243. *Elimination Reactions of Esters. Part I. The Formation of αβ-Unsaturated Acids from β-Acyloxy-compounds.*

By R. P. LINSTEAD, L. N. OWEN, and R. F. WEBB.

The action of alkali on β-acyloxy-esters $>C(OY)\cdot CH_2\cdot CO_2R$, under conditions when the parent β-hydroxy-compounds (Y = H) are not dehydrated, gives the unsaturated product $>C{:}CH\cdot CO_2H$ when Y = Ac, COPh, PO_3H_2, $PO(OPh)_2$, NO_2, SO_2Me, or $SO_2\cdot C_6H_4Me$-*p*, the proportion of elimination to hydrolysis (at the β-carbon atom) increasing with the strength of the acid YOH. The proportion of elimination is also greater when the resulting unsaturated acid is highly conjugated.

THIS series of papers is concerned with a novel reaction of certain esters, which can be represented by the general scheme :

$$YO\cdot CRR'\cdot CHR''\cdot X + OH^- \longrightarrow CRR'{:}CR''\cdot X + YO^- + H_2O$$

where X = an electron-attracting group, such as carbalkoxyl, and Y = an acyl group, such as R·CO, or $R\cdot SO_2$. Thus, when β-hydroxy-esters and similar compounds are acylated and subsequently treated with alkali, the normal hydrolysis of the acyl group (Y) may be either partly or wholly superseded by elimination, with the formation of an αβ-double bond. The present paper is concerned with the simple cases in which R, R′, and R″ are all hydrogen, alkyl, or aryl. As the general reaction has not previously been examined we have begun with a survey of its scope and potentialities and have not as yet studied the mechanism in detail.

The reaction is related to the formation of αβ-unsaturated products by the action of bases on the corresponding β-halides. Whilst there are many examples of this, the observed eliminations of β-acyloxy-groups are few and scattered. Blaise and Maire (*Ann. Chim. Phys.*, 1908, **15**, 556) found that the ketone (I) on treatment with hot aqueous alkali gave the unsaturated compound (II). Schmidt and Rutz (*Ber.*, 1928, **61**, 2142) converted a series of β-acetyloxynitro-compounds (III) into the nitro-olefins (IV) by reaction with potassium hydrogen carbonate in ether. In applying the latter reaction to carbohydrate chemistry, Fischer and Sowden (*J. Amer. Chem. Soc.*, 1947, **69**, 1048) showed

$$\underset{\text{(I)}}{\mathrm{CH_3{\cdot}CH(OAc){\cdot}CHEt{\cdot}COEt}} \longrightarrow \underset{\text{(II)}}{\mathrm{CH_3{\cdot}C{:}CEt{\cdot}COEt}} \qquad \underset{\text{(III)}}{\mathrm{R{\cdot}CH(OAc){\cdot}CH_2{\cdot}NO_2}} \longrightarrow \underset{\text{(IV)}}{\mathrm{R{\cdot}CH{:}CH{\cdot}NO_2}}$$

$$\underset{\text{(V)}}{\mathrm{AcO{\cdot}CH_2{\cdot}[CH(OAc)]_4{\cdot}CH_2{\cdot}NO_2}} \longrightarrow \underset{\text{(VI)}}{\mathrm{AcO{\cdot}CH_2{\cdot}[CH(OAc)]_3{\cdot}CH{:}CH{\cdot}NO_2}}$$

that only β-acetoxy-groups were eliminated; thus (V) gave (VI). The isomerisation of certain lactones to unsaturated compounds by bases is a related process, first observed by Beschke (*Annalen*, 1911, **384**, 143) and by Pauly and Will (*ibid.*, 1918, **416**, 1) and since studied in detail by Elvidge, Linstead, Sims, and others (*J.*, 1950, 2228, 2235; 1951, 3386; 1952, 1026).

In our experimental work three structural features have been modified. The electron-attracting groups X used were ester and carboxylic acid; the carbon skeletons were butyric, β-phenylpropionic, δ-phenylvaleric, and *cyclo*hexylacetic; and the acyl groups Y were acetyl, benzoyl, methanesulphonyl, toluene-*p*-sulphonyl, nitro-, phosphonyl, and diphenylphosphonyl. The results are summarised in the Table and special features of interest are discussed in the subsequent paragraphs.

The Alkaline Hydrolysis of β-Acyloxy-esters.

						Unsaturated acid	
No.	Compound	Alkali	Solvent	Time (hr.)	Temp.	formed (%)	isolated (%)
(VII)	Me·CH(OAc)·CH$_2$·CO$_2$Et	N-Na$_2$CO$_3$	*a*	8	Reflux	54	30
		0·8N-NaOH	*a*	4	,,	44	30
	Me·CH(OBz)·CH$_2$·CO$_2$Et	N-Na$_2$CO$_3$	*a*	8	,,	73	35
		0·8N-NaOH	*a*	4	,,	60	40
	Me·CH(OMs)·CH$_2$·CO$_2$Et	N-Na$_2$CO$_3$	*a*	8	,,	85	63
		0·8N-NaOH	*a*	2	,,	98	68
(X)	Me·CH(OTs)·CH$_2$·CO$_2$Et	N-Na$_2$CO$_3$	*a*	8	,,	79	61
		0·8N-NaOH	*a*	2	,,	96	65
(XI)	Me·CH(O·NO$_2$)·CH$_2$·CO$_2$Me	N-KOH	*a*	,,	,,	—	80
(XII)	Me·CH(O·PO$_3$Ph$_2$)·CH$_2$·CO$_2$Et	N-KOH	*a*	,,	,,	—	75
(XIII)	Me·CH(O·PO$_3$H$_2$)·CH$_2$·CO$_2$Et ...	N-KOH	*a*	,,	,,	—	33
(XIV)	C$_6$H$_{10}$(OAc)·CH$_2$·CO$_2$Et	0·25N-Na$_2$CO$_3$	*d*	28	,,	—	23
		0·1N-KOH	*b*	160	R.t.	—	26
		0·5N-KOH	*b*	48	,,	—	24
		0·1N-NaOEt	*e*	17	Reflux	—	23 *
(XVII)	Ph·CH(OAc)·CH$_2$·CO$_2$H	N-Na$_2$CO$_3$	*d*	2	90°	—	11
		N-NaOH	*d*	20	R.t.	—	14
		0·1N-KOH	*b*	2	Reflux	—	0
		0·1N-Ba(OH)$_2$	*d*	,,	90°	—	0
(XVIII)	Ph·CH(OAc)·CH$_2$·CO$_2$Me	N-Na$_2$CO$_3$	*d*	2·5	,,	—	49
		N-NaOH	*b*	48	R.t.	—	54
		0·1N-KOH	*b*	2·5	Reflux	—	55
		0·1N-Ba(OH)$_2$	*b*	,,	,,	—	0
(XXI)	Ph·[CH$_2$]$_2$·CH(OAc)·CH$_2$·CO$_2$Et	N-Na$_2$CO$_3$	*c*	48	R.t.	14	—
		0·5N-Na$_2$CO$_3$	*c*	8	Reflux	22	—
		0·1N-KOH	*c*	,,	,,	19	—
		0·2N-KOH	*c*	48	R.t.	15	12
(XXI)	Ph·[CH$_2$]$_2$·CH(OBz)·CH$_2$·CO$_2$Et	N-Na$_2$CO$_3$	*c*	,,	,,	33	—
		0·5N-Na$_2$CO$_3$	*c*	8	Reflux	34	—
		0·1N-KOH	*c*	,,	,,	29	—
		0·2N-KOH	*c*	48	R.t.	24	—

Solvents: (*a*) 1 : 1 Aq. dioxan; (*b*) 1 : 1 aq. MeOH; (*c*) 1 : 1 aq. EtOH; (*d*) H_2O; (*e*) EtOH.
* Partly as ethyl ester.
R.t. = room temperature.
Ms = methanesulphonyl; Ts = toluene-*p*-sulphonyl.

When ethyl β-acetoxybutyrate (VII) was treated with the alkaline solutions mentioned in the Table, in boiling aqueous dioxan, a mixture of crotonic (VIII) and β-hydroxybutyric acid (IX) was found. The crotonic acid was easily isolated by preferential extraction of the hydroxy-acid with water. For quantitative purposes the yield was estimated by bromine addition to an aliquot portion of the reaction mixture. Control experiments showed that ethyl β-hydroxybutyrate was not dehydrated even with higher concentrations of alkali, and the unsaturated acid is therefore formed by an elimination reaction involving the acetoxy-group. Similar results were obtained with ethyl β-benzoyloxybutyrate, the yield of unsaturated acid then being much greater.

Since sulphonic esters, even when not activated by electron-attracting groups, show a readiness to undergo elimination reactions, particularly when they are derivatives of secondary alcohols (see, *inter al.*, Clarke and Owen, *J.*, 1950, 2103), higher yields of crotonic acid would be expected on alkaline hydrolysis of the toluene-*p*-sulphonate (X) or methanesulphonate of ethyl β-hydroxybutyrate. This was found to be true. These derivatives were readily obtained by treatment of the hydroxy-ester with the appropriate sulphonyl chloride in pyridine, and under optimum conditions gave crotonic acid practically exclusively. The only simple β-sulphonyloxy-ester previously described appears to be ethyl β-toluene-*p*-sulphonyloxypropionate; this was reported by Clemo and Walton (*J.*, 1928, 723) to be converted (in unspecified yield) into ethyl acrylate when treated with cold aqueous alkali. More recently, Eglinton and Whiting (*J.*, 1950, 3650) have used the toluene-*p*-sulphonates of β-acetylenic alcohols for the preparation of vinylacetylenes, elimination occurring readily when the esters are heated with aqueous or alcoholic alkali.

The esters of other strong acids behaved similarly. The nitrate of β-hydroxybutyric acid (Duval, *Bull. Soc. chim.*, 1904, **31**, 245) with diazomethane afforded the methyl ester (XI), which on alkaline hydrolysis gave crotonic acid in high yield. Ethyl β-hydroxybutyrate and diphenyl phosphorochloridate in pyridine gave the diphenyl phosphate (XII); hydrogenolysis of this over a platinum catalyst proceeded very slowly and was not complete, but the free phosphate (XIII) was separated from the mixture by conversion into the benzylamine salt, from which it was regenerated by interaction with a cation-exchange resin. Alkaline hydrolysis of the diphenyl phosphate gave a much higher yield of crotonic acid than was obtained from the phosphate. In an attempt to prepare the sulphate, ethyl β-hydroxybutyrate was treated with chlorosulphonic acid and pyridine, but only ethyl crotonate was obtained.

The greater tendency to elimination shown by the derivatives of the strong acids is significant. The elimination reaction must involve "alkyl–oxygen" fission at the β-position, and it is recognised that toluene-*p*-sulphonates and methanesulphonates readily undergo this type of cleavage; there is also evidence that esters of nitric acid can behave in the same way (J. W. Baker, *J.*, 1952, 1193; see also Ansell and Honeyman, *J.*, 1952, 2778). Simple aliphatic phosphates, acetates, and benzoates, however, usually undergo only acyl–oxygen fission under alkaline conditions, and the occurrence of alkyl–oxygen fission in their present reactions is of some interest, although establishment of the precise mechanism of the elimination is not at present possible.

$\mathrm{Me{\cdot}CH(OR){\cdot}CH_2{\cdot}CO_2Et} \longrightarrow \mathrm{Me{\cdot}CH{:}CH{\cdot}CO_2H}$ (VIII)

(VII; R = Ac)

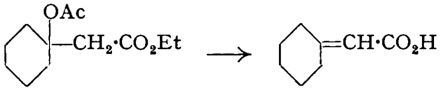
(X; $\mathrm{R = SO_2{\cdot}C_6H_4Me\text{-}}p$)

(XI; Me ester, $\mathrm{R = NO_2}$)

(XII; $\mathrm{R = PO_3Ph_2}$)

(XIII; $\mathrm{R = PO_3H_2}$)

$\searrow \mathrm{Me{\cdot}CH(OH){\cdot}CH_2{\cdot}CO_2H}$ (IX)



(XIV) (XV)

$\mathrm{Ph{\cdot}CH(OH){\cdot}CH_2{\cdot}CO_2H} \longleftarrow \mathrm{Ph{\cdot}CH(OAc){\cdot}CH_2{\cdot}CO_2R} \longrightarrow \mathrm{Ph{\cdot}CH{:}CH{\cdot}CO_2H}$

(XVI) (XVII; R = H) (XIX)

(XVIII; R = Me)

$\mathrm{Ph{\cdot}[CH_2]_2{\cdot}CH(OH){\cdot}CH_2{\cdot}CO_2H} \longleftarrow \mathrm{Ph{\cdot}[CH_2]_2{\cdot}CH(OR){\cdot}CH_2{\cdot}CO_2Et} \longrightarrow \mathrm{Ph{\cdot}[CH_2]_2{\cdot}CH{:}CH{\cdot}CO_2H}$

(XX) (XXI; R = Ac or Bz) (XXII)

$\uparrow$

$\mathrm{Ph{\cdot}CH_2{\cdot}CH{:}CH{\cdot}CH_2{\cdot}CO_2H} \longleftarrow \mathrm{\{Ph{\cdot}[CH_2]_2{\cdot}CH(OAc){\cdot}CH_2{\cdot}CO\}_2O}$

(XXIV) (XXIII)

Methyl α-methanesulphonyloxybutyrate, prepared from the α-hydroxy-ester, gave only a very small amount of crotonic acid when treated with alkali under conditions effective for the β-isomer; the elimination reaction is therefore characteristic of the β-hydroxy-ester derivatives.

Examination of ethyl 1-acetoxy*cyclo*hexylacetate (XIV) threw some light on the choice of position taken up by the double bond formed in elimination. The position of prototropic equilibrium between the corresponding unsaturated acids is 88% βγ $\rightleftharpoons$ 12% αβ (Linstead, *J.*, 1927, 362, 2579). Treatment of the acetate (XIV) with alkali under various conditions (none of which led to the dehydration of the free hydroxy-ester) led to some 25% of acyl elimination and the elimination product was exclusively the αβ-acid (XV). The formation of the labile isomer in this way contrasts with the dehydration of hydroxy*cyclo*hexylacetic ester which normally yields largely βγ-unsaturated material. Attempts in the present work to prepare the methanesulphonyloxy- and toluene-*p*-sulphonyloxy-ester gave only βγ-unsaturated ester.

Experiments with β-hydroxy-β-phenylpropionic acid (XVI) (Fittig and Slocum, *Annalen*, 1885, **227**, 59) showed an enhanced tendency for elimination, due to the additional conjugation of the double bond with phenyl. The β-hydroxy-acid itself was dehydrated to cinnamic acid by alkali under conditions where β-hydroxybutyric acid was unaffected. Furthermore, reaction of the ethyl ester with acetic anhydride resulted in the formation of much ethyl cinnamate; this was also the main product when the hydroxy-ester was treated with benzoyl chloride, methanesulphonyl chloride, or toluene-*p*-sulphonyl chloride in cold pyridine. However, the hydroxy-acid itself undergoes normal acetylation to give (XVII), and subsequent treatment with ethereal diazomethane gave methyl β-acetoxy-β-phenylpropionate (XVIII). Reaction of these compounds with alkali under mild conditions (when hydrolysis of the hydroxy-ester proceeded normally) gave cinnamic acid, the yield, as expected, being much greater from (XVIII) than from (XVII).

Different results were obtained when the phenyl group was in a more remote position. Ethyl β-hydroxy-δ-phenylvalerate reacted normally with acetyl or benzoyl chloride in pyridine, to give the derivatives (XXI), without any unsaturated product (compare the reactions of ethyl β-hydroxy-β-phenylpropionate, above). Alkaline hydrolysis of these derivatives gave a mixture of the hydroxy-acid (XX) and the αβ-unsaturated acid (XXII); as with the derivatives of 1-hydroxy*cyclo*hexylacetic ester, no βγ-unsaturated acid was detected. In this series of experiments, the yield of unsaturated acid was conveniently estimated by quantitative hydrogenation. Elimination occurred to a much smaller extent than with ethyl β-acetoxy-β-phenylpropionate; the ultimate formation of a highly conjugated system therefore favours the elimination reaction, probably because of the greater stability of the transition state.

Reaction of β-hydroxy-δ-phenylvaleric acid with acetic anhydride gave the acetoxy-anhydride (XXIII), which on treatment with aqueous alkali gave the αβ-unsaturated acid (XXII). On distillation, however, the anhydride gave a mixture of (XXII) and a different unsaturated acid, probably the βγ-unsaturated isomer (XXIV).

Finally it should be pointed out that in all the ester eliminations which have yielded unsaturated products of known configuration that configuration is *trans*. This is consistent with either a unimolecular or a bimolecular heterolytic mechanism. Further preliminary evidence bearing on the mechanism and stereospecificity of ester eliminations is given in Part II.

EXPERIMENTAL

Ethyl β-hydroxybutyrate, b. p. 74°/11 mm., n_D^{17} 1·4221, was prepared by hydrogenation of ethyl acetoacetate at room temperature and 50 atm. over Raney nickel. With the appropriate acid chloride in pyridine at 0° it gave ethyl β-acetoxybutyrate, b. p. 72°/0·4 mm., n_D^{20} 1·4284 (Found: equiv., 87·0. Calc. for $C_8H_{14}O_4$: equiv., 87), and ethyl β-benzoyloxybutyrate, b. p. 95°/3 × 10^{-4} mm. (slight decomp.), n_D^{19} 1·5000 (Found: equiv., 117·8. Calc. for $C_{13}H_{16}O_4$: equiv., 118).

Ethyl β-Methanesulphonyloxybutyrate.—A solution of the hydroxy-ester (40 g.) in pyridine (30 c.c.) was cooled to −5° and methanesulphonyl chloride (40 g.) in pyridine (40 c.c.) was added, with stirring, during 1·5 hours. The mixture was set aside at 0° for 12 hours, cooled to

$-5°$, and diluted with ice-water (220 c.c.); the precipitated oil was extracted with chloroform (3×60 c.c.), the extracts were washed with ice-cold 20% sulphuric acid, sodium hydrogen carbonate solution, and water, dried (Na_2SO_4) and evaporated. The residue on distillation afforded the *methanesulphonate* (52 g.), f. p. *ca.* 6°, b. p. 90°/10^{-4} mm. (Found: S, 15·2. $C_7H_{14}O_5S$ requires S, 15·2%), which soon became yellow.

The *toluene*-p-*sulphonate*, prepared as above from the hydroxy-ester (24 g.) and toluene-*p*-sulphonyl chloride (42 g.) in pyridine (80 c.c.), was a viscous non-distillable oil (37 g.) (Found: S, 11·1. $C_{13}H_{18}O_5S$ requires S, 11·2%).

Methyl β-*Nitratobutyrate*.—β-Nitratobutyric acid was prepared from sodium β-hydroxybutyrate (12 g.), fuming nitric acid (20 g.), and sulphuric acid (100 g.) at $-15°$ (Duval, *Bull. Soc. chim.*, 1904, **31**, 245). The *methyl* ester, obtained with ethereal diazomethane, was an oil (6·6 g.), b. p. 94°/17 mm., n_D^{21} 1·4253 (Found: C, 37·0; H, 5·7; N, 8·5. $C_5H_9O_5N$ requires C, 36·8; H, 5·6; N, 8·6%).

Ethyl β-(*Diphenoxyphosphinyloxy*)*butyrate*.—To ethyl β-hydroxybutyrate (26·4 g.) in pyridine (40 c.c.), diphenyl phosphorochloridate (41·1 g.) (Brigl and Müller, *Ber.*, 1939, **72**, 2123) in pyridine (40 c.c.) was added at 0° during an hour. After 20 hours at 0° the mixture was diluted with ice-water (150 c.c.). The *diphenoxyphosphinyloxy*-derivative, isolated by chloroform extraction, was an oil (46 g.) which could be distilled in small quantities and had b. p. 120° (bath)/0·0003 mm., n_D^{23} 1·5319 (Found: C, 59·2; H, 5·95; P, 8·1. $C_{18}H_{21}O_6P$ requires C, 59·4; H, 5·9; P, 8·6%).

Ethyl β-*Phosphonyloxybutyrate*.—The foregoing ester (17·8 g.) and Adams' platinum catalyst (0·9 g.) in ethyl acetate (400 c.c.) were shaken with hydrogen at room temperature and pressure. Uptake was slow and incomplete. Evaporation of the filtered solution gave an oil (12·4 g.), n_D^{24} 1·4840 (Found: P, 10·6%); a portion (0·5 g.) in dry ether (8 c.c.) with benzylamine (0·5 g.) gave, after 2 hours at 0°, a precipitate (0·2 g.) which on crystallisation from benzene afforded the *dibenzylamine* salt, m. p. 144°, of ethyl β-phosphonyloxybutyrate (Found: N, 6·4. $C_{20}H_{31}O_6N_2P$ requires N, 6·6%).

A solution of this salt (0·5 g.) in water (40 c.c.) and ethanol (160 c.c.) was passed through a cation exchange column (Zeo-karb); evaporation under reduced pressure then gave the β-phosphonyloxy-ester as an acidic oil (0·2 g.) which was immediately used for the hydrolysis experiments; it rapidly decomposed on storage.

Control Hydrolysis of Ethyl β-*Hydroxybutyrate*.—Ethyl β-hydroxybutyrate (0·5 g.) when refluxed for 2 hours with 0·8N-sodium hydroxide (20 c.c.) in dioxan–water (1 : 1) afforded β-hydroxybutyric acid (0·3 g.) and no unsaturated material. The ester (13·2 g.) when refluxed for 12 hours with 2N-potassium hydroxide in aqueous ethanol (1 : 1) (100 c.c.) gave only β-hydroxybutyric acid (9·65 g., 93%).

Action of Alkali on the Derivatives of Ethyl β-*Hydroxybutyrate*.—(i) *Isolation experiments.* In a typical experiment ethyl β-acetoxybutyrate (10·55 g.) was refluxed for 4·5 hours with 0·8N-sodium hydroxide in aqueous dioxan (1 : 1) (185 c.c.); the solution was then partly neutralised with hydrochloric acid, concentrated under reduced pressure, acidified with hydrochloric acid, and continuously extracted with ether. The ethereal extract was washed once with an equal volume of water, dried (Na_2SO_4), and evaporated to yield crotonic acid (1·59 g., 30%) which crystallised from water in needles, m. p. and mixed m. p. 72°. The aqueous washing was continuously extracted with ether, and the extract dried (Na_2SO_4) and evaporated to an oil which was freed from acetic acid by storage *in vacuo* over potassium hydroxide. The residue (4·27 g.) was mainly β-hydroxybutyric acid, containing a little crotonic acid.

In some experiments, extraction with chloroform was used; this gave rather better recoveries of crotonic acid.

In the hydrolyses of the benzoate, the solution after removal of dioxan was acidified, cooled to 0°, and filtered from precipitated benzoic acid before extraction.

In the hydrolysis of the diphenyl phosphate, the ethereal extract, containing crotonic acid, β-hydroxybutyric acid, and phenol, was washed with sodium hydrogen carbonate to remove the acids, which were then recovered by acidification and extraction, and separated in the usual way.

(ii) *Titrimetric experiments.* A known weight (*ca.* 0·5 g.) of the appropriate ester was refluxed with excess of alkali as in the isolation experiments, cooled, and diluted to 100 c.c. Aliquots (25 c.c.) were acidified with hydrochloric acid, treated with 50 c.c. of 0·1N-potassium bromate containing an excess of potassium bromide, and kept for 15 minutes in the dark; potassium iodide (200% excess) was then added and the iodine titrated with sodium thiosulphate.

Ethyl α-Methanesulphonyloxybutyrate.—Treatment of ethyl α-hydroxybutyrate (1·5 g.) in pyridine (10 c.c.) with methanesulphonyl chloride (1·5 g.) for 16 hours at 0°, as described for the β-isomer, gave the *methanesulphonate* (1·7 g.), b. p. 65°/0·005 mm., n_D^{18} 1·4363 (Found: C, 40·15; H, 6·9. $C_7H_{14}O_5S$ requires C, 40·0; H, 6·7%).

Alkaline hydrolysis. The α-methanesulphonate (0·5 g.) was boiled under reflux for 4 hours with N-sodium hydroxide in 1 : 1 aqueous dioxan (10 c.c.). The yield of crotonic acid, estimated by the bromine addition method described above, was 8%.

*Control Hydrolysis of Ethyl 1-Hydroxy*cyclo*hexylacetate.*—Ethyl 1-hydroxy*cyclo*hexylacetate (18·6 g.) (*Org. Reactions*, **1**, 17) when refluxed for 8 hours with N-sodium hydroxide (300 c.c.) in aqueous ethanol (1 : 1) afforded 1-hydroxy*cyclo*hexylacetic acid (12·1 g., 90%) and no unsaturated material. Recrystallisation from benzene–light petroleum afforded the hydroxy-acid (9·8 g.), m. p. and mixed m. p. 64°.

*Action of Alkali on Ethyl 1-Acetoxy*cyclo*hexylacetate.*—In a typical experiment the acetoxy-ester (5·0 g.), b. p. 116—118°/4 mm., n_D^{25} 1·4557 (Auwers and Ellinger, *Annalen*, 1912, **387**, 228), was set aside for 48 hours with 100 c.c. (10% excess) of 0·5N-potassium hydroxide in aqueous methanol (1 : 1); the solution was then acidified with 2N-hydrochloric acid (50 c.c.) and diluted to 250 c.c., and the unsaturated acids were removed by exhaustive steam-distillation. The distillate was extracted with ether (4 × 50 c.c.), and the extract dried (Na_2SO_4) and evaporated to a solid residue, m. p. 87—88° (0·75 g., 24%). Crystallisation from aqueous ethanol gave needles of *cyclo*hexylideneacetic acid, m. p. and mixed m. p. 90°. The crude material was shown to contain no βγ-isomer by the iodine-addition method of Linstead and May (*J.*, 1927, 2567), the absorption being only 2·9%. The residue from the steam-distillation was continuously extracted with ether and gave 1-hydroxy*cyclo*hexylacetic acid (1·2 g.), which after crystallisation from benzene–light petroleum had m. p. and mixed m. p. 64°.

*Reaction of Ethyl 1-Acetoxy*cyclo*hexylacetate with Sodium Ethoxide.*—The ester (15 g.) was boiled under reflux for 17 hours with 0·1N-sodium ethoxide in ethanol (1500 c.c.), cooled, and diluted with water (100 c.c.). The excess of alkali was neutralised with carbon dioxide, the sodium carbonate filtered off, and the filtrate evaporated under reduced pressure to 500 c.c. Water (1 l.) was added, the solution was extracted with ether (3 × 200 c.c.), and the extract was dried ($MgSO_4$) and evaporated. The residue (6·3 g.) on fractionation gave (i) unsaturated ester (2·0 g.), b. p. 62—70°/1 mm., n_D^{20} 1·4790, and (ii) hydroxy-ester (4·1 g.) b. p. 94—100°/1 mm., n_D^{20} 1·4681. The iodine-addition value of (i) was 4·9%. Linstead and May (*loc. cit.*) give 4·2 ± 0·5% for ethyl *cyclo*hexylideneacetate, and record n_D^{18} 1·4799.

The aqueous solution was acidified and the acids were evaporated by steam-distillation, to give the αβ-unsaturated acid (0·4 g.) (iodine addition, 2·4%) and the β-hydroxy-acid (0·9 g.).

*Reaction of Ethyl 1-Hydroxy*cyclo*hexylacetate with Toluene-*p*-sulphonyl Chloride.*—The chloride (1·3 g.) was added during ½ hour to the ester (1 g.) in pyridine (10 c.c.) at 0°. After 6 days at 0°, ice-water was added and the product was extracted with chloroform, washed with cold 2N-sulphuric acid, sodium hydrogen carbonate, and water, and isolated by evaporation. The residual oil (0·9 g.) on distillation afforded only ethyl *cyclo*hexenylacetate (0·83 g.), b. p. 66°/0·7 mm., n_D^{22} 1·4622 (Kon and Linstead, *J.*, 1929, 1278, give n_D^{24} 1·4621).

Methyl β-Acetoxy-β-phenylpropionate.—β-Acetoxy-β-phenylpropionic acid (Fittig and Slocum, *Annalen*, 1885, **227**, 59) with ethereal diazomethane gave the *methyl* ester, b. p. 84°/0·03 mm., n_D^{25} 1·5139 (Found: C, 65·4; H, 6·45. $C_{12}H_{14}O_4$ requires C, 64·9; H, 6·35%).

Control Hydrolysis of Methyl β-Hydroxy-β-phenylpropionate.—The ester (1·8 g.) was kept with N-sodium hydroxide (25 c.c.) in 1 : 1 aqueous methanol at room temperature for 48 hours; water (20 c.c.) was then added and the alkali neutralised with hydrochloric acid. The methanol was removed under reduced pressure, and the solution acidified and cooled to 0°; no precipitation of cinnamic acid occurred. Extraction with ether (3 × 10 c.c.) gave the β-hydroxy-acid (1·4 g., 84%) which on crystallisation from water had m. p. 100°.

Similar experiments with ethyl β-hydroxy-β-phenylpropionate showed that no cinnamic acid was formed when the ester was hydrolysed under reflux with (i) N-barium hydroxide, (ii) N-sodium carbonate, (iii) 0·1N-potassium hydroxide, all in 1 : 1 ethanol–water. When, however, the ester was hydrolysed with boiling aqueous-alcoholic (1 : 1) 2N-potassium hydroxide, acidification of the solution (after removal of ethanol) gave a precipitate of cinnamic acid (yield, 10%), m. p. 133° after recrystallisation from water.

Action of Alkali on β-Acetoxy-β-phenylpropionic Acid.—In a typical experiment the β-acetoxy-acid (1·0 g.) was dissolved in N-sodium carbonate (11 c.c.), heated on the steam-bath for 2½ hours, cooled to 0°, acidified with concentrated hydrochloric acid, and set aside at 0° for 1 hour. The precipitated cinnamic acid (0·08 g., 11%), on recrystallisation from water, had

m. p. and mixed m. p. 133°. The main filtrate was extracted with ether (3 × 8 c.c.), and the extract dried (Na_2SO_4), evaporated and freed from acetic acid by storage *in vacuo* over potassium hydroxide. The residue of hydroxy-acid (0·59 g., 76%), when recrystallised from water, had m. p. and mixed m. p. 100°.

Action of Alkali on Methyl β-*Acetoxy*-β-*phenylpropionate*.—The ester (*ca.* 1 g.) was treated with alkali (2·2 equiv.) in aqueous methanol (1 : 1) under the conditions indicated in the Table. The alkali was then exactly neutralised (phenolphthalein) with N-hydrochloric acid, the methanol removed under reduced pressure, and any neutral material extracted with ether. The solution was then acidified and the acid products isolated as previously described.

In a typical experiment, the ester (1·0 g.) when set aside at room temperature for 48 hours with N-sodium hydroxide in aqueous methanol (1 : 1) (10 c.c.) gave cinnamic acid (0·36 g., 54%) and hydroxy-acid (0·29 g., 38%).

Methyl β-*Hydroxy*-δ-*phenylvalerate*.—β-Hydroxy-δ-phenylvaleric acid (Farmer and Hose, *J.*, 1933, 962) with methanol and sulphuric acid gave the *methyl* ester, b. p. 114—116°/0·5 mm., n_D^{20} 1·5100 (Found : C, 69·1; H, 7·8. $C_{12}H_{16}O_3$ requires C, 69·2; H, 7·7%).

Ethyl β-*Acetoxy*-δ-*phenylvalerate*.—Ethyl β-hydroxy-δ-phenylvalerate (Farmer and Hose, *loc. cit.*) (11 g.), acetyl chloride (8·5 g.), and pyridine (25 c.c.) were mixed and kept at 0° for 6 hours; ice-water (100 c.c.) was then added and the oil was extracted into chloroform (3 × 20 c.c.), washed with 2N-sulphuric acid and with water, dried (Na_2SO_4), and evaporated, and the residue distilled to give *ethyl* β-*acetoxy*-δ-*phenylvalerate* (10 g.), b. p. 100°/10^{-5} mm. (Found : C, 68·4; H, 7·7. $C_{15}H_{20}O_4$ requires C, 68·2; H, 7·6%).

Ethyl β-*Benzoyloxy*-δ-*phenylvalerate*.—The hydroxy-ester (11 g.) in pyridine (25 c.c.) on similar treatment with benzoyl chloride (7·8 g.) gave the *benzoate* (15 g.), a viscous oil, b. p. 120°/10^{-5} mm., which solidified (needles) on storage (m. p. *ca.* 25°) (Found : C, 73·5; H, 6·8. $C_{20}H_{22}O_4$ requires C, 73·6; H, 6·8%).

5-*Phenylpent*-2-*enoic Acid* (CO_2H = 1).—Distillation of β-hydroxy-δ-phenylvaleric acid at 160°/1·0 mm. furnished 5-phenylpent-2-enoic acid, which after crystallisation from water had m. p. 104° (Farmer and Hose, *loc. cit.*, give m. p. 103°).

Control Hydrolysis of Ethyl β-*Hydroxy*-δ-*phenylvalerate*.—Treatment of the ester with an excess of aqueous alcoholic alkali, under the conditions specified below, gave only the hydroxy-acid, m. p. 130°, and no unsaturated material : (i) 0·25N-KOH at room temperature; (ii) N-Na_2CO_3 at room temperature; (iii) 0·1N-KOH under reflux; (iv) 0·5N-Na_2CO_3 under reflux.

With boiling 0·5N-sodium hydroxide, some unsaturated acid, m. p. 90°, was formed, possibly 5-phenylpent-4-enoic acid (Farmer and Hose, *loc. cit.*, give m. p. 90°).

Action of Alkali on Ethyl β-*Acetoxy*-δ-*phenylvalerate*.—The acetoxy-ester (2·5 g.) was treated with 0·2N-potassium hydroxide in 1 : 1 aqueous ethanol (100 c.c.) at room temperature for 48 hours; the solution was then neutralised with hydrochloric acid, ethanol removed under reduced pressure, and the solution acidified and extracted with ether (3 × 15 c.c.). The extract was dried (Na_2SO_4) and evaporated, and the residue (1·6 g.) was extracted with carbon disulphide. The insoluble portion (0·6 g.), β-hydroxy-δ-phenylvaleric acid, after crystallisation from water had m. p. and mixed m. p. 130°. The carbon disulphide extract was evaporated and the solid extracted with light petroleum (b. p. 60—80°); the insoluble material (0·67 g.) was more of the β-hydroxy-acid. The petroleum extract on evaporation gave 5-phenylpent-2-enoic acid (0·2 g.) which after recrystallisation from water had m. p. and mixed m. p. 103°.

Action of Alkali on Ethyl β-*Acetoxy*(*and* β-*Benzoyloxy*)-δ-*phenylvalerate and Estimation of the Unsaturated Products by Catalytic Hydrogenation*.—The ester (*ca.* 0·8 g.) was treated with alkali (2·2 equiv.) in aqueous ethanol (1 : 1) under various conditions (see Table); the excess of alkali was then neutralised, the ethanol evaporated under reduced pressure, and the solution acidified strongly with hydrochloric acid and extracted thrice with ether. The extract was dried (Na_2SO_4) and evaporated, and the solid residue dissolved in ethanol and hydrogenated at room temperature over palladium–charcoal. The proportion of unsaturated acid was then calculated from the amount of hydrogen absorbed. The filtered solution was evaporated and the residue was extracted with carbon disulphide; the insoluble portion was β-hydroxy-δ-phenylvaleric acid, m. p. 130° (after recrystallisation from water). The δ-phenylvaleric acid, recovered from the carbon disulphide solution, crystallised from water in plates, m. p. 58°.

Anhydride of β-*Acetoxy*-δ-*phenylvaleric Acid*.—A mixture of β-hydroxy-δ-phenylvaleric acid (1·1 g.) and acetic anhydride (10 c.c.) was heated at 80° for 2½ hours and then evaporated under reduced pressure, to give the *acetoxy-anhydride* as a neutral oil (1·1 g.), which was saturated to aqueous permanganate, and dissolved slowly in hot 2N-sodium hydroxide (Found : C, 69·2; H, 6·8. $C_{28}H_{30}O_7$ requires C, 68·7; H, 6·7%). Distillation of a portion (0·5 g.) at 140°/1 mm.

gave an oil which partly solidified. The solid (0·2 g.) was sublimed at 115°/0·4 mm., and then crystallised from water to give 5-phenylpent-2-enoic acid, m. p. 98°, not depressed on admixture with the pure acid, m. p. 104° (Found : C, 75·0; H, 6·9. Calc. for $C_{11}H_{12}O_2$: C, 75·0; H, 6·9%). The liquid portion (0·2 g.) slowly solidified and had m. p. 28° (Farmer and Hose, *loc. cit.*, give m. p. 30° for 5-phenylpent-3-enoic acid).

Treatment of the anhydride (0·28 g.) with 0·1N-potassium hydroxide (50 c.c.) at 90° for 1½ hours, followed by concentration, acidification, and extraction with ether, gave 5-phenylpent-2-enoic acid, m. p. and mixed m. p. 104°.

Micro-analyses in this and the two following papers were carried out in the Micro-analytical Laboratory of this Department (Mr. F. H. Oliver).

DEPARTMENT OF ORGANIC CHEMISTRY,
IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY,
S. KENSINGTON, LONDON, S.W.7.

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