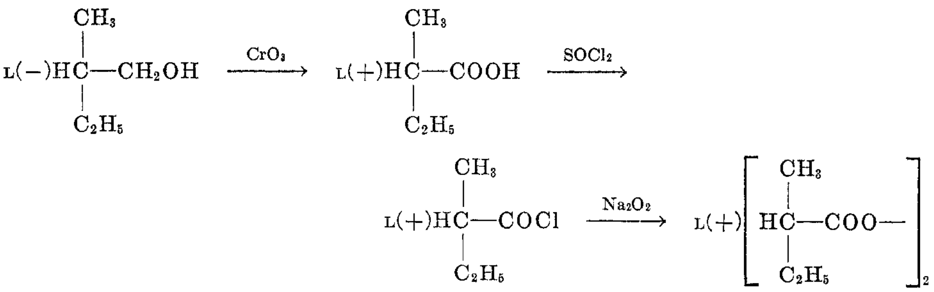
$$1.\quad (CH_3\overset{\overset{O}{\|}}{C}{-}O)_2 \rightarrow CH_3COOCH_3 + CO_2$$

$$2.\quad (CH_3CH_2COO)_2 \rightarrow CH_3CH_2CH_2COOC_2H_5 + CO_2$$

$$3.\quad (CH_3CH_2CH_2COO)_2 \rightarrow CH_3CH_2CH_2COOC_3H_7 + CO_2$$

It was realized early in the investigations that ester formation might be brought about by several mechanisms (1), but on the basis of the data then available it was difficult to assess the importance of any one of these. The importance of the mechanism suggested in the equations given above (namely spontaneous decomposition into an ester and carbon dioxide without generation of free radicals) could, however, be tested by employing an optically active peroxide and noting whether the alcohol group in the ester was or was not optically active. If it were optically active, the study of the series to which the alcohol belonged would indicate whether the ester formation proceeded with or without a Walden inversion.

The aliphatic peroxide selected for this study was L(+)methylethylacetyl peroxide. It was prepared by the following sequence of reactions:



$$\text{L}(-)H\overset{\overset{CH_3}{|}}{\underset{\underset{C_2H_5}{|}}{C}}{-}CH_2OH \xrightarrow{CrO_3} \text{L}(+)H\overset{\overset{CH_3}{|}}{\underset{\underset{C_2H_5}{|}}{C}}{-}COOH \xrightarrow{SOCl_2}$$

$$\text{L}(+)H\overset{\overset{CH_3}{|}}{\underset{\underset{C_2H_5}{|}}{C}}{-}COCl \xrightarrow{Na_2O_2} \text{L}(+)\left[H\overset{\overset{CH_3}{|}}{\underset{\underset{C_2H_5}{|}}{C}}{-}COO{-}\right]_2$$

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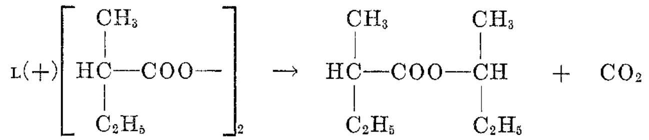
[1] This work was done in 1948 and submitted to the Graduate School of the University of Chicago in partial fulfillment of the requirements for the doctorate degree.

The first two steps in the synthesis of the optically active peroxide offered no difficulty; but the third step in the synthesis was less satisfactory. However‘ consistent yields of about 50% of optically active peroxide were readily obtained. This material was considered quite suitable for the purpose of this study, since the impurities (optically active and inactive acid, small amounts of ether, etc.) have an effect only on the yield of the ester, but not on the mechanism of its formation.

4.



$$\text{L}(+)\left[\underset{C_2H_5}{\overset{CH_3}{HC}}-COO-\right]_2 \rightarrow \underset{C_2H_5}{\overset{CH_3}{HC}}-COO-\underset{C_2H_5}{\overset{CH_3}{CH}} + CO_2$$

The decomposition of the optically active peroxide was carried out as follows: the peroxide, dissolved in benzotrichloride, was introduced slowly into benzotrichloride maintained at 75–80°. The gases evolved (carbon dioxide, butane, and butene) were collected in the usual way. Other reaction products such as *sec*-butyl chloride and tolane tetrachloride were also isolated. These products have no bearing on the problem here under investigation. The only questions bearing on the problems here at issue are whether in the ester (*sec*-butyl methylethylacetate) both the acid and alcohol are optically active and whether they both belong to the same series.

The ester (*sec*-butyl methylethylacetate) isolated had the following physical constants: b.p. 161–164°; n_D^{18} 1.4070; $[\alpha]_D^{24}$ + 27°. Hydrolysis with potassium hydroxide gave *sec*-butyl alcohol (b.p. 97°; n_D^{20} 1.3960; $[\alpha]_D^{25}$ + 10.2°) and methylethylacetic acid (b.p. 171°; n_D^{20} 1.4047; $[\alpha]_D^{25}$ + 10°). The low rotation of the acid thus obtained, compared with acid used in the preparation of the peroxide ($[\alpha]_D^{24}$ + 18.3°), is undoubtedly due to partial racemization of the acid during the hydrolysis of the ester. On the other hand, the somewhat lower rotation of the *sec*-butyl alcohol ($[\alpha]_D^{25}$ + 10.2°; Levene and Marker, $[\alpha]_D^{22}$ + 13.0°) is in part due to the fact that the methylethylacetic acid used by us as well as the peroxide were not of the highest optical purity.

It is obvious that ester formation, in which both the acid and the alcohol are optically active, could arise by elimination of carbon dioxide from the optically active methylethylacetyl peroxide with or without a Walden inversion. If and only if no Walden inversion occurred, the methylethylacetic acid and the *sec*-butyl alcohol should belong to the same series. The sequence of reactions outlined in Scheme I indicates that (+)methylethylacetic acid and (+)*sec*-butanol belong to the same series; hence, it is reasonable to assume that little if any Walden inversion takes place in the decomposition of the methylethylacetyl peroxide into carbon dioxide and *sec*-butylmethylethyl acetate.[2]

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[2] The critical reader will note that the fact that we have placed (−)*sec*-butylcarbinol and (+)*sec*-butyl alcohol in the L series, is of no consequence. The important fact, insofar

EXPERIMENTAL

REAGENTS

L(−)*sec-Butylcarbinol*[3] was isolated from fusel oil by repeated fractionation through a 200-plate Podbielniak-Heligrid column. The samples used in the present investigation were of a rather high degree of optical purity: b.p. 128°/760 mm.; n_D^{20} 1.4109; $[\alpha]_D^{24}$ −5.65°. The specific rotation for this alcohol given in the literature (2) is $[\alpha]_D^{18}$ −5.88°.

Oxidation of L(−)*sec-butylcarbinol to* L(+)*methylethylacetic acid.* The conversion of the active alcohol to the corresponding acid without loss of optical activity was successfully carried out in an acidic medium by the method of Marckwald (3). Potassium dichromate (156 g., 0.53 mole) was dissolved in 1980 ml. of distilled water contained in a 3-liter flask equipped with a stirrer, dropping-funnel, and reflux condenser, and 210 g. of conc'd sulfuric acid was slowly added to the rapidly agitated solution. Then 60 g. (0.68 mole) of L(−)-*sec*-butylcarbinol was added dropwise over a period of 20 minutes. The oxidation was completed at the reflux temperature, and steam-distillation of the reaction mixture yielded L(+)methylethylacetic acid, together with its amyl ester and unchanged alcohol. Following saponification with sodium hydroxide and a second distillation to remove the regenerated alcohol and other products, the acid was obtained by acidification with sulfuric acid and repeated ether extraction. Evaporation of the ether and distillation through a ten-inch Vigreux column at reduced pressure gave an acid, which had the following physical constants: b.p. 77–78°/12 mm.; n_D^{20} 1.4057; $[\alpha]_D^{24}$ +17.5°. Marckwald (3) cites the observed rotation of this acid as α_D +8.75° (l = 0.5 dm.). If the recovery of unreacted alcohol (and

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as this work is concerned, is that both compounds are in the same series. The reader will also note that the data here recorded do not eliminate the following reaction mechanisms:

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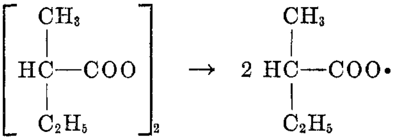
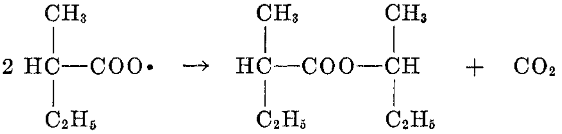
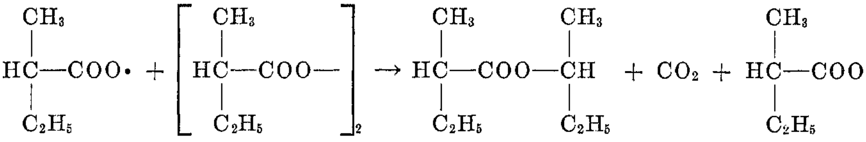


$$\left[\underset{\underset{\mathrm{C_2H_5}}{|}}{\overset{\overset{\mathrm{CH_3}}{|}}{\mathrm{HC}}}\mathrm{—COO}\right]_2 \longrightarrow 2\ \underset{\underset{\mathrm{C_2H_5}}{|}}{\overset{\overset{\mathrm{CH_3}}{|}}{\mathrm{HC}}}\mathrm{—COO}\cdot$$

6.


$$2\ \underset{\underset{\mathrm{C_2H_5}}{|}}{\overset{\overset{\mathrm{CH_3}}{|}}{\mathrm{HC}}}\mathrm{—COO}\cdot \longrightarrow \underset{\underset{\mathrm{C_2H_5}}{|}}{\overset{\overset{\mathrm{CH_3}}{|}}{\mathrm{HC}}}\mathrm{—COO—}\underset{\underset{\mathrm{C_2H_5}}{|}}{\overset{\overset{\mathrm{CH_3}}{|}}{\mathrm{CH}}} + \mathrm{CO_2}$$

7.


$$\underset{\underset{\mathrm{C_2H_5}}{|}}{\overset{\overset{\mathrm{CH_3}}{|}}{\mathrm{HC}}}\mathrm{—COO}\cdot + \left[\underset{\underset{\mathrm{C_2H_5}}{|}}{\overset{\overset{\mathrm{CH_3}}{|}}{\mathrm{HC}}}\mathrm{—COO—}\right]_2 \longrightarrow \underset{\underset{\mathrm{C_2H_5}}{|}}{\overset{\overset{\mathrm{CH_3}}{|}}{\mathrm{HC}}}\mathrm{—COO—}\underset{\underset{\mathrm{C_2H_5}}{|}}{\overset{\overset{\mathrm{CH_3}}{|}}{\mathrm{CH}}} + \mathrm{CO_2} + \underset{\underset{\mathrm{C_2H_5}}{|}}{\overset{\overset{\mathrm{CH_3}}{|}}{\mathrm{HC}}}\mathrm{—COO}\cdot$$

While past experience is not a rigorous criterion, nevertheless one would expect reactions 6 and 7 to proceed with a Walden inversion, unless reaction 6 is strongly favored by a tendency to recombination of the free radicals. The evidence, therefore, strongly favors reaction scheme 4.

[3] The specific rotations of the optically active compounds here recorded were calculated from the relations $[\alpha]_D^t = \frac{a}{ld}$ and $[\alpha]_D^t = \frac{100\alpha}{lc}$, where α is the observed rotation at temperature t, l = length of tube, d = density and c = concentration (grams/100 ml.). The specific rotation of the methylethylacetyl peroxide was calculated by allowing for the rotation of the optically active acid (in benzotrichloride) which was present as an impurity.

also that regenerated from the ester) is considered in the calculation of the yield, it was found that conversions up to 64% of the calculated could be realized. The recovered alcohol was found to have suffered no loss of optical rotatory power during the oxidation process.

The alkaline oxidation of the active alcohol to the acid by means of potassium permanganate was investigated following the method used by Fournier (4) for many carbinols of this type. However, this method did not prove to be satisfactory since the resulting acid was extensively racemized, $[\alpha]_D^{24}$ +6.4°.

Conversion of L(+)*methylethylacetic acid to* L(+)*methylethylacetyl chloride.* The active acyl chloride was obtained in a state of high optical purity by employing the method used by Levene (5). Dropwise addition of 42.1 g. (0.41 mole) of L(+)methylethylacetic acid to 98.5 g. (0.83 mole) of carefully purified thionyl chloride (cooled with the aid of a salt-ice bath) was carried out over a period of three hours. The flask was frequently agitated, but little evidence of reaction was observed. The reactants were allowed to remain at 0° for several hours, and then were brought gradually to room temperature (25°). The reaction began slowly and continued at room temperature for 12 hours. At the end of that time the mixture was refluxed for ten minutes and then cooled. Dry air was bubbled through the reaction product at 0° for 30 minutes. The acid chloride [b.p. 62° at 182 mm. (115°/760 mm.), n_D^{20} 1.4173, $[\alpha]_D^{24}$ +17.2°] was obtained by careful but rapid fractionation through a ten-inch Vigreux column. The yield was 37.5 g., or 76% (yields up to 86% were obtained in some experiments).

An attempt to convert the active acid to the acid chloride with the aid of phthalyl chloride gave an extensively racemized product.

Preparation of L(+)*methylethylacetyl peroxide.* L(+)Methylethylacetyl chloride [$[\alpha]_D^{24}$ +17.2° (31.3 g.; 0.26 mole)], in 230 cc. of dry ether was cooled to −3° and 14.1 g. (0.18 mole) of sodium peroxide was cautiously added. After cooling the slurry to −6°, approximately 70 g. of chipped ice was slowly fed into the stirred mixture over a period of 45 minutes. The emulsion was broken by adding 60 cc. of ice-water and after stirring for 15 minutes, the ethereal layer was decanted, washed with ice-water, and dried over Na_2SO_4. Titratoin of the ethereal solution showed the presence of 12 g. of peroxide, or 46% of the calculated amount and an indicated purity of *ca.* 50%. Efforts to purify the peroxide by washing with cold aqueous bicarbonate followed by ice-water were limited due to the instability of the compound in basic media. The combined ethereal extracts of several preparations were carefully washed in the manner described above and the solvent was removed with a current of dry air. An attempt was made to remove the rest of the ether from the residue (kept at 0°) at reduced pressure. This procedure resulted in reduction by about 5–10% of the peroxide titer. Final titration indicated 0.14 mole (28 g.) of active peroxide, $[\alpha]_D^{24}$ +34° (in benzotrichloride),[3] in a total of 67 g. of a colorless transparent oil. The impurities were presumably some of the active and inactive acids and some ether. The oil gave a negative test for halogen.

REACTIONS

Decomposition of L(+)*methylethylacetyl peroxide in benzotrichloride.* The reaction was carried out by dropwise addition of the active peroxide (0.14 mole, $[\alpha]_D^{24}$ +34°) dissolved in some benzotrichloride,[4] over a period of seven hours, to the remainder of the solvent (total solvent, 1.3 moles) preheated to 75–80°. Dry nitrogen was then bubbled through the reaction mixture as it was being cooled to sweep the last traces of volatile products into the absorption train and cold traps. Carbon dioxide was obtained as determined by the increase in weight of the Ascarite tubes. The gases (*n*-butane and butenes) were collected in the

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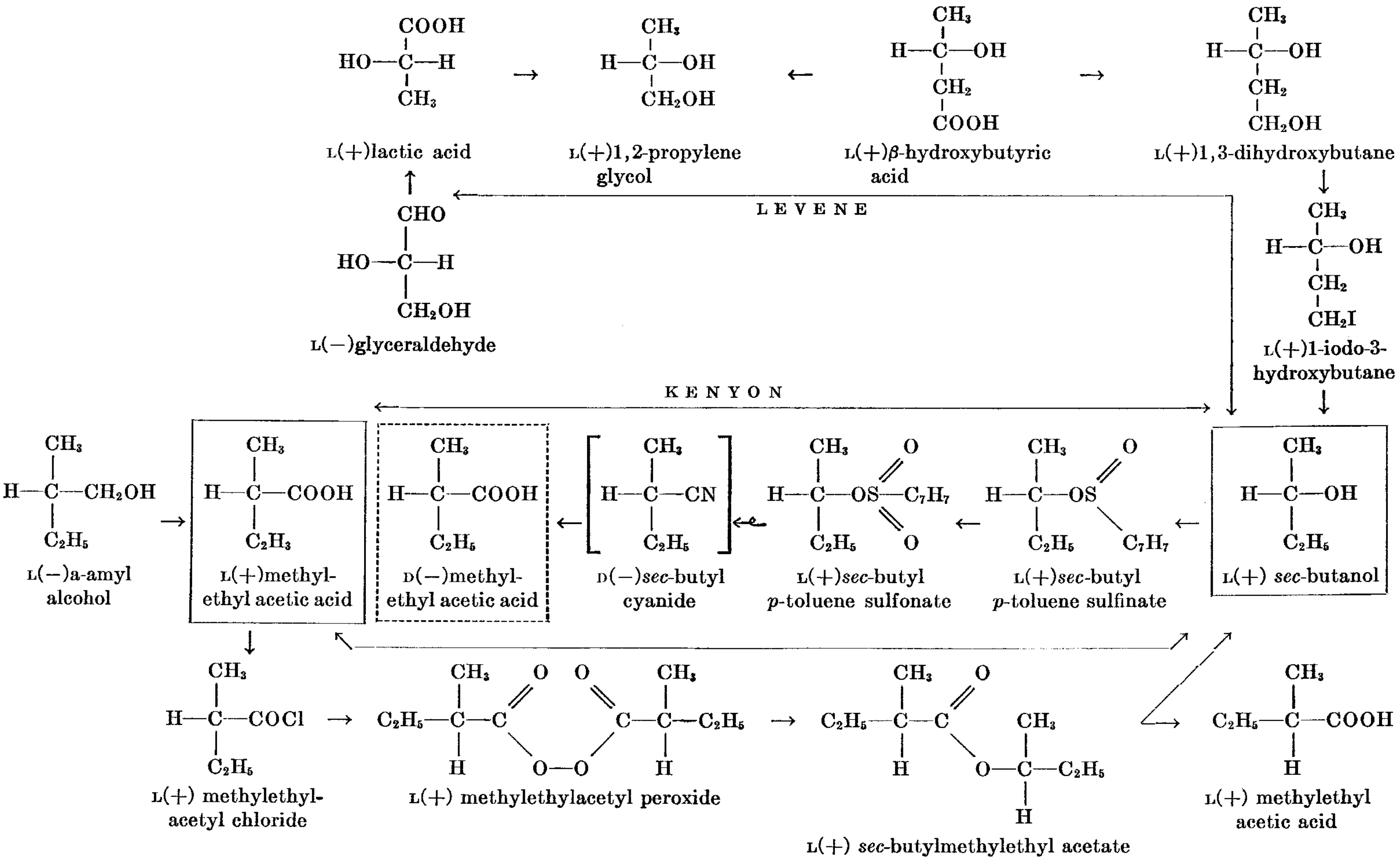
[4] The peroxide, prepared as here described, is rather unstable. Some decomposition was noted after 15–20 minutes at room temperature; hence, the importance of keeping it cold prior to addition.

SCHEME I



1. Kenyon, Phillips, and Pittman, J. Chem. Soc., 1072 (1935).

2. (a) Levene and Haller, *J. Biol. Chem.*, **67,** 329 (1926); (b) *J. Biol. Chem.*, **65,** 49 (1925); (c) *J. Biol. Chem.*, **69,** 165 (1926); (d) Levene, Walti, and Haller, *J. Biol. Chem.*, **71,** 465 (1927).

usual way. The *sec*-butyl chloride and 2-chloro-1-butene were distilled from the reaction mixture through a well-insulated micro helix-packed column at atmospheric pressure.

Distillation of the reaction mixture was then continued at reduced pressure in order to strip off the products boiling lower than benzotrichloride and the tolane tetrachloride. Redistillation of this fraction was then undertaken at atmospheric pressure using a semimicro helix-packed column enclosed in a Dewar flask. Two fractions, both optically active, predominated:

(A) *Ethyl* L(+)*methylethyl acetate*, b.p. 132–133°, n_D^{20} 1.3976, d_4^{22} 0.86, $[\alpha]_D^{24}$ +17.8°. [Physical constants given in the literature (6) for the optically pure ester are: b.p. 131–133°, n_D^{20} 1.3964, d_4^{22} 0.864, $[\alpha]_D^{24}$ +17.6°]. The rotation recorded is one derived by correction of an observed value.

(B) *sec-Butyl* L(+)*methylethyl acetate*, b.p. 161–164°, n_D^{18} 1.4070, $[\alpha]_D^{24}$ +27°. The latter ester has not been previously characterized in the literature; only an optically impure form is mentioned (7). Both products were identified by saponification to alcohol and acids, characteristic derivatives of which were prepared, as later described. Three fractions intermediate between the two pure esters (5–6 g.) also had high optical activities, and were probably mixtures of these products. It is estimated that the ethyl L(+)methylethyl acetate[5] was formed in an amount of 0.2 mole and *sec*-butyl L(+)methylethyl acetate in 0.3–0.4 mole per mole of peroxide used, respectively.

Saponification of L(+)*sec-butyl*-L(+)*methylethyl acetate* $[\alpha]_D^{24}$ +27°. A representative fraction of the ester (5.7 g.) was saponified in 20 cc. of diethylene glycol containing 3 g. of KOH and 3 cc. of distilled H_2O. The alcohol was distilled directly from the reaction mixture and the fraction boiling between 60–65° was dried over Na_2SO_4 and redistilled through a short Vigreux column. The product (about 2–3 g.) was an optically active *sec*-butanol having the following constants: b.p. 97°, n_D^{20} 1.3960, $[\alpha]_D^{25}$ +10.2°. The alcohol was converted to the phenyl urethan in the usual manner, and crystallized from 110° petroleum ether [m.p. 60°, $[\alpha]_D^{25}$ +22° (in ethyl acetate)]. Levene and Marker (8) report the preparation of a sample of (+)*sec*-butanol having an optical rotation in alcohol solution of $[\alpha]_D^{22}$ +13.0°, and which was converted to the urethan, m.p. 62°, $[\alpha]_D^{22}$ +26.5° (in alcohol). The acid fraction from the saponification of the active ester was recovered and identified as L(+)methylethylacetic acid, b.p. 171°, n_D^{20} 1.4047, $[\alpha]_D^{25}$ +10°. Racemization of the acid was thus extensive under the conditions of the hydrolysis. However, it is extremely interesting to observe that both centers of asymmetry in the ester are optically active and contribute to the observed rotation of the product. The active alcohol obtained, although having a positive rotation, is a member of the L series (related to glyceraldehyde) as shown in the accompanying chart. Thus, the alcohol has been formed with *retention* of configuration relative to the original source, the L peroxide.

Saponification of ethyl L(+)*methylethyl acetate.* The ester was saponified following the procedure used for the (+)*sec*-butyl (+)methylethylacetate. Ethanol (b.p. 78–80°, n_D^{20} 1.3631) together with (+)methylethylacetic acid, $[\alpha]_D^{20}$ +10° were obtained. They were converted to their crystalline derivatives, the 3,5-*dinitrobenzoate*, m.p. 93–94°, and the *p-bromphenacyl ester*, m.p. 54–55°, respectively.

SUMMARY

1. It has been shown that upon decomposition (+)methylethylacetyl peroxide gives the ester *sec*-butyl methylethyl acetate in which both the acid and the alcohol are optically active.

2. It has also been established that the (+)*sec*-butanol and the (+)methyl-

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[5] This product is probably formed from the peroxide and the diethylether present as an impurity. Note, for instance, that Kharasch, Kane, and Brown [*J. Am. Chem. Soc.*, **63**, 526 (1941)] found ethyl-*n*-butyrate and ethyl isobutyrate when *n*-butyryl and isobutyryl peroxides were decomposed in carbon tetrachloride containing some ether.

ethylacetic acid are in the same series, and hence, the elimination of carbon dioxide from the peroxide took place without a Walden inversion.

CHICAGO 37, ILLINOIS

REFERENCES

(1) KHARASCH, KANE, AND BROWN, *J. Am. Chem. Soc.*, **63**, 526 (1941); KHARASCH, FRIEDLANDER, AND URRY, *J. Org. Chem.*, **16**, 531 (1951); see also other papers in this series.
(2) LECOUTEUR, KENYON, AND ROHAN, *J. Appl. Chem.*, **1**, 344 (1951).
(3) MARCKWALD, *Ber.*, **37**, 1045 (1904).
(4) FOURNIER, *Bull. soc. chim.*, [4] **5**, 920 (1909).
(5) LEVENE, *J. Bio. Chem.*, **88**, 27–59 (1930).
(6) GUYE, *Bull. soc. chim.*, [3], **25**, 550 (1901).
(7) GUYE, *Compt. rend.*, **124**, 232 (1897).
(8) LEVENE AND MARKER, *J. Bio. Chem.*, **74**, 350 (1927).