Synthesis of Some Carboxybutenolide Derivatives.

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The Reformatsky reaction between ethyl α-acetoxyacetoacetate and ethyl α-bromopropionate, followed by mild alkaline hydrolysis, yielded 4-carboxy-4-hydroxy-2 : 3-dimethylbut-2-enoic lactone* (X; R = CO_2H). ($\pm$)-Anhydromonocrotalic acid (XII; R = CO_2H) has been synthesised by an analogous route. The infra-red and ultra-violet absorption spectra of these carboxy-lactones and various derivatives are discussed.

FOR another investigation it became necessary to synthesise 4-carbamyl-4-hydroxy-2 : 3-dimethylbut-2-enoic lactone * (I; R = H). Compounds of this type have not been synthesised previously although an anhydromonocrotalamide (I; R = Me) has been prepared from (+)-methyl anhydromonocrotalate, a degradation product of the alkaloid monocrotaline (Adams and Wilkinson, *J. Amer. Chem. Soc.*, 1943, **65**, 2203; cf. Adams and Govindachari, *ibid.*, 1950, **72**, 158).

One route envisaged was based upon Rosenmund reduction of αβ-dimethylsuccinic half-ester chloride (II) to the aldehyde (III). Bromination followed by dehydrobromination to (IV) and then lactonisation of the derived cyanohydrin were expected to give (V), the nitrile corresponding to the required amide. The Rosenmund reduction of (II) gave (III) in 50% yield; the product apparently contained both diastereoisomers, even when a single isomer of methyl hydrogen αβ-dimethylsuccinate was used as starting material, for the derived 2 : 4-dinitrophenylhydrazone was evidently a mixture although the elementary analysis was satisfactory. One of the isomeric dinitrophenylhydrazones was isolated by fractional crystallisation. Attempts to brominate the aldehydic ester (III) were unsuccessful, and this approach to the problem was therefore abandoned.

The following alternative synthesis was also examined :

the Reformatsky reaction between ethyl α-bromopropionate and ethyl α-acetoxyaceto-acetate in benzene gave an impure product, presumably containing the β-hydroxy-ester (VI) or the corresponding lactone, since light absorption at *ca.* 2200 Å was of low intensity. Attempts to isolate a pure product by fractional distillation were unsuccessful, and dehydration of the crude product in benzene with phosphoric oxide yielded complex mixtures.

The use of boiling xylene as solvent for the Reformatsky reaction resulted in simultaneous dehydration and lactonisation of the intermediate (VI). Three modes of dehydration of the latter are formally possible giving, after lactonisation, (VII), (VIII), or (IX); the crude ester, which boiled over a wide temperature range, may have contained all three. The light absorption data showed that (IX), which alone contains no conjugated chromophore, could not be a major component. Repeated fractional distillation of the crude material resulted in extensive decomposition and a pure ester could not be isolated. The conversion of the ester into a crystalline amide by treatment with aqueous, ethanolic, ethereal, and liquid ammonia was investigated without success.

The ester did, however, react with anilinomagnesium bromide to give a crystalline

* Geneva nomenclature, CO_2H = 1.

anilide which probably contained an αβ-unsaturated lactone grouping since the light absorption showed a maximum at 2200 Å (ε 13,800) (see Table 2), and this was subsequently shown to have structure (X; R = CO·NHPh). The use of an aminomagnesium halide in an analogous manner, however, failed to yield the required amide (cf. Oddo and Calderaro, *Gazzetta*, 1923, **53**, 64).

On partial hydrolysis of the crude ester by *ca.* 0·05N-sodium hydroxide in aqueous ethanol (1 hr. at room temperature), one mol. of alkali was consumed, and a crystalline acid (yield about 30%), but no other crystalline product, was obtained. Elementary analysis of this acid indicated the formula, $C_7H_8O_4$, which proved that the ethoxycarbonyl group, not the lactone ring, had been hydrolysed. The light absorption properties (Table 2) excluded the structure corresponding to the ester (IX). αβ-Unsaturated esters are known to be more resistant to hydrolysis than the βγ-isomers (Kon and Linstead, *J.*, 1929, 1274) and hydrolysis of the ethoxycarbonyl group in (VII) would be expected, whereas in

Me·CH——C·Me	Me·CH——C:CH₂	Me·C══C·Me	Me·CH——CHMe	Me·C══C·Me
OC C·CO₂Et	OC CH·CO₂Et	OC CHR	OC CHR	OC CMeR
\ /	\ /	\ /	\ /	\ /
O	O	O	O	O
(VIII)	(IX)	(X)	(XI)	(XII)

the case of (VIII) the lactone ring would more probably be attacked, giving a ketone, since (VIII) is derived from an enol. Moreover, hydrogenation of the acid led to the formation of the corresponding saturated lactonic acid (XI; R = CO₂H) and this behaviour is characteristic of αβ-unsaturated lactones whereas lactones derived from enolised keto-acids undergo hydrogenolysis to deoxy-acids (Jacobs and Scott, *J. Biol. Chem.*, 1930, **87**, 601; Elvidge, Linstead, Orkin, Sims, Baer, and Pattison, *J.*, 1950, 2228). The crystalline acid must therefore be 4-carboxy-4-hydroxy-2 : 3-dimethylbut-2-enoic lactone (X; R = CO₂H). This α-hydroxy-acid structure is consistent with its strongly acidic properties (pK_a 2·58). It was unexpectedly found that this acid was decarboxylated rapidly at the melting point (105°) to give the lactone (X; R = H) which was also obtained from the crude lactonic ester by treatment with hydrogen bromide in acetic acid.

With oxalyl chloride in benzene (X; R = CO₂H) gave the acid chloride whence the required amide was prepared by use of ethereal ammonia. The anilide, previously obtained from the crude lactonic ester, was proved to be (X; R = CO·NHPh) by its preparation from the acid chloride.

The lactonic acids (X and XI; R = CO₂H) were esterified by diazomethane, so that the partial hydrolysis of these esters and of the lactones (X and XI; R = H) could be examined. Under the conditions of hydrolysis employed in the case of the crude Reformatsky reaction product (*viz.*, N/20-alkali in aqueous ethanol), the methoxycarbonyl groups and saturated lactone rings were rapidly hydrolysed whereas the unsaturated lactone groups were unaffected. These results are in accord with Tommila and Ilomäki's finding (*Acta Chem. Scand.*, 1952, **6**, 1249) that γ-valerolactone is rapidly hydrolysed by cold dilute alkali, the rate of hydrolysis being of the same order as that of carboxylic esters.

Adams and Wilkinson (*loc. cit.*) obtained (+)-anhydromonocrotalic acid (4-carboxy-4-hydroxy-2 : 3 : 4-trimethylbut-2-enoic lactone) from monocrotaline. We have now synthesised the (±)-acid by Reformatsky reaction between ethyl α-bromopropionate and ethyl α-acetoxy-α-methylacetoacetate and partial hydrolysis of the resulting (XII; R = CO₂Et). Attempts to hydrogenate the acid at atmospheric pressure were unsuccessful (cf. Adams, Rogers, and Long, *J. Amer. Chem. Soc.*, 1939, **61**, 2823).

The infra-red spectra of saturated and unsaturated lactones have been investigated by a number of workers (Grove and Willis, *J.*, 1951, 877, and references cited therein; Pinder, *J.*, 1952, 2238). In lactones containing a five-membered saturated ring, the C══O absorption band occurs at about 1770 cm.⁻¹ and a shift of *ca.* 20 cm.⁻¹ to lower frequencies is produced by αβ-unsaturation. These effects are observed in the spectra of the carboxy-lactone derivatives described above, despite the fact that the substituents include highly polar groups. In passing from the lactones of type (XI) to these of type (X), there is a shift of 9—31 cm.⁻¹ to lower frequencies for pairs of compounds containing the same substituents (see Table 1). The spectra of the (±)-anhydromonocrotalic acid derivatives are very

similar to those of (X; R = CO$_2$H) but the saturated compounds of this series are not available for comparison.

Measurements of the ultra-violet absorption spectra of the unsaturated lactones confirmed the nature of the chromophoric system and also disclosed an unusually large solvent effect on the spectra of the amides (X and XII; R = CO·NH$_2$). For the former an aqueous

TABLE 1. *Lactone C=O absorption frequencies (cm.$^{-1}$).*

	Frequency			Frequency
R	(XI) (Sat.)	(X) (Unsat.)	Shift	(XII)
H	1776 [b]	1761 [b]	15	—
CO$_2$H	1767 [a]	1758 [a]	9	1758 [a]
CO$_2$Me	1789 [b]	1773 [b]	16	1764 [b]
CO·NH$_2$	1789 [a] *	1758 [a]	31	1761 [a]
CO·NHPh	1776 [a]	1764 [a]	12	1754 [a]

* Lactone and ester bands not resolved. [a] Nujol mull. [b] Liquid film.

solution showed a maximum at 2240 Å (ε 8900) which was shifted to 2130 Å (ε 9300) for a solution in 96% ethanol. Aqueous-ethanolic solutions showed maxima or inflections at both wave-lengths but no isosbestic point was observed. (±)-Anhydromonocrotalamide gave very similar results, and the acid (X; R = CO$_2$H) showed a smaller shift (*ca.* 30 Å). These results appear to be due to some form of association, probably with water rather than ethanol since, for the latter solvent, these spectra closely resemble those of the related compounds (Table 2). It seems unlikely that this effect can be due to excessive absorption by the solvent, as in a case investigated by Vandenbelt, Henrich, and Bash (*Science*, 1951, **114**, 576) because the maximum at longer wave-length is observed for a solution in the solvent which shows the lower absorption, namely, water. The possibility of chemical change on treatment with water has been excluded by crystallisation of (±)-anhydromonocrotalamide from water without change.

TABLE 2. *Absorption spectra of unsaturated lactones.*

		(X)		(XII)	
R	Solvent	λ$_{max.}$ (Å)	ε	λ$_{max.}$ (Å)	ε
H	EtOH	2130	13,400	—	—
CO$_2$H	EtOH (96%)	2250	8,200	2300	9,300
	H$_2$O	2280	9,800	2290	9,300
CO$_2$Me	EtOH (96%)	2150	12,100	2130	11,700
CO·NH$_2$	EtOH (96%)	2130	9,300	2105	8,500
				2280 *	6,600
	H$_2$O	2240	8,900	2275	9,000
CO·NHPh	*cyclo*Hexane	2200	13,800	2210	14,800
		2410	14,600	2410	14,300

* Inflection.

EXPERIMENTAL

Ethyl Butane-2 : 2 : 3-tricarboxylate.—Ethyl methylmalonate (218 g.) and ethyl α-bromopropionate (228 g.) were added successively to sodium ethoxide solution (from 29 g. of sodium and 500 c.c. of ethanol). After 2 hours' refluxing, excess of dilute sulphuric acid was added and the product isolated with ethyl acetate in the usual manner. The yield of material, b. p. 106—110°/1 mm., was 180 g.

β-*Methoxycarbonyl-αβ-dimethylpropionyl Chloride.*—The foregoing triester (180 g.) was refluxed with concentrated hydrochloric acid (600 c.c.) until it had completely dissolved (20 hr.) and the solution was evaporated to dryness, finally under reduced pressure. Acetic anhydride (300 c.c.) was added to the residue, and the mixture distilled until all acetic acid had been removed; more acetic anhydride (150 c.c.) was then added and the solution refluxed for 30 min. After evaporation under reduced pressure the residual αβ-dimethylsuccinic anhydride (mixed isomers) was refluxed with methanol (80 c.c.) for 1 hr. Evaporation furnished the crude half-ester which was warmed at 35—40° with thionyl chloride (80 c.c.) until gas evolution ceased (cf. Ruggli and Maeder, *Helv. Chim. Acta*, 1942, **25**, 936; 1943, **26**, 1476). Excess of thionyl chloride was removed at 40°/10 mm. and the *ester-chloride* then distilled as a colourless, mobile oil, b. p. 58—60°/1·5 mm. (Found : Cl, 19·6. C$_7$H$_{11}$O$_3$Cl requires Cl, 19·9%).

Methyl β-Formyl-αβ-dimethylpropionate.—(a) Xylene was desulphurised by treatment with sodium hydroxide solution and Raney nickel alloy, washed with water, and distilled. The foregoing acid chloride (57 g.) in xylene (180 c.c.) was stirred with palladised barium sulphate (8 g.; 5% Pd) at 110° (bath) while a stream of hydrogen was passed through. The reaction was stopped when 85% of the calculated quantity of hydrogen chloride had been evolved in $4\frac{1}{2}$ hr. Barium carbonate was added and the filtered solution was then fractionated through a short Fenske column, the crude product being collected at 40—44°/0·4—0·8 mm. Refractionation furnished the *aldehyde* (22 g., 50%) as a colourless oil, b. p. 50—53°/0·5 mm., n_D^{20} 1·4321 (Found : C, 58·1; H, 8·8. $C_7H_{12}O_3$ requires C, 58·3; H, 8·4%).

This product apparently contained both *erythro-* and *threo-*isomers for it furnished mixed 2 : 4-dinitrophenylhydrazones, m. p. 85—100° (Found : C, 48·1; H, 5·3; N, 17·7. $C_{13}H_{16}O_6N_4$ requires C, 48·1; H, 5·0; N, 17·3%). Repeated recrystallisations from methanol, ethanol, and ethyl acetate–light petroleum (b. p. 60—80°) yielded yellow plates of one *isomer*, m. p. 124—125° (Found : C, 47·9; H, 4·9; N, 16·8%).

(b) Methyl hydrogen αβ-dimethylsuccinate (54 g.; isomer melting at 38°; Bone, Sudborough, and Sprankling, *J.*, 1904, **85**, 545) was warmed with thionyl chloride (50 c.c.) until reaction ceased. Distillation of the mixture yielded the ester-chloride (48 g.) as a colourless oil, b. p. 62—64°/2 mm. (Found : Cl, 19·4%). Reduction as in (a) yielded the ester-aldehyde which again contained both isomers (derived 2 : 4-dinitrophenylhydrazone, m. p. 85—100°) (Found : C, 48·1; H, 4·9; N, 16·6%).

Ethyl α-Acetoxyacetoacetate.—The following procedure was found convenient for the preparation of considerable quantities of this ester (cf. Dimroth and Schweizer, *Ber.*, 1923, **56**, 1380). A mixture of glacial acetic acid (1100 c.c.), acetic anhydride (280 c.c.), and ethyl acetoacetate (195 g.) was stirred at 70° and red lead (600 g.) added at such a rate that the temperature remained at 70—80°. After a further hour's stirring the mixture was poured into water (3 l.), and the separated aqueous layer extracted four times with benzene–ethyl acetate (1 : 1). The combined organic layers were washed with water and dried (MgSO₄). Fractional distillation through a short Fenske column furnished ethyl α-acetoxyacetoacetate (180 g., 28%) as a pale yellow oil, b. p. 80—85°/0·6 mm., n_D^{20} 1·4299.

Reformatsky Reaction between Ethyl Acetoxyacetoacetate and Ethyl α-Bromopropionate.— (a) *In benzene.* Zinc wool was washed successively with dilute alkaline and acid solutions, water, ethanol, and acetone and then dried at 100°. After the zinc (40 g.) and " AnalaR " benzene (500 c.c.) had deen dried azeotropically, the mixed esters (76 g. of each) were added and reaction was initiated by means of iodine and methylmagnesium iodide. The mixture was refluxed for 6 hr. and poured into N-hydrochloric acid (1 l.), the product being isolated with ethyl acetate in the usual manner. Distillation yielded unchanged starting material and then a crude product (28 g.), b. p. 90—143°/0·6 mm., n_D^{20} 1·4487, light absorption : max. (in EtOH) at 2230 Å ($E_{1\,cm.}^{1\%}$ 37) (Found : C, 55·1; H, 6·4%).

(b) *In xylene.* Xylene (1200 c.c.; purified as described above) was added to zinc (150 g.), and remaining traces of water were removed by distillation. A portion of a mixture of ethyl α-acetoxyacetoacetate (227 g.) and ethyl α-bromopropionate (206 g.) was added together with a crystal of iodine. The mass was then refluxed (bath, 160°) for 8 hr., the remainder of the mixed esters being added gradually during the first 2—3 hr. No vigorous reaction occurred but most of the zinc eventually dissolved and a red-brown gum was deposited. This was dissolved by addition of hydrochloric acid (700 c.c.; 2N) and ethyl acetate; the separated aqueous layer was extracted twice with ethyl acetate, and the combined organic layers were washed with water and dried (MgSO₄). Fractional distillation through a short Fenske column yielded the crude *ethyl ester* (42 g.) as a yellow oil, b. p. 100—130°/1—1·5 mm., n_D^{20} 1·4721. Light absorption : max. at 2130 Å (ε 8100) (Found : C, 59·0; H, 6·8. $C_9H_{12}O_4$ requires C, 58·7; H, 6·6%).

4-Carboxy-4-hydroxy-2 : 3-dimethylbut-2-enoic Lactone.—The foregoing lactonic ester (20 g.) in ethanol (200 c.c.) was treated with 0·1N-sodium hydroxide solution (1400 c.c.). After 1 hr. at room temperature, the mixture was acidified with hydrochloric acid (80 c.c.; 2N) and extracted six times with ethyl acetate. The combined extracts were washed twice with water and evaporated *in vacuo* (bath <30°). Trituration of the residual gum with benzene gave crystalline material (5·3 g.), m. p. 102—104°. The *lactone-acid* separated from benzene in colourless plates, m. p. 103—104° (with decarboxylation) (Found : C, 53·8; H, 5·1%; equiv., 156. $C_7H_8O_4$ requires C, 53·8; H, 5·2%; equiv., 156). Infra-red spectrum (Nujol mull) : max. at 2747, 2703, 2611, 1758, 1724, 1664, 1522, 1409, 1391, 1335, 1314, 1269, 1205, 1174, 1111, 1067, 980, 935, 902, 888, 812, 763, and 732 cm.⁻¹.

4-Hydroxy-2 : 3-dimethylbut-2-enoic Lactone.—(a) A solution of the lactonic ester (6 g.) in

hydrogen bromide–acetic acid (60 c.c.; 25% w/v) was kept at room temperature for 20 hr. and then refluxed (bath-temperature rising from 80° to 100° during 2 hr. and then kept at 100° for 4 hr.). After removal of hydrogen bromide and acetic acid under reduced pressure, the residue was distilled, to give a pale yellow oil (2·5 g.), b. p. 70—75°/0·5 mm., n_D^{20} 1·4813, which partially crystallised. Redistillation through a short Vigreux column afforded an almost colourless oil, b. p. 68—71°/0·5 mm., which crystallised in large plates. The solid was washed with benzene–light petroleum (b. p. 60—80°) and then recrystallised from the same solvent mixture. The *lactone* separated in large plates, m. p. 33—34° (Found : C, 64·3; H, 7·2; *C*-Me, 16·9. $C_6H_8O_2$ requires C, 64·3; H, 7·2; 2*C*-Me, 26·8%). Infra-red spectrum (liquid film) : max. at 2967, 1761, 1686, 1522, 1449, 1393, 1374, 1330, 1205, 1083, 1035, 890, and 760 cm.$^{-1}$.

(*b*) 4-Carboxy-4-hydroxy-2 : 3-dimethylbut-2-enoic lactone (1·05 g.) was heated (bath, 115°) until decarboxylation ceased and the residue was then distilled, to give the colourless lactone (0·65 g.), b. p. 73—75°/1 mm., m. p. 32—33° undepressed by admixture with the sample from (*a*).

4-*Methoxycarbonyl-4-hydroxy-2 : 3-dimethylbut-2-enoic Lactone.*—An ethereal solution of diazomethane was gradually added to the lactonic acid (1·0 g.) in ether (20 c.c.) until the vigorous reaction ceased and the yellow colour just persisted. Glacial acetic acid was immediately added to destroy the excess of diazomethane, and the solution was washed with sodium hydrogen carbonate solution and water, dried (MgSO$_4$), and evaporated *in vacuo*. Distillation of the residue furnished the *methyl ester* (0·9 g.) as a colourless oil, b. p. 123—125°/2 mm., n_D^{20} 1·4758 (Found : C, 56·8; H, 6·2. $C_8H_{10}O_4$ requires C, 56·5; H, 5·9%). Infra-red spectrum (liquid film) : max. at 3584, 3003, 1773, 1684, 1441, 1391, 1339, 1325, 1285, 1214, 1174, 1135, 1094, 1065, 1018, 956, 924, 862, 804, 770, and 751 cm.$^{-1}$.

4-*Carbamyl-4-hydroxy-2 : 3-dimethylbut-2-enoic Lactone.*—The foregoing lactonic acid (0·45 g.), suspended in benzene (20 c.c.), was treated with oxalyl chloride (6 c.c.), and the mixture warmed (bath, 60—70°) until all the solid had dissolved. After evaporation under reduced pressure, more benzene was added and the solution again evaporated to remove all oxalyl chloride. The resulting crude acid chloride was dissolved in benzene (20 c.c.) and mixed with saturated ethereal ammonia (25 c.c.). When the filtered solution was concentrated to small volume the crude product (0·25 g.), m. p. 85—95°, separated. Recrystallisation from benzene gave fine, colourless needles (0·13 g.) of the *carbamyl-lactone*, m. p. 139—140° (Found : C, 54·5; H, 5·9; N, 9·1; *C*-Me, 18·0. $C_7H_9O_3N$ requires C, 54·2; H, 5·9; N, 9·0; 2*C*-Me, 19·4%). Infra-red spectrum (Nujol mull) : max at 3436, 3300, 1758, 1689, 1623, 1407, 1330, 1302, 1271, 1183, 1101, 1047, 894, and 762 cm.$^{-1}$.

4-*Hydroxy-2 : 3-dimethyl-4-phenylcarbamylbut-2-enoic Lactone.*—(*a*) Aniline (8 g.) and the crude lactonic ester (2 g.) were added successively to the Grignard reagent prepared from ethyl bromide (10 g.) and magnesium (2 g.) in ether. The mixture was refluxed for 10 min. and then treated with excess of dilute hydrochloric acid (cf. Hardy, *J.*, 1936, 398). The separated aqueous layer was extracted twice with ethyl acetate, and the combined organic layers were washed with water, sodium hydrogen carbonate solution, and water, dried (MgSO$_4$) and evaporated under reduced pressure. Trituration of the residual gum with ethyl acetate–light petroleum (b. p. 60—80°) gave crystalline material, m. p. 160—164° (0·9 g.). The *anilide* separated from methanol or benzene in thin plates, m. p. 165—166° (Found : C, 67·3; H, 5·5; N, 6·0. $C_{13}H_{13}O_3N$ requires C, 67·5; H, 5·7; N, 6·1%). Infra-red spectrum (Nujol mull) : max. at 3356, 1764, 1684, 1600, 1543, 1493, 1443, 1387, 1331, 1314, 1252, 1181, 1094, 1049, 979, 919, 902, 865, 722, 754, and 724 cm.$^{-1}$.

(*b*) 4-Carboxy-4-hydroxy-2 : 3-dimethylbut-2-enoic lactone (0·50 g.) was converted into the acid chloride as already described, and aniline (2·0 g.) was added to a solution of the crude chloride in benzene (20 c.c.). After 30 min. ethyl acetate (50 c.c.) was added and the mixture was washed with dilute hydrochloric acid and water, dried (MgSO$_4$), and evaporated. Recrystallisation of the residue from benzene yielded the anilide (0·4 g.), m. p. and mixed m. p. 163—164°.

4-*Hydroxy-2 : 3-dimethylbutanoic Lactone.*—The unsaturated lactone (0·52 g.) in ethanol (50 c.c.) was hydrogenated in presence of palladised strontium cabonate catalyst (5% of Pd) until absorption ceased. Distillation of the filtered solution furnished the *lactone* (0·20 g.) as a colourless oil, b. p. 65—68°/1 mm., n_D^{20} 1·4342 (Found : C, 63.4; H, 8·9. $C_6H_{12}O_2$ requires C, 63·1; H, 8·8%). Infra-red spectrum (liquid film) : max at 3597, 3030, 1776, 1484, 1458, 1391, 1372, 1328, 1284, 1247, 1223, 1181, 1159, 1124, 1100, 1056, 1029, 1011, 1002, 981, 829, 776, 723, and 707 cm.$^{-1}$.

4-*Carboxy-4-hydroxy-2 : 3-dimethylbutanoic Lactone.*—Hydrogenation of the unsaturated lactonic acid (1·0 g.) in a similar manner gave the saturated *acid* (0·9 g.) which separated from benzene–ethyl methyl ketone in plates, m. p. 122—123° (Found : C, 53·3; H, 6·5. $C_7H_{10}O_4$

requires C, 53·2; H, 6·4%). Infra-red spectrum (Nujol mull) : max. at 3279, 1767, 1403, 1389, 1350, 1335, 1284, 1174, 1159, 1130, 1085, 1062, 1040, 1019, 960, 873, 855, 808, 796, 750, 728, and 686 cm.⁻¹. It is of interest that hydrogenation gave entirely, or almost entirely, one isomeric form of this acid although *cis*-addition might be expected to produce a mixture of two isomers.

The derived *anilide*, prepared *via* the acid chloride as already described, crystallised from benzene–light petroleum (b. p. 60—80°) in fine needles, m. p. 146—147° (Found : C, 67·0; H, 6·3; N, 5·9. $C_{13}H_{15}O_3N$ requires C, 66·9; H, 6·5; N, 6·0%). Infra-red spectrum (Nujol mull) : max. at 3311, 1776, 1669, 1597, 1543, 1502, 1462, 1445, 1341, 1326, 1263, 1232, 1160, 1126, 1083, 1055, 1034, 1017, 1000, 966, 913, 888, 869, 846, 792, 768, 760, 722, and 695 cm.⁻¹. Hydrogenation of the corresponding unsaturated anilide furnished the same product (m. p. and mixed m. p.).

4-*Carbamyl*-4-*hydroxy*-2 : 3-*dimethylbutanoic lactone*, prepared from the acid chloride by ethereal ammonia, separated from benzene in fine needles, m. p. 187—188° (Found : C, 53·6; H, 7·2; N, 9·3. $C_7H_{11}O_3N$ requires C, 53·5; H, 7·1; N, 8·9%). Infra-red spectrum (Nujol mull) : max. at 3448, 3236, 1789, 1664, 1626, 1344, 1330, 1282, 1170, 1159, 1131, 1109, 1080, 1060, 1035, 1009, 956, 822, 792, 743, and 696 cm.⁻¹. This material was also obtained by hydrogenation of the unsaturated amide.

A portion (0·4 g.) of the lactonic acid was methylated by ethereal diazomethane ; the *methyl ester* distilled as a colourless oil (0·2 g.), b. p. 115—120°/1 mm., n_D^{20} 1·4525 (Found : C, 56·0; H, 7·0. $C_8H_{12}O_4$ requires C, 55·8; H, 7·0%). Infra-red spectrum (liquid film) : max. at 3636, 3030, 1789, 1805, 1443, 1387, 1344, 1306, 1277, 1221, 1164, 1133, 1094, 1080, 1063, 1031, 1005, 981, 938, 913, 859, 803, 769, and 735 cm.⁻¹.

Alkaline Hydrolysis of Lactones and Lactone-esters.—An ethanolic solution of the substance was treated with approx. 0·1N-sodium hydroxide solution (*ca.* 2 equivs.), the volume of ethanol used being equal to that of the alkali solution. After 1 hr. at room temperature (18—23°), the consumption of alkali (in equivs.) was : 4-hydroxy-2 : 3-dimethylbut-2-enoic lactone (X; R = H), 0·02; 4-hydroxy-2 : 3-dimethylbutanoic lactone (XI; R = H), 0·97; 4-methoxy-carbonyl-4-hydroxy-2 : 3-dimethylbut-2-enoic lactone (X; R = CO₂Me), 1·03; and 4-meth-oxycarbonyl-4-hydroxybutanoic lactone (XI; R = CO₂Me), 1·54.

Reactions with Aminomagnesium Bromide.—Experiments were carried out with different solvents and with the reactants in various proportions. The most satisfactory results were obtained by the following procedure : To a stirred solution (182 c.c.; 0·48M) of ammonia in dioxan, ethereal ethylmagnesium bromide (93 c.c.; 0·94M) and ethyl benzoate (1·6 g.) were added successively. After 1 hour's refluxing the ether was replaced by dioxan by distillation, and refluxing then continued for a further 1 hr. (bath 90—100°). The mixture was decomposed with ammonium chloride solution, extraction with ethyl acetate in the usual manner affording benzamide (0·43 g., 33%), m. p. 118—121°.

Application of this procedure to the lactonic ester, mainly (X; R = CO₂Et), yielded a viscous gum.

Ethyl α-*Acetoxy*-α-*methylacetoacetate.*—This ester was prepared in 26% yield by the procedure already described.

(±)-*Ethyl Anhydromonocrotalate.*—The Reformatsky reaction was carried out as in the previous example, with the foregoing acetoxy-ester (75 g.), ethyl-α-bromopropionate (65 g.), xylene (450 c.c.), and zinc (50 g.). The crude ester (23 g.) was obtained as a yellow oil, b. p. 100—140°/1·5 mm., n_D^{20} 1·4675. Fractional distillation of this material through a short Fenske column furnished the *ethyl ester* as a pale yellow oil, b. p. 93—94°/0·5 mm., n_D^{20} 1·4679 (Found : C, 61·0; H, 7·4. $C_{10}H_{14}O_4$ requires C, 60·6; H, 7·1%). Light absorption (in ethanol) : max. at 2100° Å (ε 10,600).

(±)-*Anhydromonocrotalic Acid.*—The foregoing ester (21 g.) in ethanol (200 c.c.) was treated with 0·1N-sodium hydroxide (1400 c.c.). After 1 hr. at room temperature the mixture was acidified with hydrochloric acid (100 c.c.; 2N) and extracted with ethyl acetate (10 × 100 c.c.). The combined extracts were washed with water (2 × 50 c.c.) and evaporated *in vacuo* (bath <30°). Trituration of the residual oil with benzene gave crystals (7·7 g.), m. p. 104—106° ; (±)-*anhydromonocrotalic acid* crystallised from benzene in thin plates, m. p. 114—115° (with decarboxylation) (Found : C, 56·3; H, 6·0%; equiv., 169. $C_8H_{10}O_4$ requires C, 56·5; H. 5·9%; equiv., 170). Infra-red spectrum (Nujol mull) : max. at 2660, 1758, 1721, 1681, 1531, 1449, 1339, 1284, 1244, 1186, 1147, 1129, 1103, 1073, 972, 929, 899, 835, 773, 759, and 709 cm.⁻¹.

A suspension of the acid (3·0 g.) in ether (100 c.c.) was treated with ethereal diazomethane until the yellow colour persisted. Isolated in the usual manner, the *methyl ester* (2·6 g.) was a colourless oil, b. p. 96—98°/0·6 mm., n_D^{20} 1·4712 (Found : C, 58·3; H, 6·7. $C_9H_{12}O_4$ requires

C, 58·7; H, 6·6%). Infra-red spectrum (liquid film) : max. at 3597, 3021, 1764, 1692, 1441, 1389, 1381, 1326, 1272, 1259, 1178, 1136, 1123, 1099, 1065, 977, 936, 888, 845, 780, and 750 cm.$^{-1}$.

The methyl ester (1·0 g.) was shaken with aqueous ammonia (15 c.c.; *d* 0·88) for 30 min., the crystalline product being collected and washed with water (yield, 0·8 g. of material, m. p. 174—176°). Recrystallisation from benzene furnished fine needles of the *amide*, m. p. 177—178° (Found : C, 56·6; H, 6·6 ; N, 8·7. $C_8H_{11}O_3N$ requires C, 56·8; H, 6·6; N, 8·3%). Infra-red spectrum (Nujol mull) : max. at 3345, 3279, 1761, 1689, 1462, 1405, 1389, 1325, 1258, 1183, 1149, 1124, 1114, 1091, 1064, 970, 733, 811, and 765 cm.$^{-1}$.

(±)-Ethyl anhydromonocrotalate (2·0 g.) was treated with anilinomagnesium bromide as in the previous example. The resulting *anilide* (0·6 g.) separated from light petroleum (b. p. 80—100°) containing a little ethyl methyl ketone in elongated hexagonal plates, m. p. 156—157° (Found : C, 68·5; H, 6·2; N, 6·0. $C_{14}H_{15}O_3N$ requires C, 68·5; H, 6·2; N, 5·7%). Infra-red spectrum (Nujol mull) : max. at 3345, 1754, 1678, 1597, 1543, 1502, 1488, 1441, 1389, 1370, 1316, 1247, 1178, 1124, 1099, 1063, and 866 cm.$^{-1}$.