371. *Novel Reactions of Some α-Acyloxy Acid Chlorides.*

By A. R. Mattocks.

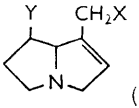
Three abnormal reactions of α-acetoxy-α-methylbutyryl chloride are reported. Certain diols are converted into chloroalkyl acetates and α-hydroxy-α-methylbutyric acid (IIa), instead of into esters of α-acetoxy-α-methylbutyric acid; with excess of methanol, methyl α-hydroxy-α-methylbutyrate (IIh) is formed instead of the acetoxy-ester (IIg); with alcohols and triethylamine, it forms novel cyclic dioxolanones (V), instead of α-acetoxy-α-methylbutyryl esters. Some of these reactions are given by certain other α-acyloxy acid chlorides, and there is evidence that the extent of " abnormal " reaction depends on steric factors. Mechanisms are proposed, involving intramolecular reaction of the acyloxy and acyl chloride groups. The first reaction provides a means of synthesizing chloro-esters from suitable diols in one step.

An unexpected reaction of α-acetoxy-α-methylbutyryl chloride (IIc) was encountered in attempts to prepare α-acetoxy-α-methylbutyryl esters of retronecine (5,6,7,7a-tetrahydro-7β-hydroxy-1-hydroxymethyl-7aα-3*H*-pyrrolizine) (Ia), as part of a study of semi-synthetic pyrrolizidine alkaloids.[1]

(±)-α-Hydroxy-α-methylbutyric acid (IIa) was prepared in the usual way,[2] and resolved through the brucine salts. The (±)-acid was used for most experiments. The hydroxy-acid was acetylated to give α-acetoxy-α-methylbutyric acid (IIb), which was

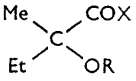
[1] Schoental and Mattocks, *Nature*, 1960, **185**, 842; and further work to be published.
[2] Young, Dillon, and Lucas, *J. Amer. Chem. Soc.*, 1929, **51**, 2532.

converted into the acid chloride (IIc) using oxalyl chloride [3] or thionyl chloride.[4] The infrared spectrum of the acid chloride was identical for all samples used in subsequent experiments. Acetyl chloride and the mixed anhydride (IIe) were shown to be absent by mild alkaline hydrolysis followed by paper chromatography; a single spot was found, corresponding to α-acetoxy-α-methylbutyric acid, and no acetic acid was present. Stronger alkaline hydrolysis gave acetic acid and α-hydroxy-α-methylbutyric acid; no oxalic acid was present.



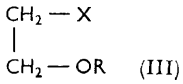
(I)

(a) X = Y = OH
(b) X = Y = EtCMe(OAc)·CO_2
(c) X = Cl, Y = OAc
(d) X = Cl, Y = EtCMe(OH)·CO_2
(e) X = Cl, Y = OH



(II)

(a) R = H, X = OH
(b) R = Ac, X = OH
(c) R = Ac, X = Cl
(d) R = Ac, X = NHPh
(e) R = Ac, X = OAc
(f) R = Pr^iCO, X = Cl
(g) R = Ac, X = OMe
(h) R = H, X = OMe



(III)

(a) R = H, X = OH
(b) R = Ac, X = Cl
(c) R = Pr^iCO, X = Cl

Because the reaction with retronecine necessitated strong heating of the mixture initially, a sample of α-acetoxy-α-methylbutyryl chloride (IIc) was heated alone to a higher temperature (about 180°) for a similar time (2 minutes). This caused only slight decomposition; the infrared spectrum was essentially unchanged, and mild hydrolysis gave the acetoxy-acid (IIb) and only a trace of an unidentified acid.

Reaction of α-Acetoxy-α-methylbutyryl Chloride with Retronecine (Ia).—When retronecine hydrochloride was heated with an excess of α-acetoxy-α-methylbutyryl chloride (IIc), the expected diester (Ib) was not obtained. Instead, two bases were isolated as their picrates. The free bases, which both polymerized rapidly, were identified as 7β-acetoxy-1-chloromethyl-5,6,7,7a-tetrahydro-7aα-3*H*-pyrrolizine (Ic) (54% yield) and the 1-chloromethyl-7β-(α-hydroxy-α-methylbutyryl) derivative (Id) (20%). The identification was based on the following grounds. Compound (Ic) was identical with material prepared by acetylating the known [5] monochlororetronecine (Ie). A small yield of (Id) was obtained when the hydrochloride of monochlororetronecine (Ie) was treated with α-acetoxy-α-methylbutyryl chloride (the main product was Ic); thus it is a 1-chloromethylpyrrolizine derivative. Furthermore, (Id) on strong alkaline hydrolysis gave α-hydroxy-α-methylbutyric acid (IIa) but no acetic acid.

Reaction with Ethylene Glycol.—Clearly, the main reaction of α-acetoxy-α-methylbutyryl chloride (IIc) with retronecine (whose hydroxyl groups are close together, as in a vicinal diol), is to chlorinate and acetylate, respectively, the primary and secondary hydroxyl groups. To study this reaction further, a simple diol, ethylene glycol (IIIa), was used. Equimolecular amounts of glycol (IIIa) and the acid chloride (IIc) reacted rapidly at room temperature to give α-hydroxy-α-methylbutyric acid (IIa) (90%) and 2-chloroethyl acetate (IIIb) (<82%). As no other products were detected in significant amounts, it is likely that this surprising reaction is nearly quantitative. To test whether related compounds react in the same way, α-isobutyroxy-α-methylbutyryl chloride (IIf) was prepared. This reacted with ethylene glycol in the same way as the acetyl homologue, giving α-hydroxy-α-methylbutyric acid (IIa) (89%) and 2-chloroethyl isobutyrate (IIIc) (70%).

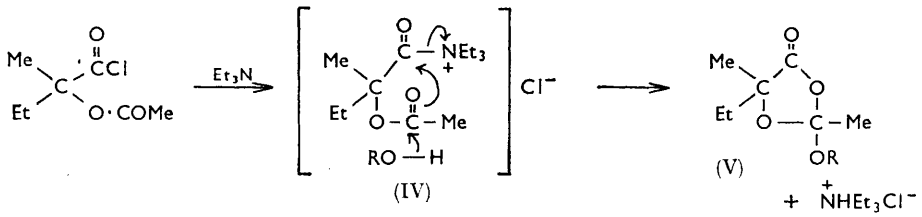
Reaction with Mono-alcohols under Basic Conditions.—In seeking a clue to the mechanism of the above reaction, a study was made of the reaction of α-acetoxy-α-methylbutyryl chloride (IIc) with some mono-alcohols. With an excess of methanol and of

[3] Hancock and Linstead, *J.*, 1953, **3490**.
[4] (*a*) Anschutz, *Ber.*, 1903, **36**, 467; (*b*) Benington and Morin, *J. Org. Chem.*, 1961, **26**, 194.
[5] Adams and Van Duuren, *J. Amer. Chem. Soc.*, 1954, **76**, 6379.

triethylamine, the expected methyl α-acetoxy-α-methylbutyrate (IIg) was not obtained; instead, the only product, compound M, was a neutral oil (~90%) with a camphor-like odour [a comparable product was formed when the isobutyroxy-acid chloride (IIf) was used]. Using ethanol in place of methanol, a similar compound, E, was obtained. A compound of this type was not isolated when the alcohol was omitted; with triethylamine in acetone, α-acetoxy-α-methylbutyric acid (IIb) was the only product.

The interesting compounds M and E are formulated as 5-ethyl-2-methoxy-2,5-dimethyl-1,3-dioxolan-4-one (V; R = Me) and its 2-ethoxy-homologue (V; R = Et), respectively, on the basis of the following evidence. (i) Compound M is hydrolysed slowly by hot water to α-acetoxy-α-methylbutyric acid (IIb), *i.e.*, the intact acetyl group is restored by mild hydrolysis; alkaline hydrolysis gives α-hydroxy-α-methylbutyric acid (IIa), acetic acid, and methanol; compound E behaves similarly, giving ethanol instead of methanol. (ii) When compound M is hydrolysed by aqueous acid, about equal amounts of methyl acetate and methanol are produced, together with the hydroxy- and acetoxy-acids (IIa) and (IIb); this supports the view that the methoxy-group is located on C-2. Similarly, E gives ethyl acetate and ethanol. (iii) In their infrared spectra (in chloroform), M and E both show a single strong carbonyl absorption at 1802 cm.$^{-1}$; no ester carbonyl band is present (cf. 1748 cm.$^{-1}$ for α-acetoxy-α-methylbutyric acid, and 1733 cm.$^{-1}$ for the acid chloride). Evidently the carbonyl character of the acetyl group has been lost in these compounds, yet the (modified) group is retained in the molecule. The absorption at 1802 cm.$^{-1}$ is consistent with a strained lactone ring (cf. β-propiolactone, 1841 cm.$^{-1}$; γ-butyrolactone, 1783 cm.$^{-1}$ in carbon tetrachloride [6]); M and E cannot be acid anhydrides, which would show two carbonyl absorption bands.[7a] Both M and E also show characteristic absorption at 911 cm.$^{-1}$, and a strong doublet at 1056—1058 and 1037—1040 cm.$^{-1}$. The latter could be due to the group C–O–C–O–C; diethers, including cyclic dioxolans, containing this group are reported [7b] to show four characteristic bands between 1200 and 1000 cm.$^{-1}$, and a strong doublet between 1150 and 1080 cm^{-1} is allocated to this group in saturated ethers.

The following mechanism is suggested for the formation of compounds M and E:



In the intermediate (IV), first formed, the strongly electrophilic carbon atom attached to the quaternary nitrogen reacts with the carbonyl oxygen atom of the acetyl group, which is sterically in a favourable position; simultaneous electrophilic attack by the carbonyl carbon atom of the acetyl group on an alcohol molecule leads to the cyclic compound (V; R = Me or Et).

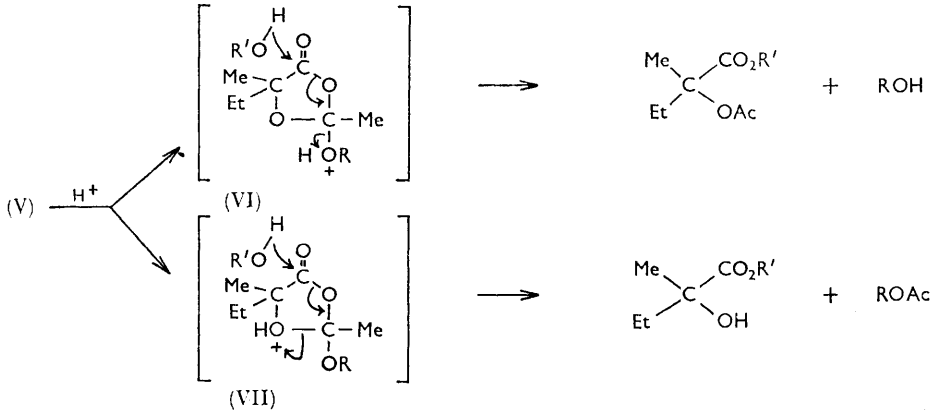
When pyridine was used in place of triethylamine for the reaction of methanol with the acid chloride (IIc), the product was a ~60 : 40 mixture of methyl α-acetoxy-α-methylbutyrate (IIg) and compound M. The ester (IIg) could not have been formed from M, since a pure sample of the latter was recovered almost unchanged after treatment with methanol and pyridine under similar conditions. Its formation directly from methanol and the acid chloride is explicable on steric grounds; in the intermediate (IV), the bulky triethylammonium group makes reaction of the adjacent carbon atom with another

[6] Searles, Tamres, and Barrow, *J. Amer. Chem. Soc.*, **1953**, **75**, 71.

[7] Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen, London, **1958**, (*a*) p. 127; (*b*) p. 116.

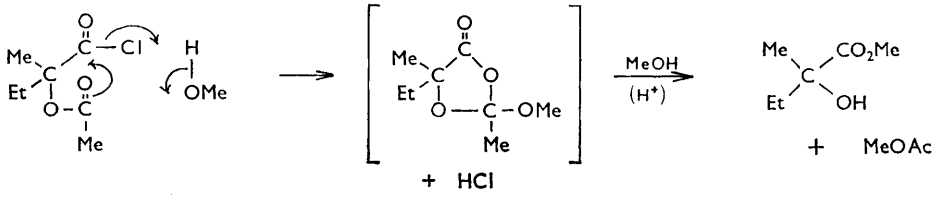
molecule very unlikely, compared with the ease of the intramolecular reaction. The smaller pyridinium group gives the intermolecular reaction a better chance of occurring. In agreement with this, the less hindered acetoxyacetyl chloride (XIIIc) and α-acetoxypropionyl chloride (XIIId) both react with methanol and triethylamine to give only the corresponding methyl esters (XIIIg) and (XIIIh).

Compounds M and E are hydrolysed slowly by water, as mentioned above, but rapidly in acid. Thus M was almost unchanged after shaking to an emulsion with water at room temperature for 1·5 hours, whereas with one equivalent of water containing hydrochloric acid (0·4 equivalent) hydrolysis was exothermic, and complete in a few minutes. The formation of both methyl acetate and methanol is consistent with the following mechanism:



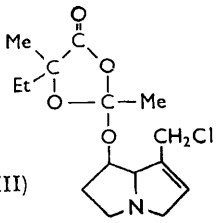
Protonation of an ether-oxygen atom of M (V; R = Me) leads to (VI; R = Me) or (VII; R = Me), which can react with water (R′ = H) to give, respectively, methanol and α-acetoxy-α-methylbutyric acid, and methyl acetate and α-hydroxy-α-methylbutyric acid. Similarly, in acidic methanol (R′ = Me), M should be converted into methyl α-acetoxy- or α-hydroxy-butyrate. In fact, when M was treated at room temperature with an equimolecular amount of hydrochloric acid in excess of methanol, the only high-boiling ester isolated was methyl α-hydroxy-α-methylbutyrate (IIh) (40%); thus it seems that this reaction proceeds only through (VII).

Reaction with Alcohols under Acid Conditions.—When the acid chloride (IIc) was refluxed with a ten-fold excess of methanol, the only high-boiling product (68% yield) was methyl α-hydroxy-α-methylbutyrate (IIh). (No attempt was made to isolate products boiling below 100°.) At or below room temperature, the product was the same, but in lower yield (54 and 10%, respectively); no acetoxy-ester (IIg) was obtained. The ester was identified by comparison with authentic methyl α-hydroxy- and α-acetoxy-α-methylbutyrate, prepared from the acids and diazomethane. To decide whether the hydroxy-ester (IIh) was formed simply by hydrolysis or methanolysis of initially formed acetoxy-ester (IIg), a sample of the latter was treated with methanolic hydrogen chloride under conditions similar to those for the esterification. An equimolecular amount of hydrochloric acid under reflux gave 95% of hydroxy-ester, but at room temperature a four-fold excess of hydrochloric acid gave only 15% of hydroxy-ester. Hence, in the reaction of methanol with α-acetoxy-α-methylbutyryl chloride, at least in the cold, the acetyl group must be removed from the latter either before or during the formation of the methyl ester group. Evidence for this is provided by the reaction of the acid chloride with only a small excess of methanol (1·2 equivalents). This gave compound M (51% yield), but no more than traces of (IIg) or (IIh). Compound M, with excess methanol and hydrochloric acid would, as already shown, give methyl α-hydroxy-α-methylbutyrate and methyl acetate:



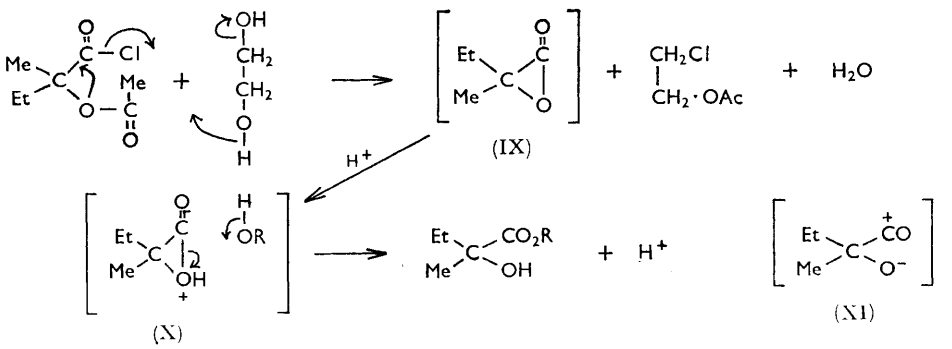
(The reaction with limited methanol also yielded some α-hydroxy-α-methylbutyric acid (31% yield) and methyl acetate. These could result, together with methyl chloride, from the acid chloride and two equivalents of methanol, in a similar way to the reaction with glycols.)

The reaction of α-acetoxy-α-methylbutyryl chloride with monochlororetronecine can be similarly explained. When an excess of the acid chloride (IIc) reacted with the hydrochloride of monochlororetronecine (Ie) under the same conditions as the reaction with retronecine hydrochloride, the main product (66% yield), as in the latter reaction, was the 7-acetyl derivative (Ic). The acetylation could occur through an intermediate (VIII) similar to M; hydrolysis of this (during working-up) by way of an intermediate of type (VII) would give the acetyl derivative (Ic). Alcoholysis of (VIII) by unreacted monochlororetronecine, again through (VII), could account for the small amount of 7-(α-hydroxy-α-methylbutyryl)-ester (Id) which was also formed.



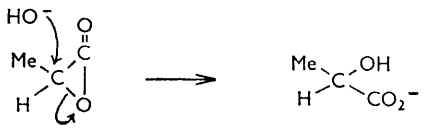
(VIII)

Mechanism of the Reaction of α-Acetoxy-α-methylbutyryl Chloride with Certain Diols.—A two-stage reaction, where the diol is first acetylated to give a hydroxy-ester, which later reacts with hydrochloric acid to form the chloro-ester, is unlikely for the following reasons: a large excess of hydrogen chloride is usually needed to give good yields of alkyl chloride from an alcohol; further, the more reactive allylic primary hydroxyl group of retronecine should be the first acetylated, to give a 1-acetoxymethyl compound, whereas in fact the 7-position is acetylated. It is significant that diacetyl and/or dichloro-derivatives have not been found among the major reaction products. The mechanism is thus likely to be one by which chlorination and transacylation occur simultaneously, the hydroxyl groups being suitably orientated with the appropriate groups on the acetoxy-acid chloride. It is also noteworthy that where, in retronecine (Ia), a choice of primary allylic hydroxyl and secondary hydroxyl groups is presented to the reagent, the allylic group is chlorinated, and the secondary group acetylated. The former, as would be expected, undergoes alkyl–oxygen fission whilst the latter is acylated through fission of the O–H bond. That the removal of the acetyl group from the reagent occurs not through alkyl–oxygen fission (like a t-butyl ester) but through acyl fission, is shown by the retention of configuration at the optical centre when the optically active acid chloride (IIc) reacts with ethylene glycol.



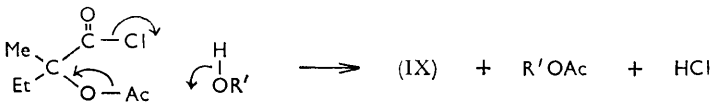
Scheme 1.

A mechanism which satisfies these requirements (Scheme 1) involves the transient formation of an α-lactone (IX). Such a labile intermediate has been proposed [8] to explain the stereochemistry of hydrolysis of α-bromopropionate ion in weakly alkaline solution, the lactone being hydrolysed by attack (S_N2) of hydroxyl ion on the optical centre, with inversion of configuration:



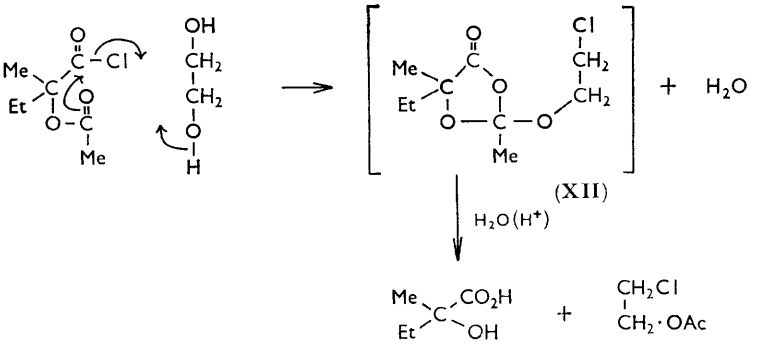
In the present case, (IX) can be hydrolysed in acid by way of (X; R = H), without affecting the optical centre, in agreement with the experimental results. It is possible, however, that an α-lactone is not formed at all, the labile intermediate being an ionic species such as (XI).

This mechanism is consistent with the very rapid formation of hydroxy-acid (IIa) when the acid chloride (IIc) reacts with ethylene glycol. It also provides an alternative or additional pathway for the previously discussed reaction of the acid chloride (IIc) with mono-alcohols (R'OH). Thus an alcohol (*e.g.*, methanol or monochlororetronecine hydrochloride) would be acetylated:



Any excess of alcohol would react with (IX) to give (*via* X; R = H) only the α-hydroxy-α-methylbutyryl ester of the alcohol [*e.g.*, (IIh) or (Id)]; in the absence of more alcohol, any water present would give the hydroxy-acid (IIa).

The discovery of compounds M and E, described above, suggests another mechanism by which α-acetoxy-α-methylbutyryl chloride might react with diols (Scheme 2). This involves the formation of a cyclic intermediate, similar to M, which is rapidly hydrolysed to a chloroalkyl acetate and α-hydroxy-α-methylbutyric acid. To test this, α-acetoxy-α-methylbutyryl chloride (IIc) was allowed to react with a slight excess of ethylene oxide. The only product was an oil G. This was closely similar to M and E, having characteristic strong infrared absorption bands at 1802, 1067, 1037, and 913 cm.$^{-1}$; hydroxyl and



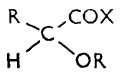
Scheme 2.

ester-carbonyl bands were absent. Hence G is formulated as (XII). However, G, which was fairly stable in cold water, was hydrolysed by aqueous acid almost entirely to α-acetoxy-α-methylbutyric acid and 2-chloroethanol; only a trace of 2-chloroethyl acetate was

[8] Waley, "Mechanisms of Organic and Enzymic Reactions," Oxford, 1962, p. 98.

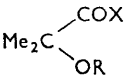
obtained. Hence it is likely that Scheme 2 accounts for only a small part of the reaction of the acid chloride with glycols; another mechanism, such as Scheme 1, being the major pathway.

Reactions of Other α-Acetoxy Acid Chlorides.—As a step towards defining the scope of the reactions discussed above, derivatives of the three simplest α-hydroxy-acids, glycollic acid (XIIIa), lactic acid (XIIIb), and α-hydroxy-isobutyric acid (XIVa), were used. With an equimolar amount of ethylene glycol, acetoxyacetyl chloride (XIIIc) gave a small yield of 2-chloroethyl acetate (IIIb); α-acetoxypropionyl chloride (XIIId) gave this product in much higher yield (at least 62%). The other products were esters, presumably



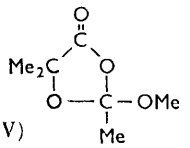
(XIII)

(a) R = R′ = H, X = OH
(b) R = Me, R′ = H, X = OH
(c) R = H, R′ = Ac, X = Cl
(d) R = Me, R′ = Ac, X = Cl
(e) R = H, R′ = Ac, X = OH
(f) R = Me, R′ = Ac, X = OH
(g) R = H, R′ = Ac, X = OMe
(h) R = Me, R′ = Ac, X = OMe



(XIV)

(a) R = H, X = OH
(b) R = Ac, X = Cl
(c) R = Ac, X = OMe



(XV)

of ethylene glycol with the acetoxy-acids (XIIIe) or (XIIIf). This is entirely consistent with the proposed mechanisms (Schemes 1 and 2). These both depend on the interaction of the two acyl groups, which are forced together by substituents on the common α-carbon atom, with one another and/or with adjacent hydroxyl groups. Acid chlorides, such as (XIIIc) and (XIIId), with small α-substituents have less chance of assuming the necessary configuration for this " abnormal " reaction; hence, more of the " normal " esters are formed. This steric factor is reflected, as already mentioned, in the formation, from (XIIIc) or (XIIId) with methanol and triethylamine, of only the " normal " methyl esters (XIIIg) and (XIIIh), and no cyclic compound comparable with (V). The fact that, in spite of this, (XIIIc) and (XIIId) still undergo the " abnormal " reaction with glycols, is further evidence in favour of a mechanism like Scheme 1, rather than Scheme 2, for this reaction.

α-Acetoxy-isobutyryl chloride (XIVb) gave the " abnormal " reaction with methanol and triethylamine, forming a cyclic compound, 2-methoxy-2,5,5-trimethyl-1,3-dioxolan-4-one (XV), and not the methyl ester (XIVc). Thus, two methyl groups are the minimum substituents needed on the α-carbon atom of an α-acetoxy-acid chloride to provide sufficient steric hindrance for the " abnormal " reaction with methanol and triethylamine to take place. With ethylene glycol, the acid chloride (XIVb) gave 2-chloroethyl acetate (IIIb) (at least 70%) and an almost quantitative yield of α-hydroxyisobutyric acid (XIVa).

The reactions described in this Paper suggest possible synthetic applications; *e.g.*, for the one-step preparation of chloro-esters from certain α-acyloxy-acid chlorides and suitable diols. The proposed mechanism (Scheme 1) suggests that a way might be found of demonstrating the existence of an α-lactone. Dioxolanones like (V) may be of value for synthesizing esters of α-hydroxy-α-methylbutyric and similar acids.

The formation of the dioxolanones (V) is an example of an intramolecular attack by an electrophilic group (COCl or $CO{\cdot}NR_3^+$) on a neighbouring carbonyl group. A number of examples are known [9] where hydrolysis or transesterification reactions are enhanced by neighbouring-group participation; the catalytic activity of some enzymes (esterases) is

[9] See, *e.g.*, Bruice and Sturtevant, *J. Amer. Chem. Soc.*, 1959, **81**, 2860; Bernhard, Berger, Carter, Katchalski, Sela, and Shalitin, *ibid.*, 1962, **84**, 2421; Ringold, Burstein, and Gut, *J. Org. Chem.*, 1963, **28**, 575; also refs. 8 and 10.

attributed to this type of reaction, and has been demonstrated with model compounds; in some cases cyclic intermediates were isolated; examples are the hydrolysis of phthalic acid mono-amide,[10a] and monomethyl ester,[10b] which proceed through phthalic anhydride. These are reactions of nucleophilic groups (O^- or N:) with the carbonyl-carbon atom of an ester or amide. The interesting feature of the present reaction is the incorporation of the carbonyl-oxygen atom into a ring structure.

Experimental

Paper Chromatography.—Descending chromatograms of the acids, as ethylamine salts [11] were run on Whatman No. 1 paper using butan-1-ol–ethylamine–water as solvent. Descending chromatograms of retronecine derivatives were run on Whatman No. 1 paper buffered with 0·1M-sodium acetate,[12] using butan-1-ol–acetic acid–water.[13] Spraying was with an aqueous solution of platinic chloride (0·003M) and potassium iodide (0·2M).

α-Hydroxy-α-methylbutyric Acid.—This, prepared by the method of Young *et al.*,[2] crystallized from benzene–light petroleum (b. p. 60—80°) as needles, m. p. 71·5°, R_F 0·35, of the (±) acid. To resolve it, the acid (10·2 g.) was neutralized with brucine (39·45 g.) in acetone, and the two brucine salts were recrystallized from methanol–acetone. The less-soluble salt (11·1 g.) had m. p. 194—195°, $[\alpha]_D^{20}$ −14·45° (*c* 6·29 in abs. EtOH); nine extractions of an acidified (HCl) aqueous solution of this salt with ether gave the (−)-acid, m. p. 76·5—77·5°, $[\alpha]_D^{20}$ −3·85° (*c* 14·74 in abs. EtOH). The more soluble brucine salt (8·5 g.), m. p. 178—180°, $[\alpha]_D^{20}$ −15·25° (*c* 6·48 in abs. EtOH) gave the (+)-acid, m. p. 76—77°, $[\alpha]_D^{20}$ +3·75° (*c* 16·0 in abs. EtOH).

α-Acetoxy-α-methylbutyric Acid.—α-Hydroxy-α-methylbutyric acid (100 g.) and acetyl chloride (200 ml.) were refluxed together on a steam-bath for 2 hr. Excess of reagent was removed under reduced pressure. The residue was shaken with water (200 ml.), adjusted to pH 9 (NaOH and $NaHCO_3$), washed twice with ether, and re-acidified (HCl). The product was extracted 5 times with ether, and the dried ($MgSO_4$) extract concentrated and distilled, to give the (±)-*α-acetoxy-acid* as a colourless syrup (80 g., 59%), b. p. 107°/0·2 mm., n_D^{20} 1·4312, R_F 0·50 (Found: C, 51·7; H, 7·3. $C_7H_{12}O_4$ requires C, 52·5; H, 7·5%).

Similarly were prepared the (−)-acetoxy-acid, n_D^{20} 1·4310, $[\alpha]_D^{20}$ −3·6° (*c* 8·3 in CCl_4), and the (+)-acetoxy-acid, n_D^{18} 1·4329, $[\alpha]_D^{20}$ +3·2° (*c* 1·77 in CCl_4), from the (−)- and (+)-hydroxy-acids, respectively.

α-Acetoxy-α-methylbutyryl Chloride.—(*a*) A mixture of (±)-α-acetoxy-α-methylbutyric acid (25 g.), oxalyl chloride (20 ml.), and benzene (50 ml.) was kept at 35—40° for 3 hr. The benzene and excess of reagent were removed under reduced pressure at about 40°. Benzene (15 ml.) was added, and removed in the same way; this was repeated twice. The residue yielded a colourless liquid (20 ml.), b. p. 49—52°/0·7—0·8 mm., n_D^{20} 1·4355. This was fractionally distilled through a 4 in. column of glass helices, to give pure (±)-*α-acetoxy-α-methylbutyryl chloride*, b. p. 43—45°/0·3—0·4 mm., n_D^{20} 1·4353 (Found: C, 47·1; H, 6·1; Cl, 19·9. $C_7H_{11}ClO_3$ requires C, 47·0; H, 6·2; Cl, 19·9%).

In the same way, from the (−)-acetoxy-acid (1·7 g.) the (+)-*acid chloride* was prepared (1·35 g.), b. p. 47—48°/0·6—0·7 mm., n_D^{20} 1·4355, $[\alpha]_D^{20}$ +27·8° (*c* 9·0 in CCl_4). Similarly, the (+)-acetoxy-acid gave the (−)-*chloride*, n_D^{18} 1·4365, $[\alpha]_D^{20}$ −24·0° (*c* 5·0 in CCl_4).

(*b*) Crude (±)-α-hydroxy-α-methylbutyric acid (99 g.) and acetyl chloride (180 ml.) were mixed cautiously and refluxed together for 2 hr. After removal of the excess acetyl chloride under reduced pressure, the residue was refluxed with thionyl chloride (115 g.) for 2 hr. Excess of reagent was removed under reduced pressure. Benzene (50 ml.) was added, and removed under reduced pressure at about 50°. This was repeated twice. The residue gave pure (±)-α-acetoxy-α-methylbutyryl chloride (101 g., 67%), b. p. 51°/0·7 mm., n_D^{20} 1·4355.

The (±)-acid chloride reacted with an excess of aniline in benzene to give *α-acetoxy-α-methylbutyranilide*, needles from ether–light petroleum (b. p. 30—40°), m. p. 71—72° (Found: C, 66·5; H, 7·5; N, 6·1. $C_{13}H_{17}NO_3$ requires C, 66·4; H, 7·2; N, 6·0%).

Alkaline Hydrolysis of α-Acetoxy-α-methylbutyryl Chloride.—(*a*) The (+)-acid chloride (110

[10] (*a*) Bender, Yuan-Lang Chow, and Chloupek, *J. Amer. Chem. Soc.*, 1958, **80**, 5380; (*b*) Bender, Chloupek, and Neveu, *ibid.*, 1958, **80**, 5384.
[11] Manganelli and Brofazi, *Anal. Chem.*, 1957, **29**, 1441.
[12] Munier, Macheboeuf, and Cherrier, *Bull. Soc. Chim. biol.*, 1952, **34**, 204.
[13] Crawley and Culvenor, *Austral. J. Chem.*, 1959, **12**, 694.

mg.) was shaken with saturated sodium hydrogen carbonate solution (4 ml.) at 0—10° for 10 min.; the solution was washed with ether, acidified (HCl), and extracted with ether, to give (−)-α-acetoxy-α-methylbutyric acid (95 mg., 96%), R_F 0·50, $[\alpha]_D^{15}$ −3·6° (*c* 6·1 in CCl_4).

(*b*) The (+)-acid chloride (0·3 g.) was hydrolysed with 3N-sodium hydroxide solution (2 ml.) at 100° for 30 min., and the cooled solution acidified (HCl), and extracted 9 times with ether. The dried (Na_2SO_4) extract was concentrated, to give (−)-α-hydroxy-α-methylbutyric acid (0·18 g., 90%) which after recrystallization had m. p. 75—76°, $[\alpha]_D^{20}$ −4·6° (*c* 7·5 in abs. EtOH). The crude extract, on chromatography, showed 2 spots, of R_F 0·18 (acetic acid), and 0·35 (α-hydroxy-acid).

Action of Heat on α-Acetoxy-α-methylbutyryl Chloride.—The (±)-chloride was heated under reflux (about 180°) for 2 min.; the pale brown material was hydrolysed with sodium hydrogen carbonate soution; a paper chromatogram showed a large spot, R_F 0·50, of α-acetoxy-α-methylbutyric acid, and a very small spot, R_F 0·79 (unknown acid). There was no trace of acetic acid (R_F 0·17).

Methyl α-Hydroxy-α-methylbutyrate.—Prepared from (±)-α-hydroxy-α-methylbutyric acid and diazomethane in ether solution, the ester had b. p. 150°, n_D^{20} 1·4155 (Found: C, 54·0; H, 9·0. Calc. for $C_6H_{12}O_3$: C, 54·5; H, 9·1%) [lit.,[14] b. p. 153°, n_D^{25} 1·4137 for the (−)-methyl ester].

Methyl α-Acetoxy-α-methylbutyrate.—Prepared from (±)-α-acetoxy-α-methylbutyric acid and diazomethane in ether solution, the *ester* had b. p. 186°, n_D^{20} 1·4200 (Found: C, 55·1; H, 8·0. $C_8H_{14}O_4$ requires C, 55·2; H, 8·0%).

α-Isobutyroxy-α-methylbutyric Acid.—A mixture of (±)-α-hydroxy-α-methylbutyric acid (10 g.) and isobutyryl chloride (20 g.) was heated under reflux for 1 hr. on a steam-bath. Excess of acid chloride was removed under reduced pressure and the residue was shaken for 10 min. with water (100 ml.) and sufficient sodium hydrogen carbonate to maintain alkalinity. The solution was washed twice with ether, acidified (HCl), extracted with ether 4 times, the dried (Na_2SO_4) extract concentrated, and the residue distilled, to give the *α-isobutyroxy-acid* as a syrup (8 g., 50%), b. p. 120°/0·8 mm., n_D^{20} 1·4302, R_F 0·72 (Found: C, 57·3; H, 8·6. $C_9H_{16}O_4$ requires C, 57·5; H, 8·5%).

α-Isobutyroxy-α-methylbutyryl Chloride.—Prepared from the acid (5 g.) and oxalyl chloride (6 g.) as described for the α-acetoxy-acid chloride, the *chloride* (5·1 g., 93%) had b. p. 65—68°/0·8—0·9 mm., n_D^{20} 1·4554 (Found: C, 52·4; H, 7·3; Cl, 17·1. $C_9H_{15}ClO_3$ requires C, 52·3; H, 7·3; Cl, 17·2%).

Reaction of α-Acetoxy-α-methylbutyryl Chloride with Retronecine Hydrochloride.—A mixture of finely powdered retronecine hydrochloride (0·8 g.; prepared by hydrolysis of the alkaloid monocrotaline, from *Crotalaria retusa* [15]) and the acid chloride (2 g.) was heated for 1—2 min. at 150—160°, until the solid dissolved, and then at 100° for 1 hr. The cooled mixture was diluted with water (10 ml.) and washed with ether. The aqueous solution was made alkaline with disodium phosphate, extracted twice with ether, further basified with sodium hydroxide, and again extracted with ether. A paper chromatogram of the crude bases showed two spots, R_F 0·67 and 0·88. The combined basic extracts were at once neutralized with ethanolic picric acid. Crystals (1 g.) separated, m. p. 180—183°; 3 recrystallizations from acetone–ethanol gave needles, $[\alpha]_D^{20}$ −36·1° (*c* 3·38 in acetone), m. p. 195° (decomp.) not depressed when mixed with 7β-acetoxy-1-chloromethyl-5,6,7,7α-tetrahydropyrrolizine picrate (see below).

The mother-liquors yielded a second picrate (0·45 g.). Three recrystallizations from ethanol gave *1-chloromethyl-7β-(α-hydroxy-α-methylbutyroxy)-5,6,7,7a-tetrahydropyrrolizine picrate* as blades, m. p. 145—146°, $[\alpha]_D^{20}$ −28·9° (*c* 5·06 in acetone) (Found: C, 45·2; H, 4·3; Cl, 7·05; N, 11·4. $C_{19}H_{23}ClN_4O_{10}$ requires C, 45·4; H, 4·2; Cl, 7·1; N, 11·1%). The *hydrochloride*, obtained from this picrate using Dowex 1 (OH^- form) resin and hydrochloric acid, formed a gum, $[\alpha]_D^{20}$ −40·5° (*c* 1·72 in H_2O). The free *base*, R_F 0·88, polymerized rapidly. This base was hydrolysed by refluxing with 2N-sodium hydroxide for 1 hr.; the solution was acidified (HCl) and extracted with ether, to give a single acid with the same R_F, 0·35, as α-hydroxy-α-methylbutyric acid.

7β-Acetoxy-1-chloromethyl-5,6,7,7a-tetrahydropyrrolizine.—Monochlororetronecine hydrochloride (0·2 g.; R_F of base 0·53), prepared from retronecine and thionyl chloride,[5] was refluxed

[14] Christensen and Kjaer, *Acta Chem. Scand.*, 1962, **16**, 2466.
[15] Adams and Rogers, *J. Amer. Chem. Soc.*, 1939, **61**, 2815.

with acetyl chloride (3 ml.) in diglyme (dimethylene glycol dimethyl ether; 3 ml.) for 1·5 hr. Excess of reagent and solvent were removed on a steam-bath under reduced pressure. The residue, in water, was made alkaline with disodium phosphate, extracted twice with ether, further basified (NaOH), and extracted once more with ether. The combined extracts were neutralized at once with ethanolic picric acid, to give the *acetylchlororetronecine picrate* (0·37 g., 87%), needles (from acetone–ethanol), m. p. 195° (decomp.), $[\alpha]_D^{20}$ −36·0° (*c* 3·28 in Me_2CO) (Found: C, 43·5; H, 4·0; Cl, 7·95; N, 12·4. $C_{16}H_{17}ClN_4O_9$ requires C, 43·2; H, 3·8; Cl, 8·0; N, 12·6%). The picrate, in acetone–methanol, was passed through a column of Dowex 1 resin (OH^- form), and the eluate was immediately neutralized (ethanolic HCl) and concentrated to dryness, to give the *hydrochloride* as a colourless gum, $[\alpha]_D^{20}$ −55·5° (*c* 3·93 in H_2O). The free base, R_F 0·67, polymerized rapidly.

Reaction of α-Acetoxy-α-methylbutyryl Chloride with Monochlororetronecine.—The acid chloride (1 g.) was allowed to react with monochlororetronecine hydrochloride (0·5 g.) under the same conditions as those described for retronecine hydrochloride. Treatment of the ether extract with picric acid gave almost pure 7β-acetoxy-1-chloromethyl-5,6,7,7a-tetrahydropyrrolizine picrate (0·7 g., 66%), m. p. and mixed m. p. 195° (decomp.) (from acetone–ethanol). From the concentrated picrate mother-liquors, was obtained a second picrate (0·1 g.), m. p. 147—148° not depressed by the second picrate obtained from the acid chloride and retronecine hydrochloride.

Reactions of α-Acetoxy-α-methylbutryl Chloride.—(*a*) *With ethylene glycol.* The (±)-acid chloride (1·78 g., 10 mmoles) and glycol (0·62 g., 10 mmoles) were mixed at about 0°, emulsified by shaking, and allowed to warm to room temperature. Within a few minutes a sudden reaction took place with spontaneous warming (controlled by external cooling); the mixture became a single phase which rapidly deposited a mass of crystals. After a further 10 min. at room temperature, the mass was triturated with light petroleum (b. p. 30—40°) and filtered, yielding (±)-α-hydroxy-α-methylbutyric acid (1·1 g., 93%), m. p. and mixed m. p. 71·5° (from ether–light petroleum). The filtrate was washed with sodium hydrogen carbonate solution, concentrated, and distilled to give 2-chloroethyl acetate (1·0 g., 82%), b. p. 145°, n_D^{20} 1·4239. The infrared spectrum was identical with that of an authentic sample, b. p. 145°, n_D^{20} 1·4240.

When the above procedure was repeated using the (+)-acid chloride, the α-hydroxy-α-methylbutyric acid formed had m. p. 76—77°, $[\alpha]_D^{20}$ −4·25° (*c* 16·5 in abs. EtOH), *i.e.*, there was no change in configuration.

(*b*) *With ethylene oxide.* The acid chloride (3·6 g., 20 mmoles) and ethylene oxide (1·2 g., 27 mmoles) were mixed at 0° and allowed to warm slowly until reaction occurred, with spontaneous warming to 20—30°, for about 5 min. After 30 min. (total) the mixture was dissolved in ether, washed with water and sodium hydrogen carbonate solution, dried (Na_2SO_4), and concentrated, to give an oil (4·45 g., almost 100%) with a faint camphor-like odour. Distillation at 88—89°/0·2 mm. gave *compound G*, n_D^{20} 1·4445 (Found: C, 48·7; H, 6·8; Cl, 16·7. $C_9H_{15}ClO_4$ requires C, 48·6; H, 6·7; Cl, 15·9%).

Compound G was recovered largely unchanged after shaking to an emulsion with water for 30 min. at room temperature. When G (0·4 g.) was warmed and shaken with water (0·03 ml.) and concentrated hydrochloric acid (0·01 ml.) a rapid reaction occurred. After 10 min. at room temperature, ether was added and the mixture washed with sodium hydrogen carbonate solution. The ether yielded a mixture (15 mg.) of 2-chloroethyl acetate and (a little) 2-chloroethanol. The aqueous washings contained much 2-chloroethanol. From them, after acidification, was obtained an acid which was almost entirely α-acetoxy-α-methylbutyric acid (0·25 g., 90%).

Reactions of α-Isobutyroxy-α-methylbutyryl Chloride.—(*a*) *With ethylene glycol.* The acid chloride (2·06 g., 10 mmoles) and glycol (0·62 g., 10 mmoles) were allowed to react under the same conditions as those described for the reaction of α-acetoxy-α-methylbutyryl chloride with glycol. A similar reaction took place, yielding (±)-α-hydroxy-α-methylbutyric acid (1·05 g., 89%), m. p. mixed m. p. 71·5° (from ether–light petroleum). The filtrate gave a colourless oil (1·35 g.) which yielded 2-*chloroethyl isobutyrate* (1·05 g., 70%), b. p. 168—170°, n_D^{20} 1·4247. This was identical (infrared spectrum) with material prepared from 2-chloroethanol and isobutyryl chloride, which had b. p. 168—169°, n_D^{20} 1·4250 (Found: C, 47·9; H, 7·5; Cl, 23·8. $C_6H_{11}ClO_2$ requires C, 47·8; H, 7·3; Cl, 23·6%).

(*b*) *With methanol and triethylamine.* The acid chloride (0·5 g., 2·5 mmoles) reacted with methanol (2 ml.) and triethylamine (0·8 ml.) under similar conditions to the reaction of

α-acetoxy-α-methylbutyryl chloride with these compounds, to give an oil (0·5 g., 99%); vacuum distillation gave *5-ethyl-2-isopropyl-2-methoxy-5-methyl-1,3-dioxolan-4-one*, b. p. 56°/0·04 mm., n_D^{20} 1·4290 (Found: C, 59·4; H, 8·8. $C_{10}H_{18}O_4$ requires C, 59·4; H, 8·9%). The infrared spectrum showed a single carbonyl band at 1795 cm.$^{-1}$.

Reactions of α-Acetoxy-α-methylbutyryl Chloride.—(*a*) *With a large excess of methanol.* The acid chloride (2 g., 11 mmoles) was added to ice cold methanol (3 g., 90 mmoles); after warming slowly to room temperture the mixture was refluxed (steam-bath) for 30 min., cooled, shaken with saturated sodium hydrogen carbonate solution (15 ml.) for 5 min., and extracted 3 times with ether. The extract was washed thrice with water, dried (Na_2SO_4), and concentrated, to give methyl α-hydroxy-α-methylbutyrate (1 g., 68%), b. p. 148°, n_D^{20} 1·4159. The infrared spectrum was identical with that of an authentic specimen of the ester (see above).

The same product was obtained when the above reaction was carried out at room temperature or at 0° instead of under reflux, but the yields were lower (54 and 10%, respectively).

(*b*) *With limited methanol.* The acid chloride (1·78 g., 10 mmoles) and methanol (0·38 g., 12 mmoles) were mixed at 0° and kept at 0—10° for 5 min. (HCl was evolved), then partly distilled under reduced pressure at 10—20°. The distillate was identified by its infrared spectrum as methyl acetate with a little methanol. Crystals in the residue were collected after addition of light petroleum (b. p. 30—40°), and identified as α-hydroxy-α-methylbutyric acid, m. p. and mixed m. p. 71° (from ether–light petroleum) (0·37 g.). The light-petroleum filtrate, after washing with sodium hydrogen carbonate solution and water, drying (Na_2SO_4), and concentration, yielded an oil (0·9 g.), n_D^{20} 1·4203, almost identical with the product from (*c*) (below); only a trace of ester (weak carbonyl band at 1740 cm.$^{-1}$) was present.

(*c*) *With methanol and triethylamine.* The acid chloride (2·5 g.) was added slowly, with shaking and cooling, to a mixture of methanol (8 ml.) and triethylamine (2·5 ml.). After 30 min. at room temperature the mixture was diluted with water (20 ml.), acidified (cooling) with hydrochloric acid, and immediately extracted twice with ether. The combined extracts were washed with water, saturated sodium hydrogen carbonate solution, twice more with water, dried (Na_2SO_4), and concentrated, to give a colourless mobile oil, n_D^{20} 1·4200 (2·2 g., 91%) with a strong camphor-like odour. This decomposed when heated at 1 atm. but almost all distilled *in vacuo*, to give pure *5-ethyl-2-methoxy-2,5-dimethyl-1,3-dioxolan-4-one* (compound M), b. p. 49°/0·3 mm., n_D^{20} 1·4198 (Found: C, 55·4; H, 8·2. $C_8H_{14}O_4$ requires C, 55·1; H, 8·1%). Material prepared from the (+)-acid chloride had $[\alpha]_D^{20}$ +15·3° (*c* 3·28 in CCl_4).

Compound M contained no N or Cl, was immiscible with water, and neutral. It was unchanged (infrared spectrum) after more than 4 weeks at room temperature in a dry atmosphere. When shaken with hot water it was hydrolysed to α-acetoxy-α-methylbutyric acid (infrared spectrum, and R_F 0·50), and methanol (infrared). In 3N-sodium hydroxide it was hydrolysed to acetic acid (R_F 0·18) and α-hydroxy-α-methylbutyric acid.

(*d*) *With ethanol and triethylamine.* By the procedure described in (*c*), using ethanol instead of methanol, an oil with camphor-like odour was obtained; vacuum distillation gave *2-ethoxy-5-ethyl-2,5-dimethyl-1,3-dioxolan-4-one* (compound E), b. p. 61—62°/0·6 mm., n_D^{20} 1·4207 (Found: C, 58·0; H, 8·7. $C_9H_{16}O_4$ requires C, 57·5; H, 8·5%). Compound E had properties similar to M. It was hydrolysed by hot water to α-acetoxy-α-methylbutyric acid and ethanol.

(*e*) *With triethylamine in acetone.* When acetone was substituted for methanol in procedure (*c*), no neutral product was obtained, and only α-acetoxy-α-methylbutyric acid, R_F 0·50, was recovered from the mother-liquors.

(*f*) *With methanol and pyridine.* When the triethylamine in procedure (*c*) was replaced by an equimolar amount of pyridine, the product, n_D^{20} 1·4207, was a mixture of methyl α-acetoxy-α-methylbutyrate and compound M, in a ratio of about 6 : 4, as shown by comparison of the infrared spectrum with those of authentic mixtures. The mixture was altered in composition, but not separated, by distillation *in vacuo*.

When pure compound M was treated with pyridine and methanol under similar conditions, but for 1 hr., less than 5% of it was converted into methyl α-acetoxy-α-methylbutyrate, the rest being unchanged.

Action of Methanolic Hydrogen Chloride on Methyl α-Acetoxy-α-methylbutyrate.—Mixtures of the acetoxy-ester (0·5 g., 2·87 mmoles) and methanol (1 ml.) containing hydrogen chloride, were kept at room, or reflux, temperature for 30 min. Ether (15 ml.) was added, and the solution was washed with saturated sodium hydrogen carbonate solution (3 × 2 ml.) and water (2 ml.), dried (Na_2SO_4), and the ether removed, leaving an oil (about 0·4 g.). The percentages

of starting material and methyl α-hydroxy-α-methylbutyrate in this oil were estimated by comparing its infrared spectrum with those of mixtures of the two esters.

	Hydrogen chloride used			Product	
Run	(mmoles)	(Equiv. compared with acetoxy-ester)	Temp.	n_D^{20}	% hydroxy-ester
1	2·87	1·0	Room temp.	1·4190	15
2	11·5	4·0	Room temp.	1·4192	15
3	2·87	1·0	Reflux	1·4165	95
4	0·57	0·2	Reflux	1·4183	25

Reactions of Compound M.—(*a*) *With methanolic hydrogen chloride.* Compound M (0·435 g., 2·5 mmoles) and methanol (0·8 g., 25 mmoles) containing hydrogen chloride (2·5 mmoles) were mixed at room temperature; the mixture became warm. After standing at room temperature for 30 min., part of the mixture was distilled at 20—30° under reduced pressure. The distillate contained methyl acetate and a little methanol (infrared spectrum). The residue was dissolved in ether and the solution washed with sodium hydrogen carbonate solution and water, dried (Na_2SO_4), and concentrated. The residue, n_D^{20} 1·4146, was entirely methyl α-hydroxy-α-methylbutyrate (infrared spectrum) (0·13 g., 40%).

(*b*) *With hydrochloric acid.* Compound M (0·4 g., 2·3 mmoles) and concentrated hydrochloric acid (0·041 ml.; 2·3 mmoles water and about 0·4 mmoles HCl) were shaken to an emulsion at room temperature. The oily phase disappeared rapidly, with spontaneous heating. After 5 min., volatile material was distilled at room temperature under reduced pressure into a cold trap. The distillate consisted (infrared spectrum) of methyl acetate and methanol (about equal amounts). Acid extracted from the residue contained both α-hydroxy-α-methylbutyric acid (R_F 0·35) and α-acetoxy-α-methylbutyric acid (R_F 0·50).

(*c*) *With water.* When equimolecular amounts of compound M and water were shaken to an emulsion at room temperature for 1·5 hr., most of the compound was recovered unchanged.

Reactions of Acetoxyacetyl Chloride.—(*a*) *With ethylene glycol.* The acid chloride,[4] b. p. 33°/0·15 mm., n_D^{20} 1·4266 (lit.,[4a] b. p. 51°/14 mm.) (1·36 g., 10 mmoles), and glycol (0·62 g., 10 mmoles) were shaken to an emulsion below room temperature and allowed to warm up slowly until a vigorous exothermic reaction occurred, with evolution of some hydrogen chloride; this was moderated by external cooling. After a further 10 min. at room temperature, ether (20 ml.) was added; the solution was washed with sodium hydrogen carbonate solution (twice) and with water, dried (Na_2SO_4), and concentrated, to give an oil (1·12 g.), n_D^{20} 1·4307. Distillation gave almost pure 2-chloroethyl acetate (0·135 g., 1·1 mmoles), b. p. 144—149°, n_D^{20} 1·4235, identical (infrared spectrum) with authentic material. The remainder, b. p. 150—>220° was a mixture of unidentified esters with a little 2-chloroethyl acetate.

(*b*) *With methanol and triethylamine.* The acid chloride (0·5 g., 3·65 mmoles) was added slowly to a mixture of methanol (2 ml.) and triethylamine (0·8 ml.). After cooling to room temperature and keeping for 15 min., the mixture was diluted with water, acidified (HCl), and extracted twice with ether. The extract was washed with water, sodium hydrogen carbonate solution (twice), and water (twice), dried (Na_2SO_4), and concentrated, to give methyl acetoxyacetate (0·25 g., 52%), n_D^{20} 1·4100, identical (infrared spectrum) with authentic material, n_D^{20} 1·4110, prepared from acetoxyacetic acid and diazomethane.

Reactions of α-Acetoxypropionyl Chloride.—(*a*) *With ethylene glycol.* The acid chloride, b. p. 31°/0·25 mm., n_D^{17} 1·4230 (lit.,[16] b. p. 56°/11 mm., n_D^{17} 1·4241) (1·5 g., 10 mmoles), and glycol (0·62 g., 10 mmoles) were allowed to react under the same conditions as those described using acetoxyacetyl chloride (above); working up in the same way gave an oil (1·08 g.), n_D^{20} 1·4257, which gave almost pure 2-chloroethyl acetate (0·76 g., 6·2 mmoles), b. p. 143—149°, n_D^{20} 1·4240. The remainder, b. p. 150—>210°, probably contained more 2-chloroethyl acetate together with another ester which was not identified.

(*b*) *With methanol and triethylamine.* The acid chloride (0·5 g., 3·3 mmoles) was added to methanol (2 ml.) and triethylamine (0·8 ml.) under the conditions already described for acetoxyacetyl chloride. Working up in the same way yielded methyl α-acetoxy propionate (0·38 g., 86%), b. p. 170°, n_D^{20} 1·4093, identical (infrared spectrum) with authentic material, b. p. 170°, n_D^{20} 1·4093, obtained from acetyl-lactic acid and diazomethane. The crude material showed no band in the region of 1802 $cm.^{-1}$.

[16] Auger, *Compt. rend.*, 1905, **140**, 938.

α-Acetoxyisobutyryl Chloride.—α-Acetoxyisobutyric acid (10 g.) was refluxed with acetyl chloride (20 ml.) for 2 hr., excess of reagent was removed under reduced pressure, and the residue was refluxed with thionyl chloride (10 ml.) for 2½ hr. The excess of reagent was distilled off, and benzene (5 ml.) was added, and removed under reduced pressure; this was repeated twice. Distillation of the residue gave the *acetoxy-acid chloride* (9·45 g., 60%), b. p. 28°/0·1 mm., n_D^{20} 1·4290 (Found: C, 43·6; H, 5·3. $C_6H_9ClO_3$ requires C, 43·7; H, 5·5%).

Reactions of α-Acetoxyisobutyryl Chloride.—(*a*) *With ethylene glycol.* The acid chloride (1·645 g., 10 mmoles) and glycol (0·62 g., 10 mmoles) were allowed to react under the same conditions as described for α-acetoxy-α-methylbutyric acid and glycol. After the reaction, the mixture was cooled, giving crystals (1·02 g., 98%) of α-hydroxy-isobutyric acid, m. p. and mixed m. p. 77—79° (from ether–light petroleum). The liquor, worked up as before, yielded almost pure 2-chloroethyl acetate (0·86 g., 70%), n_D^{20} 1·4240, b. p. 144°.

(*b*) *With methanol and triethylamine.* The acid chloride (1 g., 6 mmoles) was added slowly to a mixture of methanol (4 ml.) and triethylamine (1·5 ml.), with shaking and cooling to room temperature. After standing for 10 min. at room temperature, the mixture was worked up as that from the reaction of acetoxyacetyl chloride with methanol and triethylamine, to give an oil (0·71 g., 74%). Distillation gave *2-methoxy-2,5,5-trimethyl-1,3-dioxolan-4-one*, b. p. 33°/0·02 mm., n_D^{20} 1·4115 (Found: C, 52·5; H, 7·6. $C_7H_{12}O_4$ requires C, 52·5; H, 7·5%). The infrared spectrum of the crude material showed only a slight inflexion at 1739 cm.$^{-1}$ (ester).

Infrared Spectra.—These were recorded with a Perkin-Elmer Infracord model 137 instrument. Maxima (cm.$^{-1}$) are given for solutions in dry, alcohol-free chloroform except where otherwise stated.

(±)-α-Hydroxy-α-methylbutyric acid. 3472m (OH), 2941s, 1715s (C=O), 1453m, 1370m, 1176s, 1035m, 935m.

(±)-α-Acetoxy-α-methylbutyric acid (film). 1748 (ester C=O) and 1724 (acid C=O). Also strong bands at 2985, 1466, 1370, 1250, 1142, 1022, 952, 876.

(±)-α-Acetoxy-α-methylbutyryl chloride. 2940m, 1790s (chloride C=O), 1733s (ester C=O), 1451m, 1366m, 1242s, 1205s, 1149m, 1124m, 1054m, 1024m, 952m, 872w, 844m, 813m.

(±)-α-Isobutyroxy-α-methylbutyryl chloride. 2950m, 2933m, 2857w, 1792s (chloride C=O), 1739s (ester C=O), 1462m, 1387m, 1372m, 1348w, 1259m, 1192m, 1143s, 1070m, 1020w, 1101w, 953m, 893w, 857m, 806m.

Methyl α-hydroxy-α-methylbutyrate. 3509m (OH), 2941m, 1730s (C=O), 1458m, 1433m, 1370w, 1248s, 1176s, 1035m, 1010m, 980m, 935m.

Methyl α-acetoxy-α-methylbutyrate. 2995w, 2940w, 1742s (C=O), 1458m, 1433m, 1370m, 1258s, 1160m, 1129m, 1054w, 1017m, 980w, 951w.

Compound M. 2940m, 1802s (C=O), 1456m, 1389s, 1369m, 1305m, 1274s, 1212s, 1198s, 1176s, 1151s, 1056s, 1037s, 1000m, 951m, 911s, 897m, 847w, 784w, 743w, 712w.

Compound E. 2940m, 1802s (C=O), 1450m, 1381m, 1305m, 1274s, 1241s, 1206s, 1167s, 1099m, 1058s, 1040s, 1000m, 980m, 987m, 943m, 911s, 895m, 844w, 784w, 743w, 712w.

Compound G. 2940m, 1802s (C=O), 1451m, 1389m, 1271m, 1163s, 1067s, 1037s, 1000w, 966m, 942m, 913s.

2-Methoxy-2,5,5-trimethyl-1,3-dioxolan-4-one. 2967m, 2933w, 2817w, 1802s (C=O), 1460m, 1435w, 1389s, 1368w, 1300m, 1256m, 1183s, 1157s, 1058m (infl.), 1049s, 995m, 942m, 912s, 858w.

The microanalyses were by Mrs. G. M. Ostler.

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