

161.—*Investigation on the Formation and Stability of β -Lactones.*

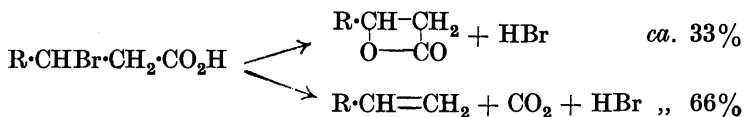
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β -LACTONES, in spite of their elementary position among the groups of organic compounds, have until recently received no adequate investigation and therefore constituted a small class of substances of which few examples were known. This is mainly to be ascribed to the general acceptance of the view of Erlenmeyer (*Ber.*, 1880, **13**, 305; 1881, **14**, 320) that β -bromo-acids, when treated with the equivalent of sodium carbonate, undergo preferential decomposition into unsaturated hydrocarbons. The formation of styrene from β -bromo- β -phenylpropionic acid (Fittig and Binder, *Annalen*, 1879, **195**, 131), of ψ -butylene from β -bromo- α -methylbutyric acid (Fittig and Pagenstecher, *Annalen*, 1879, **195**, 108), and of amylenes from β -bromo- α -ethylbutyric acid (Fittig and Howe, *Annalen*, 1880, **200**, 21) lent considerable support to this view.

The existence of β -lactones of *o*-nitro- and *p*-nitro-phenyl-lactic acids (Einhorn, *Ber.*, 1883, **16**, 2208; Basler, *ibid.*, p. 3001) was ascribed, on the grounds of analogy, to the stabilising influence of the nitro-group. It has, however, now been shown (Johannson and Hagman, *Ber.*, 1922, **55**, 647) that the formation of these lactones as well as that of quinoyl- β -hydroxypropionic acid (Einhorn and Lehnkering, *Annalen*, 1888, **246**, 160) is due to their insolubility (in water), which protects them from decomposition after formation.

As a result of careful investigation of the action of sodium carbonate on the β -bromo-derivatives of propionic, butyric, *isobutyric*, α -methyl-, and α -ethyl-butylacids, Johannson (*Dissert.*, Lund,

1916; Johannson and Hagman, *loc. cit.*) discovered that these substances underwent decomposition simultaneously in two ways :



The essential difference between the β - and the γ -lactones lies in the fact that, while the change γ -lactone \rightleftharpoons hydroxy-acid is a reversible one, that of the β -lactone \rightarrow hydroxy-acid is irreversible. It is therefore necessary, for the successful preparation of the β -lactones, to employ methods in which the decomposition of the lactone into the hydroxy-acid is prevented.

In contrast to the β -lactones derived from β -bromo-monocarboxylic acids, dimethylmalolactone (I), obtained by Baeyer and Villiger (*Ber.*, 1897, **30**, 1954) by the action of moist silver oxide on bromo- $\beta\beta$ -dimethylsuccinic acid, appeared to possess considerable stability. The isomeric lactone (II) of β -hydroxyisopropylmalonic acid (Meldrum, J., 1908, **93**, 598), on the other hand, is less stable and decomposes when heated into carbon dioxide and acetone.

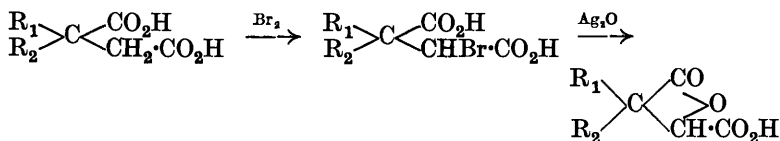


The present investigation was undertaken with the object of synthesising a series of β -lactones of the *as*-disubstituted succinic acids and the isomeric lactones of the β -hydroxymalonic acid type and comparing their stabilities. Bains and Thorpe (J., 1923, **123**, 2742), who isolated the β -lactone of $\beta\beta$ -di-*n*-propylmalic acid (III) from the products derived from tribromo- $\beta\beta$ -dipropylglutaric acid,



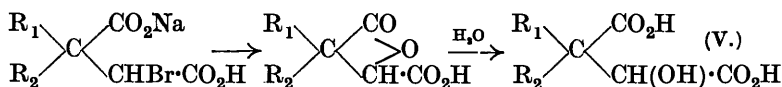
made the interesting discovery that this compound, in marked contrast to all the previously known β -lactones, behaved like the stable γ -lactones in that it could be regenerated from the salt of the hydroxy-acid (IV). These authors therefore suggested, on the basis of the valency deflexion hypothesis, that the alteration of the tetrahedral angle caused by the volumes of the two propyl groups brought the carboxyl and the hydroxyl group into the same relative distance from each other as the carboxyl and the γ -hydroxyl group in an unsubstituted chain. On this view, it is to be expected that, while the β -lactones of the dimethyl- and the *cyclopentane*-malic acids would behave like typical β -lactones, that of the *cyclohexane* analogue should simulate a γ -lactone.

The following scheme represents the method employed in the preparation of these lactones :



The bromination of the succinic acids by the Hell-Volhard-Zelinski method is much slower than that of the corresponding glutaric acids, but is considerably hastened in sunlight. The action of sodium carbonate in various concentrations and proportions on the bromo-acids was first studied. Under no conditions and in no case could the β -lactone be obtained : the product was invariably the hydroxy-acid (V). β -Lactones were, however, obtained in excellent yield by the action of moist silver oxide on an ethereal solution of the bromo-acid.

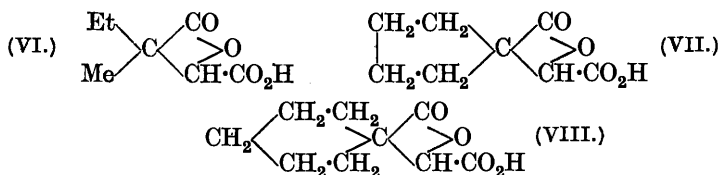
The lactonic acids thus obtained are generally well-defined crystalline solids and are distinguished from the hydroxy-acids by their solubility in hot benzene, in which the latter are practically insoluble. They form normal esters when treated with ethyl-alcoholic hydrogen chloride. The initial action of sodium carbonate on a β -bromo-acid, as on a γ -bromo-acid, is probably the elimination of sodium bromide and the formation of the β -lactone. The latter is, however, almost immediately converted into the hydroxy-acid by the action of boiling water.



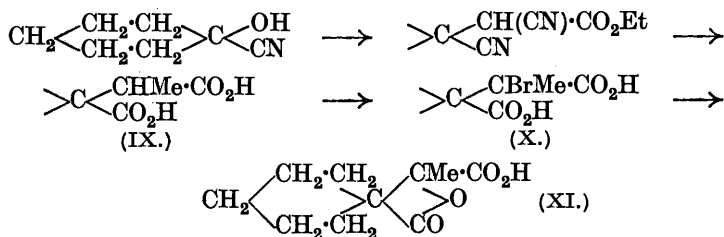
Johannson and Hagman's isolation of the β -lactone by the action of sodium carbonate on β -bromo- α -ethylbutyric acid (*loc. cit.*) depended for its success on the use of a solvent (chloroform) to remove the β -lactone from the sphere of action soon after formation and thus prevent its decomposition. It has now been found that all β -lactonic acids are converted into the corresponding hydroxy-acids by boiling water. These facts support the mechanism suggested for the formation of the hydroxy-acids from β -bromo-acids.

The β -lactonic acids, on titration, behave as monobasic acids, but become dibasic when heated with alkali. They show none of the fickleness of neutralisation which is so troublesome a feature of the γ -lactonic acids. The lactones could in no case be regenerated from the salts of the hydroxy-acids. Treatment of the hydroxy-acids with the conventional lactonising reagents (hydrochloric acid, hydrobromic acid, etc.) failed to convert them into the lactonic

acids. It was to be expected in the case of the β -lactonic acids (I; VI; VII) that once the lactone ring was opened there would be no tendency to re-form it. On the other hand, it was expected that the lactone (VIII), on the basis of a uniplanar configuration for the *cyclohexane* ring, which reduces the angle between the extra-cyclic valencies to 107.2° , would behave like a γ -lactone. Possibly



the extent of the valency deflexion even in this case is not sufficient to bring about this change. It was therefore considered desirable to study the lactone (XI), in which the effect of the *cyclohexane* ring would be supplemented by that of an α -methyl group. The 1-carboxycyclohexane-1- α -propionic acid (IX) necessary for this purpose was synthesised by Higson and Thorpe's method (J., 1906, 89, 1455) by the following series of reactions :

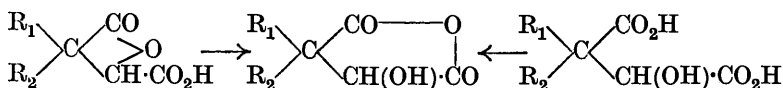


Some trouble was experienced in the bromination of the acid (IX). Considerable difficulty had previously been encountered in the preparation of bromotrimethylsuccinic acid. Komppa (*Acta Soc. Sci. Fennicæ*, 1891, 24, 1) obtained, by the action of phosphorus pentabromide on hydroxytrimethylsuccinic acid, a complex mixture of substances, from which he was unable to isolate any pure product. Bone and Sprankling (J., 1902, 81, 50) obtained, by the action of water on bromotrimethylsuccinic anhydride, a solid, m. p. $120-130^\circ$, which was a mixture of the parent anhydride and bromotrimethylsuccinic acid. It has, however, been found that the bromination of trisubstituted succinic acids proceeds smoothly in ultra-violet light.

The β -lactone (XI) behaves exactly like the other β -lactones in that it is not produced from the hydroxy-acid. The behaviour of the β -lactone of di-*n*-propylmalic acid in simulating a γ -lactone would thus seem to be an abnormal one.

Attempts to determine the difference in stability of the various lactic acids by measurement of the rate of opening of the lactone ring by means of alkali were unsuccessful. The reactions proceeded too slowly at 25–50°, and too rapidly at 80° for accurate measurements to be made.

Baeyer and Villiger found that *as*-dimethylmalolactone, in sharp contrast to the lactones derived from β -bromo-monocarboxylic acids, could be distilled under reduced pressure without loss of carbon dioxide. The product of distillation was, however, shown by Fichter and Hirsch (*Ber.*, 1900, **33**, 3270) to be dimethylmalic anhydride and not the lactone itself as Baeyer and Villiger had thought. All the β -lactones discussed in this paper undergo the same intramolecular rearrangement into the anhydrides of the corresponding hydroxy-acids on distillation: the change is not surprising when it is remembered that a not particularly stable four-membered ring is converted into a stable five-membered one. The identity of the anhydrides was established by their preparation from the hydroxy-acids.



β -Lactones of the Type (II).—Lactones of type (II), with Me and Et, Pr ^{α} , C₄H₈>, or C₅H₁₀> in place of Me₂, have been obtained either by Meldrum's original method or by the modification of it devised by Ott (*Annalen*, 1913, **401**, 1605). They are all highly crystalline substances and are regenerated from their salts on acidification. They behave as monobasic acids on titration with cold alkali and as dibasic acids at 100°. These lactones undergo ring fission by alkali much more slowly than the isomerides previously discussed. The great solubility of the resulting hydroxymalonic acids in water and their general instability make their isolation impossible.

Synthesis of Cyclic Malonic Acids.—The usual methods of preparation of cyclic malonic acids are rather involved and tedious. It is now found that *cyclohexane*- and *cyclopentane*-1 : 1-dicarboxylic acid are conveniently obtained by oxidation of the hydroxy-acids C₅H₁₀>C(CO₂H)·CH(OH)·CO₂H and C₄H₈>C(CO₂H)·CH(OH)·CO₂H respectively with permanganate.

EXPERIMENTAL.

α -Bromo-1-carboxycyclohexane-1-acetic Acid.—I-Carboxycyclohexane-1-acetic acid (Lapworth and McRae, *J.*, 1922, **121**, 2754) (162 g.) was mixed with phosphorus pentachloride (360 g.) and heated on the steam-bath for 4 hours, bromine (47 c.c.) added

during 8 hours, and the mixture gently heated until the evolution of hydrogen bromide ceased (30 hours). The product was poured into formic acid (300 c.c., *d* 1.2) and, when the vigour of the initial reaction had abated, heated on the steam-bath for 3 hours. The bromo-acid, which separated from the cooled solution, was washed with a little cold formic acid and crystallised from this solvent, forming needles, m. p. 142°; more was obtained from the concentrated filtrate (yield, 212 g.) (Found : Br, 29.9. $C_9H_{13}O_4Br$ requires Br, 30.2%).

β-Lactone of α-Hydroxy-1-carboxycyclohexane-1-acetic Acid (VIII).—Silver oxide freshly prepared from 51 g. of silver nitrate was added portionwise to a solution of the preceding bromo-acid (25 g.) in ether (250 c.c.) : silver bromide separated at once and the solvent boiled. After 6 hours, more ether was added, the mixture decomposed with just sufficient hydrochloric acid, the solution filtered and dried over anhydrous sodium sulphate, and the solvent evaporated. The oily residue solidified in a vacuum (yield, 14 g.). The *β-lactone of α-hydroxy-1-carboxycyclohexane-1-acetic acid* crystallised from benzene-petroleum (b. p. 60–80°) in rectangular prisms, m. p. 129° [Found : C, 58.5; H, 6.6; M_1 ,* 184.5; M_2 , 101. $C_9H_{12}O_4$ requires C, 58.7; H, 6.5%; M_1 (monobasic), 184; M_2 (dibasic), 101]. The *aniline* salt crystallised in lustrous plates, m. p. 116°, when the lactone and aniline were mixed in benzene solution (Found : C, 64.6; H, 7.0. $C_9H_{12}O_4 \cdot C_6H_5 \cdot NH_2$ requires C, 65.0; H, 6.9%).

α-Hydroxy-1-carboxycyclohexane-1-acetic Acid.—(1) A solution of the bromo-acid (40 g.) in 2*N*-sodium carbonate (400 c.c.) was boiled under reflux for 3 hours and evaporated on the steam-bath to a syrupy consistency. The oil which was precipitated on acidification of the solution was extracted and dried in ether, recovered, and crystallised from ethyl acetate, *α-hydroxy-1-carboxycyclohexane-1-acetic acid* being obtained in needles, m. p. 135°, sparingly soluble in chloroform and benzene (Found : C, 53.6; H, 7.0; equiv., 100.9. $C_9H_{14}O_5$ requires C, 53.5; H, 6.9%; equiv., 101).

(2) The lactonic acid (VIII) (1 g.) was heated for 1 hour with *N*/10-barium hydroxide (50 c.c.), and the solution cooled, acidified, and thoroughly extracted with ether. The acid thus obtained, after one crystallisation, melted at 135°, alone or mixed with the hydroxy-acid.

The *anhydride*, prepared by the action of excess of acetyl chloride on the acid, distilled at 170°/11 mm. and solidified. It crystallised from light petroleum (b. p. 60–80°) in stellate clusters of rods, m. p. 86° (Found : C, 58.8; H, 6.4. $C_9H_{12}O_4$ requires C, 58.7;

* Throughout this paper M_1 and M_2 denote the equivalents obtained by titration with cold and with hot alkali respectively.

H, 6.5%). The *anilic acid* separated in needles, m. p. 187°, when the anhydride and aniline were mixed in benzene solution (Found : C, 64.9; H, 6.8. $C_{15}H_{19}O_4N$ requires C, 65.0; H, 6.9%). The *anil*, formed on melting the acid, crystallised from alcohol in plates, m. p. 168° (Found : C, 69.4; H, 6.6. $C_{15}H_{17}O_3N$ requires C, 69.5; H, 6.5%).

Distillation of the Lactonic Acid.—Fumes were evolved and then a viscous liquid distilled at 164°/8 mm. This solidified on cooling and crystallised from petroleum in rosettes of needles, m. p. 85—86°.

Oxidation of α -Hydroxy-1-carboxycyclohexane-1-acetic Acid to α -Keto-1-carboxycyclohexane-1-acetic Acid.—A 4% solution of potassium permanganate (5.3 g.) was slowly added, with vigorous shaking, to the hydroxy-acid (10 g.) in water (1 l.) which had been neutralised with *N*/10-barium hydroxide. After 6 hours, the filtered solution was concentrated, acidified with hydrochloric acid, and extracted with ether. The *keto-acid*, obtained on evaporation of the solvent, was sparingly soluble in benzene and crystallised from chloroform in short needles, m. p. 132° (Found : C, 54.0; H, 5.9; equiv., 100. $C_9H_{12}O_5$ requires C, 54.0; H, 6.0%; equiv., 100). The *quinoxaline* derivative, prepared by heating the *keto-acid* and *o*-phenylenediamine (1 mol. of each) in glacial acetic acid, was obtained as a yellow precipitate on dilution of the solution; it crystallised from alcohol in buff-coloured needles, m. p. 249° (sintering at 240°) (Found : C, 66.2; H, 6.0. $C_{15}H_{16}O_3N_2$ requires C, 66.2; H, 5.9%).

Oxidation of α -Hydroxy-1-carboxycyclohexane-1-acetic Acid to cycloHexane-1:1-dicarboxylic Acid.—The acid (2 g.), suspended in water (150 c.c.) and neutralised with aqueous barium hydroxide, was stirred while a solution of potassium permanganate (4 g.) in water (100 c.c.) was added during 4 hours. After 12 hours, the filtered solution was evaporated to a small bulk and acidified with hydrochloric acid. *cycloHexane-1:1-dicarboxylic acid*, obtained by extraction of the solution with ether, solidified on trituration with benzene: it crystallised from light petroleum (b. p. 60—80°) in prisms, m. p. 17° (equiv. 86).

Bromination of 1-Carboxycyclopentane-1-acetic Acid.—The bromination was carried out exactly as described for the *cyclohexane acid*, the quantities employed being 150 g. of the acid, 364 g. of phosphorus pentachloride, 47 c.c. of bromine, and 300 c.c. of formic acid. A large proportion of the bromo-acid crystallised from the formic acid solution, and what remained dissolved was isolated by extraction with ether (yield, 200 g.). *α -Bromo-1-carboxycyclopentane-1-acetic acid* crystallised from formic acid in plates, m. p. 135° (Found : Br, 31.5. $C_8H_{11}O_4Br$ requires Br, 31.9%).

β-Lactone of α-Hydroxy-1-carboxycyclopentane-1-acetic Acid (VII).—The bromo-acid (50 g.) was dissolved in ether (300 c.c.) and treated with silver oxide freshly prepared from 100 g. of silver nitrate. The *β-lactone*, isolated in the usual manner, solidified in a vacuum after 1 day and was freed from oily impurities on porous tile (yield, 25 g.). It was freely soluble in most organic solvents, more soluble in benzene than the *cyclohexane* analogue, and crystallised from benzene–light petroleum (b. p. 40–60°) in rectangular prisms, m. p. 81° (Found : C, 56.4; H, 6.3; M_1 , 170; M_2 , 94. $C_8H_{10}O_4$ requires C, 56.4; H, 5.9%; M_1 , 170; M_2 , 94). The *aniline* salt crystallised from benzene in soft needles, m. p. 118° (Found : C, 63.9; H, 6.3. $C_8H_{10}O_4 \cdot C_6H_5 \cdot NH_2$ requires C, 63.9; H, 6.5%).

α-Hydroxy-1-carboxycyclopentane-1-acetic Acid.—A solution of the bromo-acid (25 g.) in 2*N*-sodium carbonate (250 c.c.) was boiled under reflux for 4 hours. The *hydroxy-acid*, isolated as described before, crystallised from ethyl alcohol in short prisms (14 g.), m. p. 125° (Found : C, 51.2; H, 6.3; M_1 , 93.8. $C_8H_{12}O_5$ requires C, 51.2; H, 6.4%; M_1 , 94). The *anhydride*, obtained by boiling a mixture of the acid and acetic anhydride, distilled as a viscous liquid which solidified on cooling; recrystallised from light petroleum (b. p. 60–80°), it formed needles, m. p. 141° (Found : C, 56.5; H, 5.7. $C_8H_{10}O_4$ requires C, 56.4; H, 5.9%).

Distillation of the Lactonic Acid.—There was a slight evolution of fumes at the commencement. The distillate, which solidified on cooling, had, after one crystallisation, m. p. 141° alone or mixed with the above anhydride. The *anilic acid* crystallised from benzene in prisms, m. p. 151° (Found : C, 63.8; H, 6.6. $C_{14}H_{17}O_4N$ requires C, 63.9; H, 6.5%).

Oxidation of the Hydroxy-acid to α-Keto-1-carboxycyclopentane-1-acetic Acid.—This was carried out exactly as described on p. 1221. The *keto-acid*, which was sparingly soluble in benzene, crystallised from a large volume of chloroform in rods, m. p. 133° (Found : C, 51.7; H, 5.5; equiv., 93. $C_8H_{10}O_5$ requires C, 51.6; H, 5.4%; equiv., 93).

Oxidation to cyclopentane-1 : 1-dicarboxylic Acid.—The quantities employed were : 2 g. of the acid and 4 g. of potassium permanganate (3% solution). The product, worked up in the usual way, gave an acid (1 g.) which crystallised from ether–petroleum in small prisms, m. p. 190° (Found : M , 78.5).

Bromination of β-Methyl-β-ethylsuccinic Acid.—The quantities employed for bromination were : 16 g. of the acid (Higson and Thorpe, *loc. cit.*), 42 g. of phosphorus pentachloride, and 6 c.c. of bromine. Since the bromo-acid failed to separate from the formic acid solution, the solvent was evaporated and the residue diluted

with water and extracted with ether. α -Bromo- β -methyl- β -ethylsuccinic acid, left on evaporation of the ether, solidified after 3 days and crystallised from benzene-light petroleum, b. p. 60–80°, in prisms, m. p. 126° (Found: Br, 33.0. $C_7H_{11}O_4Br$ requires Br 33.5%).

Lactone of β -Methyl- β -ethylmalic Acid.—This lactone, prepared by the usual method, did not solidify after several weeks (Found: M_1 , 156. $C_7H_{10}O_4$ requires M_1 , 158). The *aniline* salt crystallised in needles, m. p. 102° (Found: C, 62.0; H, 6.7. $C_7H_{10}O_4 \cdot C_6H_5 \cdot NH_2$ requires C, 62.1; H, 6.8%).

β -Methyl- β -ethylmalic Acid.—A solution of the bromo-acid in *N*-sodium carbonate was boiled for 3 hours. The hydroxy-acid, precipitated from the acidified solution, crystallised from chloroform-light petroleum in plates, m. p. 105° (Found: C, 47.8; H, 6.8%; M , 176).

Bromination of $\beta\beta$ -Dimethylsuccinic Acid.—The quantities used were 20 g. of the acid, 69 g. of phosphorus pentachloride, and 9 c.c. of bromine. α -Bromo- $\beta\beta$ -dimethylsuccinic acid, which separated from the formic acid solution, had m. p. 167° (Baeyer and Villiger, *loc. cit.*).

β -Lactone of $\beta\beta$ -Dimethylmalic Acid.—Prepared by the standard method, this crystallised from benzene-petroleum in plates, m. p. 56°, and m. p. 45° after drying in a desiccator. This β -lactone, unlike the others, shows an extraordinary tendency to combine with a molecule of water (Found: C, 49.9; H, 5.7; M_1 , 145. Calc.: C, 50.0; H, 5.6%; M_1 , 144).

Bromination of 2-Carboxy-trans-hexahydrohydrindene-2-acetic Acid.—This was carried out in the usual manner, the quantities used being 12 g. of the acid, 22 g. of phosphorus pentachloride, and 8 c.c. of bromine. α -Bromo-2-carboxy-trans-hexahydrohydrindene-2-acetic acid, which was isolated by extraction with ether, solidified in a vacuum after a few days and crystallised from formic acid in prisms, m. p. 136° (Found: Br, 26.1. $C_{12}H_{17}O_4Br$ requires Br, 26.3%).

β -Lactone of α -Hydroxy-2-carboxy-trans-hexahydrohydrindene-2-acetic Acid.—This β -lactone, which was prepared by the action of silver oxide on an ethereal solution of the bromo-acid, remained a sticky mass in a vacuum for several days. It crystallised from benzene, on addition of light petroleum, in clusters of silky needles, m. p. 110°; more was obtained from the mother-liquor after concentration (Found: C, 64.3; H, 7.0; M_1 , 225; M_2 , 121. $C_{12}H_{16}O_4$ requires C, 64.3; H, 7.1%; M_1 , 224; M_2 , 121). The *aniline* salt crystallised from benzene in plates, m. p. 116° (Found: C, 68.1; H, 7.2. $C_{12}H_{16}O_4 \cdot C_6H_5 \cdot NH_2$ requires C, 68.2; H, 7.2%).

α -Hydroxy-2-carboxy-trans-hexahydrohydrindene-2-acetic acid, ob-

tained by the action of sodium carbonate on the bromo-acid, had m. p. 134° after one crystallisation from ethyl acetate (Found : C, 59.5; H, 7.4; M , 120.8. $C_{12}H_{18}O_5$ requires C, 59.5; H, 7.4%; M , 121).

α -Bromo-2-carboxy-cis-hexahydrohydrindene-2-acetic acid, obtained by the bromination of the corresponding succinic acid, crystallised from benzene-light petroleum in needles, m. p. 164° (Found : Br, 25.8. $C_{12}H_{17}O_4Br$ requires Br, 26.3%).

The β -lactone of α -hydroxy-2-carboxy-cis-hexahydrohydrindene-2-acetic acid, prepared in the usual manner, is much more soluble in benzene than the *trans*-isomeride and crystallises from benzene-petroleum (b. p. $60-80^{\circ}$) in snow-white rectangular prisms, m. p. 125° (Found : C, 64.2; H, 7.3; M_1 , 224.3; M_2 , 121. $C_{12}H_{16}O_4$ requires C, 64.3; H, 7.1%; M_1 , 224; M_2 , 121). The *aniline* salt separated from benzene in needles, m. p. 135° (Found : C, 68.0; H, 7.3. $C_{12}H_{16}O_4 \cdot C_6H_5 \cdot NH_2$ requires C, 68.2; H, 7.2%).

α -Hydroxy-2-carboxy-cis-hexahydrohydrindene-2-acetic acid, obtained by the action of sodium carbonate on the bromo-acid, crystallised from chloroform in short needles, m. p. 192° (Found : C, 59.4; H, 7.6; M , 121. $C_{12}H_{18}O_5$ requires C, 59.5; H, 7.4%; M , 121).

Synthesis of 1-Carboxycyclohexane-1- α -propionic Acid (IX).—*Ethyl 1-cyanocyclohexane-1- α -cyanopropionate.* To a well-cooled solution of freshly distilled cyclohexanone cyanohydrin (186 g.) in absolute alcohol (186 c.c.) was gradually added, with vigorous shaking, a suspension of ethyl sodiocyanoacetate, obtained from ethyl cyanoacetate (168 g.), sodium (33 g.), and alcohol (500 c.c.). The mixture, after being kept in ice for 6 hours and at room temperature for 3 days, was mixed with methyl iodide (145 c.c.) and, after the initial vigorous reaction had abated, boiled under reflux until a test portion, diluted with water, was neutral to litmus. The oil thus precipitated was extracted with ether, washed with a large volume of water to remove most of the alcohol, dried, and recovered. The *ester* distilled as a viscous liquid, which solidified when cooled and crystallised from light petroleum (b. p. $60-80^{\circ}$) in large, well-defined, rhombic prisms, m. p. 51° (Found : C, 66.6; H, 7.5. $C_{13}H_{18}O_2N_2$ requires C, 66.6; H, 7.7%).

Hydrolysis. As this ester could not be hydrolysed with concentrated hydrochloric acid even on prolonged boiling, it was mixed with 6 vols. of 70% sulphuric acid and boiled under reflux for 10 hours. The solution was then diluted with water and extracted with ether and the acid thus obtained was freed from neutral matter by extraction with sodium carbonate. 1-Carboxycyclohexane-1- α -propionic acid crystallised from chloroform in prisms, m. p. 110° (Found : C, 60.0; H, 8.3; equiv., 95. $C_{10}H_{16}O_4$ requires C, 60.0;

H, 8.0%; equiv., 100). The *anhydride* distilled at 165°/10 mm. as a colourless liquid (Found: C, 65.9; H, 7.8. $C_{10}H_{14}O_3$ requires C, 65.9; H, 7.7%). The *anilic acid* crystallised in plates, m. p. 165° (Found: C, 69.5; H, 7.8. $C_{16}H_{21}O_3N$ requires C, 69.8; H, 7.6%). The *anil* separated from aqueous alcohol in lustrous needles, m. p. 100° (Found: C, 74.7; H, 7.4. $C_{16}H_{19}O_2N$ requires C, 74.7; H, 7.4%).

Bromination of 1-Carboxycyclohexane-1- α -propionic Acid.—The acid (20 g.), contained in a silica flask, was mixed with phosphorus pentachloride (40 g.) and warmed on the steam-bath until the evolution of hydrogen chloride ceased. Dry bromine (7 c.c.) was added, and the mixture kept in an ultra-violet chamber for 3 days. The solution obtained by pouring the mixture into formic acid was evaporated on the steam-bath, and the *bromo-acid* isolated by extraction with ether. It solidified after a week and, having been drained on porous tile, crystallised from formic acid in prismatic rods, m. p. 142° (Found: Br, 28.5. $C_{10}H_{15}O_4Br$ requires Br, 28.7%).

Bromination of the Anhydride.—The anhydride (5 g.), mixed with bromine (4 g.), was heated in a sealed tube in a boiling water-bath for 12 hours. The liquid product was kept in a vacuum desiccator over potash to remove the last traces of hydrogen bromide. The *bromo-anhydride* crystallised from light petroleum (b. p. 60—80°) in colourless prisms, m. p. 55° (Found: Br, 30.5. $C_{10}H_{13}O_3Br$ requires Br, 30.7%).

β -Lactone of α -Hydroxy-1-carboxycyclohexane-1- α -propionic Acid.—The bromo-acid, on treatment with silver oxide, was quantitatively converted into the *lactone*, which crystallised from benzene in rectangular prisms, m. p. 46° (Found: C, 60.6; H, 7.0; M_1 , 197.3; M_2 , 108. $C_{10}H_{14}O_4$ requires C, 60.6; H, 7.2%; M_1 , 198; M_2 , 108).

α -Hydroxy-1-carboxycyclohexane-1- α -propionic Acid.—When a solution of the bromo-acid in sodium carbonate was boiled for 3 hours and acidified, the *hydroxy-acid* separated as a snow-white solid readily soluble in benzene; it crystallised from hot water in needles, m. p. 73.4° (Found: C, 55.6; H, 7.4; M , 108. $C_{10}H_{16}O_5$ requires C, 55.5; H, 7.4%; M , 108).

Bromination of Trimethylsuccinic Acid.—Trimethylsuccinic acid was prepared by Higson and Thorpe's method (compare Bardhan, J., 1928, 2604). The bromination was carried out exactly as described above. *Bromotrimethylsuccinic acid* crystallised from formic acid in scales, m. p. 185° (Found: Br, 33.5. $C_7H_{11}O_4Br$ requires Br, 33.5%).

The β -lactone of hydroxytrimethylsuccinic acid, prepared from the bromo-acid in the usual way, crystallised from benzene-petroleum

in needles, m. p. 120° (Found: C, 53.2; H, 6.4. Calc.: C, 53.2; H, 6.3%).

α -Carboxy- β -hydroxy- β -n-propylhexolactone (as II).—When malonic acid (10 g.), dipropyl ketone (20 g.), acetic anhydride (20 c.c.), and concentrated sulphuric acid (1 c.c.) were mixed together, there was considerable development of heat and the malonic acid soon dissolved. After 24 hours, the solution was cooled in a freezing mixture and the crystalline product was collected and washed with a little water (yield, 7 g.). On removal of the ketone from the mother-liquor in a vacuum, a further quantity of the *lactonic acid* was obtained. It crystallised from light petroleum (b. p. 60 – 80°) in long needles, m. p. 89° (Found: C, 60.0; H, 8.0; *M*, 200. $C_{10}H_{16}O_4$ requires C, 60.0; H, 8.0%; *M*, 200).

1-Hydroxycyclopentane-1-malonolactone (as II).—A mixture of cyclopentanone (30 g.) and malonic-acetic anhydride (70 g.) was kept for 24 hours and then cooled in a freezing mixture; it deposited a crystalline solid (20 g.). A further quantity of the lactone was obtained by extracting the mother-liquor repeatedly with petroleum. This *lactone* crystallised from benzene-light petroleum in plates, m. p. 73° (Found: C, 56.4; H, 6.1; *M*, 170.8. $C_8H_{10}O_4$ requires C, 56.4; H, 5.9%; *M*, 170).

1-Hydroxycyclohexane-1-malonolactone.—This condensation was carried out as in the previous case, the quantities used being cyclohexanone (40 g.) and malonic-acetic anhydride (73 g.). Yield, 50 g. The *lactone* crystallised from petroleum (b. p. 60 – 80°) in plates, m. p. 95° (Found: C, 58.8; H, 6.4; *M*, 184.2. $C_9H_{12}O_4$ requires C, 58.7; H, 6.5%; *M*, 184).

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