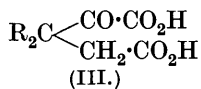
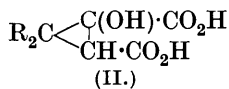
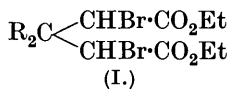


CXXXIV.—*Studies in Dicyclic Systems. Part II. The Influence of cis- and trans-Hexahydrohydrindene Nuclei on the Carbon Tetrahedral Angle.*

By ARUPPILLAI KANDIAH.

THE conclusion reached by Rao (J., 1930, 1162) as a result of experiments on derivatives of *trans*-decahydronaphthalene-2:2-diacetic acid was that *trans*-decalin is a strainless system and that the component *cyclohexane* rings must necessarily be given a strainless multiplanar configuration. It was therefore deemed desirable to determine whether *cis*- and *trans*-hexahydrohydrindenes would be comparatively strainless, indicating a strainless form for the *cyclohexane* ring, or highly strained, owing to the uniplanar structure of that component. In these condensed systems, but not in the decalin series, the *cis*-complex is according to the models strainless, whereas the *trans*-compound has an appreciable molecular strain.

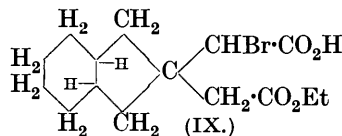
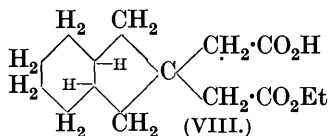
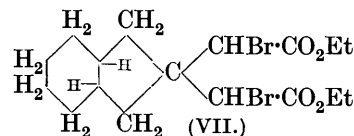
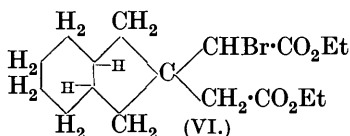
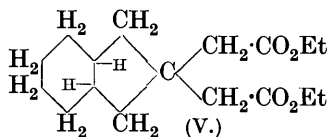
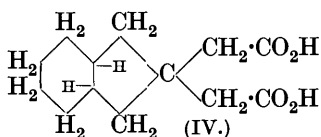
It was therefore proposed to detect the strain by means of a comparative study of the products of hydrolysis of the mono- and di-bromo-esters of *cis*- and *trans*-hexahydrohydrindene-2:2-diacetic acids. The study has for its basis Thorpe and Ingold's valency deflexion hypothesis, which postulates that, when the normal angle between two valencies of a carbon atom is altered either by their attachment to heavy groups or by participation in a ring complex, the angle between the other two valencies is correspondingly affected in the opposite direction. This hypothesis, which is based on a large body of experimental data, is the only one that explains, for instance, the observation that dibromo-esters of the type (I), when treated with aqueous potassium hydroxide, yield the hydroxyring acid (II), the keto-acid (III), or an equilibrium mixture of the



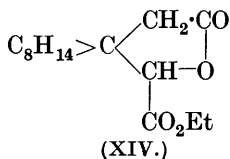
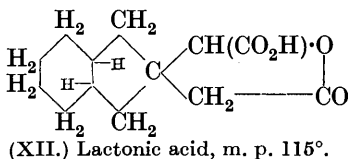
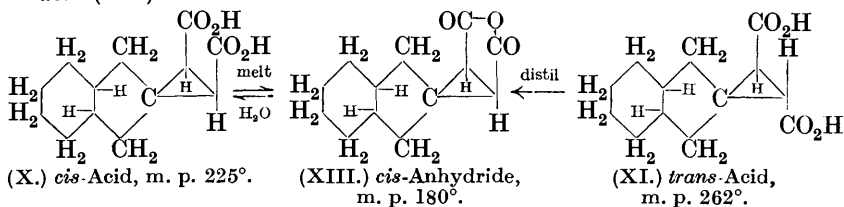
two according as R_2 represents a *cyclohexane* ring, a *cyclopentane* ring (or dimethyl), or diethyl.

Examination of Derivatives of trans-Hexahydrohydrindene.

The monobromination of the diacetic acid (IV) by the Hell-Volhard-Zelinski method usually produced mixtures of the unbrominated ester (V), the monobrominated ester (VI), and the dibromo-ester (VII). The separation of these substances by fractional distillation under reduced pressure is not possible, as the last



two substances partially lose ethyl bromide during the process. *Ethyl α -bromo-trans-hexahydrohydrindene-2:2-diacetate* (VI) was, however, obtained in a high degree of purity by the monobromination of *ethyl hydrogen trans-hexahydrohydrindene-2:2-diacetate* (VIII). [A small amount of *monobrominated acid ester* (IX) is always formed in this process.] On hydrolysis with 64% aqueous potassium hydroxide it was converted to the extent of about 40% into a mixture of *cis-1:2-dicarboxycyclopropane-3(2')-spiro-trans-hexahydrohydrindene* (X) and *trans-1:2-dicarboxycyclopropane-3(2')-spiro-trans-hexahydrohydrindene* (XI), and the rest into the *lactonic acid* (XII).

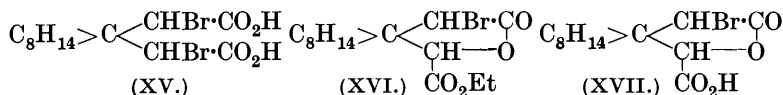


The separation of the *cis*- from the *trans*-dicarboxylic acid could not be effected by fractional crystallisation, but was achieved by means of acetyl chloride, which converted the *cis*-acid (X) into the corresponding *anhydride* (XIII) and left the *trans*-isomeride unaffected. The latter is, however, converted into the same anhydride on distillation, and this yields the *cis*-acid on hydration.

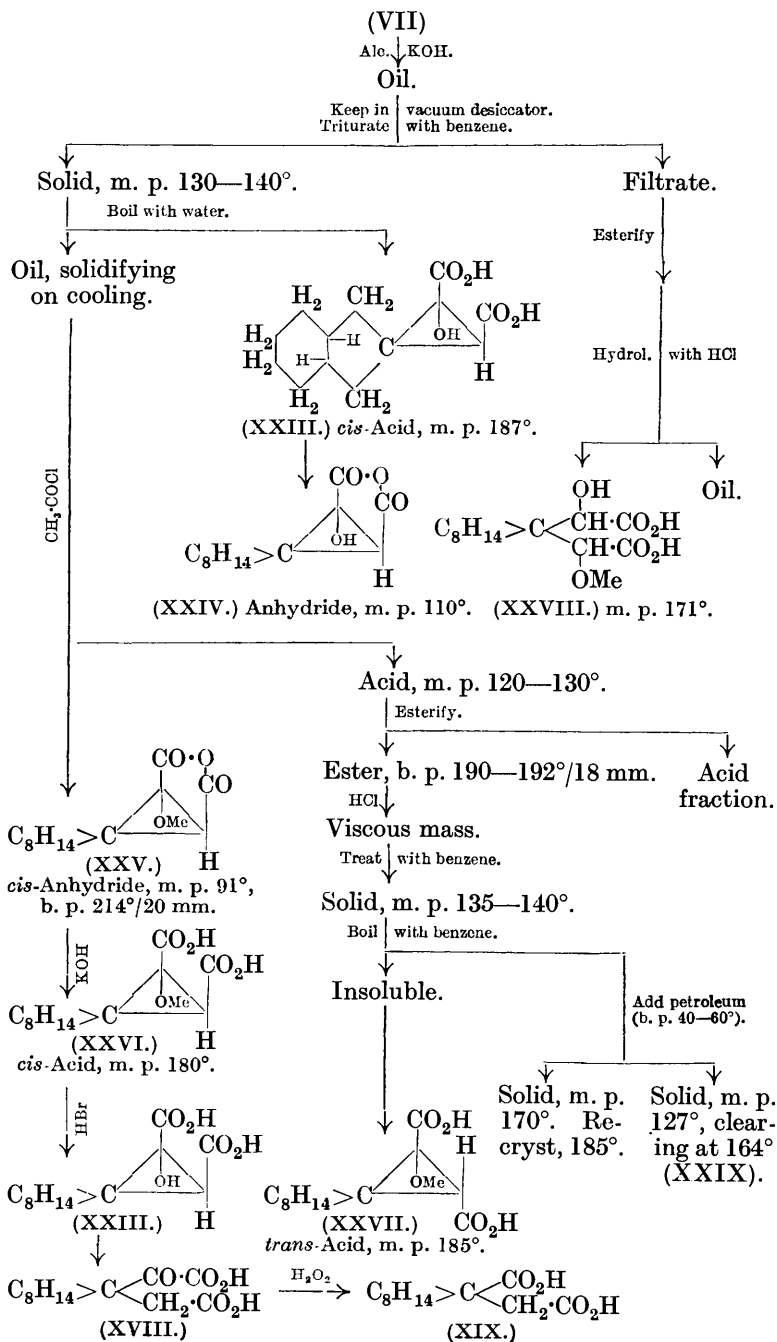
Any strain in the *trans*-hexahydrohydrindene nucleus would be expected to reveal itself in the consequential instability of the associated *cyclopropane* ring. It has already been shown (Beesley, Ingold, and Thorpe, J., 1915, **107**, 1080; Becker and Thorpe, J., 1920, **117**, 1579) that, although the *gem*-dimethyl- and the *cyclopentane-spiro*-acid are decomposed when heated at 200° with 5% hydrochloric acid, the *cyclohexane* analogue survives heating with 20% hydrochloric acid at 240° for 6 hours. The *trans*-hexahydrohydrindene-*spiro-trans*-acid (XI), though practically unaffected by 5–10% acid at 200°, is completely carbonised by 10% acid at 240°, whereas the parent diacetic acid is recovered unchanged after similar treatment. The stability of the hexahydrohydrindene *spiro*-acid towards hydrochloric acid, though very slightly greater than that of the *cyclopentane* acid, is considerably less than that of the *cyclohexane* analogue. The *spiro*-acids are stable to boiling permanganate solution and to reducing agents.

The lactonic acid (XII) is obtained by the hydrolysis of the lactonic ester (XIV) with concentrated hydrochloric acid or by treatment of either the monobromo-ester (VI) or the monobromo-acid ester (IX) with dilute sodium carbonate solution.

The dibromo-acid chloride of *trans*-hexahydrohydrindene-2 : 2-diacetic acid was easily prepared in the usual way and converted into *ethyl α'-dibromo-trans-hexahydrohydrindene-2 : 2-diacetate* (VII) together with a small amount of a viscous acidic liquid, from which some *bromo-lactonic acid* (XVII) was isolated.

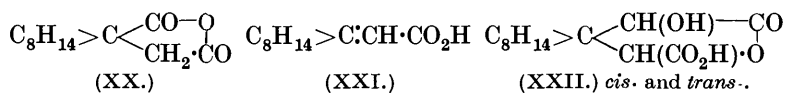


The dibromo-ester (VII), which is possibly a mixture of *meso*- and *racemic* forms, cannot be distilled under reduced pressure without undergoing partial decomposition into the bromo-lactone (XVI) and ethyl bromide. It behaves, therefore, like the dibromo-esters of the *cyclohexane* and *decalin* series. This contrast in behaviour of ethyl *α'-dibromo-trans-hexahydrohydrindene-2 : 2-diacetate* and its *cyclopentane* analogue probably depends on the dicyclic structure and the higher molecular weight and not on the presence of any strain in the molecule.



When the dibromo-ester is hydrolysed with concentrated aqueous alkali at 150° it gives mainly α -keto-*trans*-hexahydrohydrindene-2 : 2-diacetic acid (XVIII), together with a small quantity of 2-carboxy-*trans*-hexahydrohydrindene-2-acetic acid (XIX) and a trace of the unsaturated acid (XXI); the rest of the material possibly consists of a mixture of stereoisomeric hydroxy-lactonic acids (XXII), from which the *trans*-isomeride (XXX) is isolable in small amount.

Among the products of hydrolysis no trace of a hydroxy-*spiro*-acid (XXIII) was detected. The acid (XIX), which undoubtedly results from the decomposition of the keto-acid first formed, is of interest in that it is the first instance of an acid of this type being produced by hydrolysis of dibromo-esters. The keto-acid (XVIII) is characterised by the formation of a well-defined *quinoxaline* derivative, by conversion into the succinic acid (XIX) by oxidation with hydrogen peroxide, and by the production of the *anhydride* (XX)



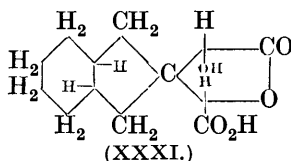
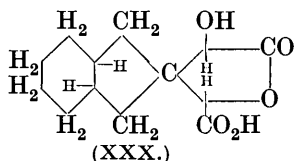
on distillation. The side chain which is eliminated, probably as glyoxylic acid, in the reaction leading to the formation of *trans*-hexahydrohydrindylidene-2-acetic acid (XXI), undergoes oxidation to oxalic acid, and is detected as such among the products of hydrolysis.

When the hydrolysis of the dibromo-ester (VII) is effected with methyl-alcoholic potash a complex mixture of products is formed : the separation of the components presented almost insuperable experimental difficulties, as indicated in the scheme on p. 955.

Many points of interest emerge from the various types of substance isolated in this reaction. In the first place, the occurrence of the *hydroxy-ring-acid* (XXIII) is remarkable. This acid, however, like its *cyclopentane* analogue, readily gives an *anhydride* (XXIV) and is therefore a *cis*-acid with the carboxyl groups in the same plane, whereas all the other hydroxy-ring-acids are *trans*-forms and fail to undergo anhydride formation. The hydroxy-ring-acid is stable towards potash, and it is evidently the *trans*-form which undergoes fission to give rise to the keto-acid (Lanfear and Thorpe, J., 1923, 123, 1683).

The *methoxy-spiro-acid* has been isolated in well-defined *cis*- and *trans*-forms (XXVI and XXVII). The *trans*-modification is converted into the *cis*- through the *anhydride* of the latter. Both substances are converted by boiling hydrobromic acid into 2-carboxy-*trans*-hexahydrohydrindene-2-acetic acid (XIX) : the initially formed *cis*- and *trans*-hydroxy-ring acids probably react with

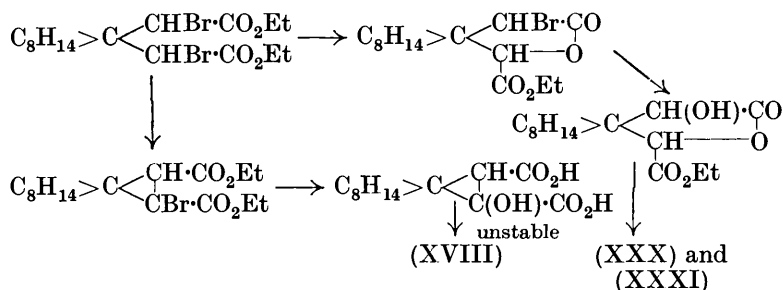
The hydroxy-lactonic acids, which would not solidify, were purified by fractional distillation of their esters, and then, by hydrolysis of the esters, three substances were isolated, namely, the *cis*- and *trans*-hydroxy-lactonic acids (XXXI) and (XXX) and the keto-acid (XVIII) (small amount).



The hydroxy-lactonic acid (XXX), m. p. 212°, is rapidly converted into the acetyl derivative by means of acetyl chloride, but the isomeride (XXXI), m. p. 195°, is unaffected by this reagent.

The large neutral fraction obtained in the above hydrolysis with sodium carbonate, on distillation under reduced pressure, furnished a thick viscous liquid which partly solidified. The solid, m. p. 129°, was the ester of one of the above hydroxy-lactonic acids, but the quantity obtained was too small for further investigation. This result shows that the difficulty of obtaining the hydroxy-lactonic acids in quantity by the above method is due to the fact that, although the replacement of bromine by hydroxyl takes place readily, the hydrolysis of the ester group by sodium carbonate is rather difficult.

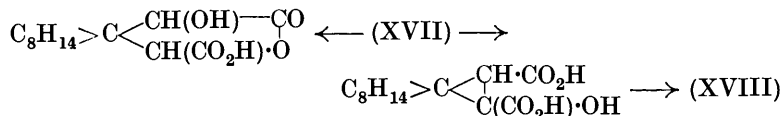
The formation of the keto-acid (XVIII) in this reaction, though unexpected, can readily be accounted for on the assumption that the hydrolysis with sodium carbonate pursues two courses (compare Ingold, J., 1921, 119, 314; Rao, *loc. cit.*):



It is thus unnecessary to assume the initial presence of any unsymmetrical dibromo-ester, the formation of which is contrary to all experience in this type of reaction. It is, however, necessary to assume that the *trans*-hydroxy-ring-acid which is one of the intermediate products, being unstable to alkali, undergoes fission

resulting in the formation of the stable open-chain isomeride (XVIII).

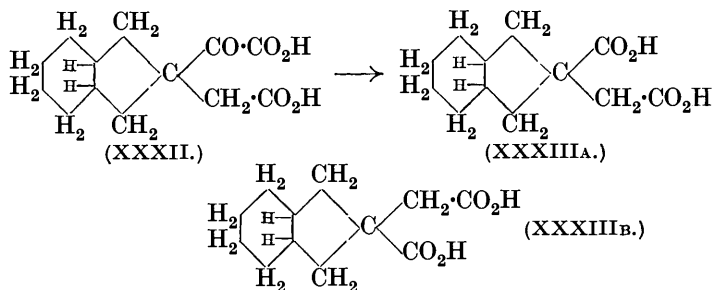
The bromo-lactonic acid (XVII) isolated in small quantity (p. 954) from the acid product of dibromination gave the keto-acid (XVIII) on hydrolysis with 2*N*-sodium carbonate.



The reaction must therefore be assumed to lead to ring formation in preference to hydroxylation.

Examination of Derivatives of cis-Hexahydrohydrindene.

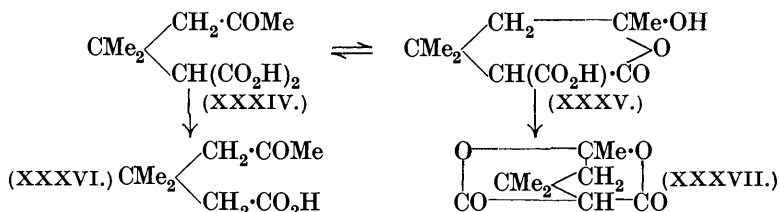
The small quantity (15 g.) of *cis*-hexahydrohydrindene-2:2-di-acetic acid that was available was dibrominated, and the dibromo-ester hydrolysed with aqueous potassium hydroxide at 150°. The product was a tarry oil which, after 3 months, gave a small amount of crystalline solid, characterised as the keto-acid both by the formation of a quinoxaline derivative and by oxidation to the succinic acid, m. p. 205° (the higher-melting of the two stereoisomerides XXXIII A and B), previously discussed (preceding paper). The difficulty of crystallisation may be due in part to the



existence of two stereoisomerides corresponding to each type of compound formed in this reaction (two keto-, one unsaturated, and four hydroxy-lactonic acids).

Although the evidence arising from the study of the decomposition products of the mono- and di-bromo-esters is in harmony with the view that both *cis*- and *trans*-hexahydrohydrindene possess strainless dicyclic nuclei, it was considered desirable to investigate the matter further by the employment of other types of reaction. One of the latest pieces of evidence supporting the validity of the Thorpe-Ingold hypothesis has been adduced by Qudrat-i-Khuda (J., 1929, 201, 713, 1913; 1930, 206), who, in his studies in keto-

lactol tautomerism, suggested that α -carboxy- γ -acetyl- $\beta\beta$ -dimethylbutyric acid exists in the liquid state as a tautomeric mixture of the keto-form (XXXIV) and the lactol form (XXXV), which when heated decompose into the keto-monobasic acid (XXXVI) and the dilactone (XXXVII) respectively.



It has been further demonstrated that when the *gem*-dimethyl group is replaced by the *cyclohexane* ring the proximity of the carbonyl and the carboxyl groups caused by the deflexion of the extracyclic valencies of the quaternary carbon atom is reflected not only in the far greater yield of dilactone but also in the fact that this substance is formed when the keto-acid is heated in an organic solvent for some time.

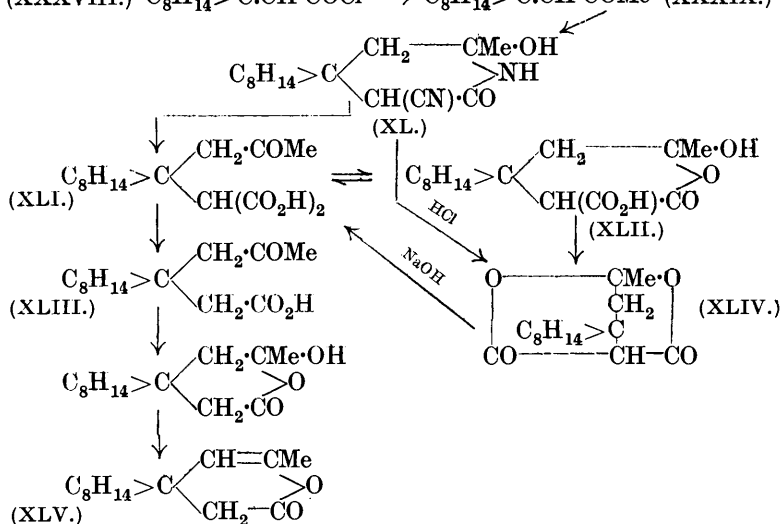
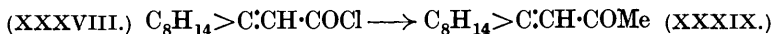
The synthesis of 2-acetonyl-trans-hexahydrohydrindene-2-malonic acid (XLI) is best achieved by the condensation of trans-hexahydrohydrindylidene-2-acetone (XXXIX) (or its $\beta\gamma$ -isomeride), obtained from the acid chloride (XXXVIII) by the Blaise-Maire reaction, with sodiocyanoacetamide in hot alcoholic solution and alkaline hydrolysis of the resulting 6-hydroxy-2-keto-3-cyano-6-methylpiperidine-4(2')-spiro-trans-hexahydrohydrindene (XL).

The hydrolysis of the compound (XL) with concentrated hydrochloric acid yields as the principal product a neutral substance, m. p. 154°, identified as the dilactone (XLIV). The ester of the keto-dibasic acid (XLI) has the normal keto-form, as shown both by its physical properties and by the ready formation of a semi-carbazone.

Since the acid (XLI) on pyrogenic decomposition gives a mixture of the dilactone (XLIV) and the monobasic keto-acid (XLIII) in the ratio 1 : 3, it probably exists in the liquid state as an equilibrium mixture of the keto-form (XLI) and the lactol form (XLII), which are the progenitors of the substances (XLIII) and (XLIV), respectively.

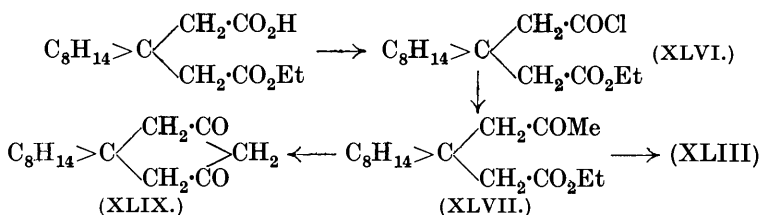
The keto-acid (XLIII), when treated with acetyl chloride (or, better, acetic anhydride), reacts in the lactol form with the production of the unsaturated lactone (XLV) by loss of a molecule of water. Esterification of (XLIII) with alcoholic hydrogen chloride gives ethyl 2-acetonyl-trans-hexahydrohydrindene-2-acetate (XLVII),

which is converted by alcoholic sodium ethoxide into cyclohexane-3 : 5-dione-1(2')-spiro-trans-hexahydrohydrindene (XLIX).

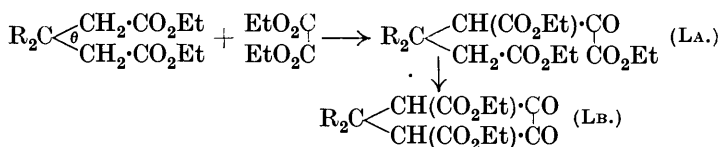


The constitution of the keto-monobasic acid (XLIII) was established by its rational synthesis from ethyl hydrogen *trans*-hexahydrohydrindene-2 : 2-diacetate by the action of zinc methyl iodide on its acid chloride (XLVI) and hydrolysis of the resulting ester.

The results here obtained show that the *trans*-hexahydrohydrindene ring closely resembles the *gem*-dimethyl group in its effect on the tautomerism of δ -keto acids.

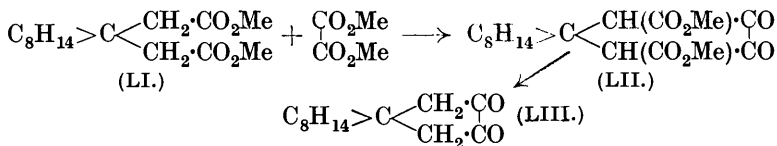


By the condensation of various substituted glutaric esters with ethyl oxalate by the Dieckmann-Komppa reaction, Dickens, Kon, and Thorpe (J., 1922, 121, 1496) obtained a series of cyclic ketones,



and showed that the ring formation occurred in two stages. The fact that the best yield of the dione (LB) was obtained with ethyl glutarate itself, in which the angle θ is much greater than that required for the *cyclopentane* ring, suggested that the necessary alteration in this angle is caused by the presence of the oxalyl group on the α -carbon atom. The correctness of this view was exemplified in the non-formation of the *cyclohexane* analogue, where the effect of substitution would be to cause overlapping of the two carbon atoms which have to be linked in order to produce the five-membered dione ring (Dickens, Kon, and Thorpe, *loc. cit.*).

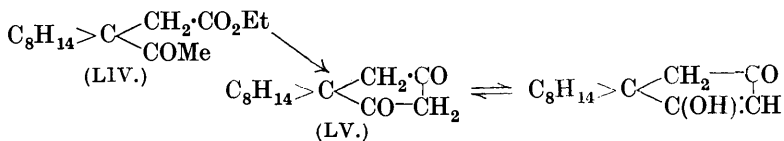
The condensation, carried out under the standard conditions, of methyl *trans*-hexahydrohydrindene-2 : 2-diacetate (LI) with methyl oxalate gave a 50% yield of 2 : 5-dicarbomethoxycyclopentane-3 : 4-dione-1(2')-spiro-*trans*-hexahydrohydrindene (LII), the rest of the material having undergone hydrolysis to the parent diacetic acid, which was isolated as such.



The diketonic ester (LII) is readily converted into *cyclopentane*-3 : 4-dione-1(2')-spiro-*trans*-hexahydrohydrindene (LIII) by boiling dilute sulphuric acid. With respect to this reaction, therefore, *trans*-hexahydrohydrindene shows a great similarity to the strainless rings, such as *cyclopentane*.

The examination was taken a stage further by the preparation of *cyclopentane* derivatives from the corresponding lævulic esters by direct ring closure with sodium ethoxide (Vorländer, *Annalen*, 1896, 294, 270; Rothstein and Thorpe, J., 1926, 2011). It has already been shown that, whereas $\beta\beta$ -dimethyl-lævulic ester gives a 20—25% yield, the *cyclohexane* compound gives as much as 48%, the difference in behaviour being another illustration of the ease of ring closure due to the deflexion of the tetrahedral angle in the latter case.

*Ethyl 2-acetyl-*trans*-hexahydrohydrindene-2-acetate* (LIV) is obtained from ethyl 2-carboxy-*trans*-hexahydrohydrindene-2-acetate through the acid chloride by means of zinc methyl iodide. It is



smoothly converted in 30% yield into cyclopentane-2 : 4-dione-1(2')-spiro-trans-hexahydrohydrindene (LV), which gives a crimson solution with ferric chloride and a solid bromide. The yield in this case, smaller than that of the corresponding cyclohexane compound, is in accordance with expectation.

The investigation into the conditions of strain in *cis*- and *trans*-hexahydrohydrindenes by the various methods that have been used for such purposes in these laboratories has revealed the absence of any considerable strain in these two dicyclic systems. Further it has demonstrated convincingly that hexahydrohydrindene simulates cyclopentane in the several reactions studied. The results, taken in conjunction with those of Rao (*loc. cit.*) in the *trans*-decalin series, lead to the conclusion that when the cyclohexane ring participates in the formation of condensed systems, it does so in its strainless "cis" and "trans" forms.

It would, however, be unsound to draw any conclusion as to the nature of the cyclohexane ring itself from a study based on the dicyclic systems of which it is a unit.

EXPERIMENTAL.

Ethyl Hydrogen trans-Hexahydrohydrindene-2 : 2-diacetate (VIII) —The anhydride (200 g.) of *trans*-hexahydrohydrindene-2 : 2-diacetic acid, dissolved in absolute alcohol (150 c.c.), was gradually added with shaking to a solution of sodium (23 g.) in absolute alcohol (350 c.c.). After 1 hour, the excess of alcohol was evaporated and the residue was diluted with water, extracted with ether to remove any unchanged anhydride, and acidified with dilute hydrochloric acid. The heavy oil which was precipitated was extracted with ether, washed, dried, and recovered. *Ethyl hydrogen trans-hexahydrohydrindene-2 : 2-diacetate* is a thick viscous liquid which is reconverted into the anhydride on distillation under diminished pressure (Found : equiv., 267. $C_{15}H_{24}O_4$ requires equiv., 268).

Monobromination : *Ethyl α -bromo-trans-hexahydrohydrindene-2 : 2-diacetate* (VI). Phosphorus pentachloride (103 g.) was added in three portions to the ester (VIII) : a reaction ensued with copious evolution of hydrogen chloride. The mixture was heated on the steam-bath until the evolution practically ceased (2 hours), dry bromine (28 c.c.) was introduced dropwise into it at 60—80°, the heating continued until no more hydrogen bromide was evolved, and the product poured into absolute ethyl alcohol (500 c.c.) cooled in ice. After $\frac{1}{4}$ hour, the solution was heated on the steam-bath for 3 hours and poured into water, and the precipitated oil extracted with ether. The extract was freed from acid product by treatment with 10% aqueous sodium carbonate, washed, and dried,

and the neutral *bromo-ester* recovered (yield, 85%) (Found : Br, 21.0. $C_{17}H_{27}O_4Br$ requires Br, 21.3%). On distillation in a vacuum it was converted into the *lactonic ester*, a thick syrup, b. p. 210—215°/12 mm., 210°/13 mm. after redistillation (Found : C, 66.5; H, 7.9. $C_{15}H_{22}O_4$ requires C, 67.7; H, 8.3%).

The above sodium carbonate extract, on acidification, gave the *monobromo-acid ester*, a viscid liquid which refused to solidify (Found : Br, 22.6. $C_{15}H_{23}O_4Br$ requires Br, 23.05%).

Hydrolysis of the Neutral Monobromo-ester, (VI), with Potassium Hydroxide Solution at 150°.—To a solution of potassium hydroxide (120 g.) in water at 150°, the monobromo-ester (40 g.) was added as quickly as was consistent with safety. When the vigorous reaction had subsided, the mixture was heated for 20 minutes, cooled, diluted, and acidified. The oil which separated solidified after some time and was then freed from adhering oil by washing with a little benzene (yield, 15 g.). The benzene solution deposited a further quantity (4 g.) of *spiro-acid* on the addition of light petroleum. The white solid thus obtained, m. p. 195—215°, was a mixture of *cis-* and *trans-spiro-acids* which could not be separated into its constituents by fractional crystallisation. It was therefore gently boiled with acetyl chloride (30 c.c.) for 3 hours, the excess of acetyl chloride removed, and the residue kept over potash in a vacuum desiccator. The solid thus obtained was separated into acid and neutral fractions by extraction with a dilute solution of sodium carbonate. The alkaline extract on acidification gave a crystalline solid, sparingly soluble in benzene and chloroform, which, recrystallised from aqueous acetone, yielded *trans-1:2-dicarboxycyclopropane-3(2')-spiro-trans-hexahydrohydrindene (XI)* in stellate clusters of short needles, m. p. 262° (Found : C, 65.5; H, 7.6; equiv., 119. $C_{13}H_{18}O_4$ requires C, 65.5; H, 7.5; equiv., 119). The *dianilide* crystallised from ethyl alcohol in silky needles, m. p. 310° (Found : C, 77.0; H, 7.1. $C_{25}H_{28}O_2N_2$ requires C, 77.3; H, 7.2%).

The ethereal solution from which the *trans-spiro-acid* had been removed left on evaporation of the solvent a thick viscid syrup which solidified over potash in a vacuum. When decomposed with dilute potash solution, it gave *cis-1:2-dicarboxycyclopropane-3(2')-spiro-trans-hexahydrohydrindene (X)*, which crystallised from much water in lustrous plates, m. p. 225° (Found : C, 65.3; H, 7.7%; equiv., 118.5).

The *anhydride (XIII)* of the *cis-spiro-acid* was obtained by warming the acid (5 g.) with acetyl chloride (10 c.c.) for 2 hours, evaporating the excess of acetyl chloride, and keeping the viscous residue over potash in a vacuum desiccator for 3 days. It crystallised

from petroleum (b. p. 60—80°) in plates, m. p. 180° (Found: C, 70·8; H, 7·4. $C_{13}H_{16}O_3$ requires C, 70·9; H, 7·3%). It was also obtained by first melting the *trans-spiro*-acid and then rapidly distilling it under ordinary pressure: the unchanged acid was removed with sodium carbonate solution, and the anhydride solidified in a vacuum.

The *anilic acid*, obtained from aniline and the anhydride in benzene, crystallised in clusters of soft needles, m. p. 175° (decomp.) (Found: C, 72·9; H, 7·1. $C_{15}H_{23}O_3N$ requires C, 72·9; H, 7·3%).

The mother-liquor from which the *trans*- and the *cis-spiro*-acid had been isolated was evaporated, the residue esterified with ethyl-alcoholic hydrogen chloride, and the esters distilled, two fractions being isolated: (1) b. p. 195—200°/15 mm. (2 c.c.), (2) b. p. 215—218°/15 mm. These fractions were separately hydrolysed with concentrated hydrochloric acid and the products were kept for several weeks in a vacuum and then triturated with benzene-petroleum (b. p. 40—60°). From fraction (1) a mixture (5 g.), m. p. 195—200°, of *cis*- and *trans-spiro*-acids was obtained, and from fraction (2) a small quantity of crystalline lactone (XII).

Action of 2N-Sodium Carbonate on the Neutral Monobromo-ester (VI): Lactone of α -Hydroxy-trans-hexahydrohydrindene-2:2-diacetic Acid (XII).—A mixture of the monobromo-ester (40 g.) and 2N-sodium carbonate (400 c.c.) was boiled under reflux for 60 hours, cooled, diluted, and extracted with ether to remove any unchanged ester. The oil precipitated on acidification of the solution was repeatedly extracted with ether, washed, and dried, and the solvent removed. The residue (20 g.), which would not solidify, was esterified with ethyl alcohol (100 c.c.) and concentrated sulphuric acid (10 c.c.). The ester was separated into two fractions: (1) b. p. 192—198°/9 mm. (14 g.), (2) b. p. 206°/9 mm. Fraction (1), when boiled with concentrated hydrochloric acid and cooled, deposited needles (2 g.), m. p. 110—112°, the rest of the product separating as a heavy oil. After 5 weeks, a considerable quantity of lactone was obtained on treating the residue with cold benzene. The lactone of *α -hydroxy-trans-hexahydrohydrindene-2:2-diacetic acid* crystallised from hot benzene in silky needles, m. p. 115° (Found: C, 65·4; H, 7·7; equiv., 237·2. $C_{13}H_{18}O_4$ requires C, 65·5; H, 7·5%; equiv., 238). The *aniline* salt separated in a few minutes after the lactone and aniline had been mixed in benzene solution. It crystallised from benzene in long needles, m. p. 192° (Found: C, 68·6; H, 7·8. $C_{13}H_{18}O_4 \cdot C_6H_5 \cdot NH_2$ requires C, 68·9; H, 7·6%).

Dibromination of trans-Hexahydrohydrindene-2:2-diacetic Acid: Ethyl $\alpha\alpha'$ -Dibromo-trans-hexahydrohydrindene-2:2-diacetate (VII).—When *trans*-hexahydrohydrindene-2:2-diacetic acid (200 g.) was

mixed with phosphorus pentachloride (450 g.), a vigorous reaction occurred and hydrogen chloride was evolved. The conversion into the acid chloride was completed by gentle heating on the steam-bath for 2 hours. Dry bromine (100 c.c.) was then added portion-wise during 10 hours, and the mixture heated until the evolution of hydrogen bromide ceased (24 hours). The product was cooled and poured slowly into absolute ethyl alcohol (800 c.c.) at 0° and the mixture was boiled for 3 hours and poured into water. The precipitated *dibromo-ester* was isolated by three extractions with ether, submitted to the usual washing with dilute sodium carbonate solution and drying, recovered, and kept over sulphuric acid in a vacuum. The yellow oil obtained could not be further purified, as it decomposed into the bromo-lactone on distillation under reduced pressure (Found: Br, 33·7. $C_{17}H_{26}O_4Br_2$ requires Br, 35·2%).

The acid product of bromination was obtained as a heavy oil when the sodium carbonate extract was acidified. After several weeks, a small amount of crystalline solid separated. The whole mixture was treated with benzene, the liquid filtered, and the crystalline solid washed with benzene. The *lactone of α -bromo- α' -hydroxy-trans-hexahydrohydrindene-2 : 2-diacetic acid* (XVII) crystallised from much petrol in lustrous plates, m. p. 145° (Found: Br, 20·5. $C_{13}H_{17}O_4Br$ requires Br, 25·2%). The benzene mother-liquor on evaporation left a residue consisting mainly of acid monobromo-ester (Found: Br, 22·2. Calc. for $C_{15}H_{23}O_4Br$: Br, 23·05%).

$\alpha\alpha'$ -Dibromo-trans-hexahydrohydrindene-2 : 2-diacetic Acid (XV).—A portion of the dibromo-acid chloride was poured into four volumes of formic acid (*d* 1·2) and after $\frac{1}{2}$ hour the solution was concentrated to a small bulk on the steam-bath. The *dibromo-acid* which crystallised was washed with a little formic acid: it separated from formic acid in short prisms, m. p. 200° (decomp.) (Found: Br, 39·8. $C_{13}H_{18}O_4Br_2$ requires Br, 40·2%).

Hydrolysis of the Dibromo-ester, (VII), with 64% Potassium Hydroxide.—A solution of potassium hydroxide (360 g.) in water (300 c.c.) was evaporated until the boiling point reached 150°. The dibromo-ester (100 g.) was then added as rapidly as possible to the boiling solution. The solution was boiled for 15 minutes, cooled, and diluted, and any unchanged ester removed by ether. The heavy oil which was precipitated on acidification of the solution was extracted (thrice) in ether, dried over anhydrous sodium sulphate, and recovered. The syrup obtained deposited a solid (2 g.) which crystallised from hot water in plates, m. p. 203° (decomp.), and was identified as 2-carboxy-*trans*-hexahydrohydrindene-2-acetic acid (XIX). The residue, which failed to solidify after several weeks, was esterified and by distillation two fractions were

then obtained : (1) b. p. 142—146°/10 mm. (2 g.), (2) b. p. 190—194°/10 mm. (30 g.). The second fraction was boiled with concentrated hydrochloric acid for 20 hours, the acid evaporated, and the residue dried in the steam-oven for 1 hour and treated with benzene. The α -keto-trans-hexahydrohydrindene-2 : 2-diacetic acid (XVIII) thus obtained (15 g.) crystallised from benzene in clusters of needles, m. p. 164°; more was obtained after addition of petroleum (b. p. 60—80°) to the mother-liquor (Found : C, 61.3; H, 7.1; equiv., 127. $C_{13}H_{18}O_5$ requires C, 61.4; H, 7.1%; equiv., 127). The acid is soluble in boiling water, acetone, and ethyl acetate. Once obtained in the solid condition, it shows an extraordinary tendency to crystallise from various solvents.

The *quinoxaline* derivative was prepared by heating the keto-acid and *o*-phenylenediamine (1 mol. each) in glacial acetic acid for 1 hour and was obtained as a yellow flocculent precipitate by diluting the solution; it crystallised from ethyl alcohol (charcoal) in short needles, m. p. 238° (Found : C, 69.8; H, 6.8. $C_{19}H_{22}O_3N_2$ requires C, 69.9; H, 6.7%).

The *phenylhydrazone*, prepared by heating the keto-acid and phenylhydrazine in dilute acetic acid on a steam-bath for 30 minutes, was crystallised from alcohol; m. p. 176° (decomp.) (Found : C, 66.3; H, 7.1. $C_{19}H_{24}O_4N_2$ requires C, 66.3; H, 7.0%).

When an aqueous solution of the keto-acid, semicarbazide hydrochloride, and sodium acetate was warmed and kept for 12 hours, the *semicarbazone* of the monosodium salt separated in prisms. After drying at 100°, it melted at 245° with frothing and decomposition (Found : Na, 6.7. $C_{14}H_{20}O_5N_3Na$ requires Na, 6.9%).

The *methyl* ester, obtained by the action of methyl-alcoholic hydrogen chloride on the keto-acid, had b. p. 208°/18 mm. (Found : C, 63.8; H, 7.9. $C_{15}H_{22}O_5$ requires C, 63.8; H, 7.8%).

The *semicarbazone* was prepared from the ester, semicarbazide hydrochloride, and sodium acetate in dilute alcohol, but it crystallised only when a speck of solid obtained by concentrating a small portion of the liquid was introduced into the bulk of the solution. It crystallised from aqueous alcohol in silky needles, m. p. 150° (decomp.) (Found : C, 56.6; H, 7.7. $C_{16}H_{25}O_5N_3$ requires C, 56.6; H, 7.4%).

The *phenylhydrazone* separated when a benzene solution of the keto-ester and phenylhydrazine was heated on the steam-bath for 2 hours and cooled; more was obtained on addition of light petroleum (b. p. 40—60°). It crystallised from benzene in silky needles, m. p. 186° (Found : C, 67.5; H, 7.6. $C_{21}H_{28}O_4N_2$ requires C, 67.7; H, 7.5%).

Distillation of the keto-acid. On distillation under reduced pres-

sure, the keto-acid lost carbon monoxide and water vapour and left an oily substance. This slowly solidified and then crystallised from light petroleum in needles, m. p. 181°, of the anhydride of 2-carboxy-*trans*-hexahydrohydrindene-2-acetic acid, identified by comparison with an authentic specimen.

Oxidation of the keto-acid with hydrogen peroxide. A large excess of hydrogen peroxide (20 vol.) was gradually added to a warm solution of the keto-acid in aqueous sodium carbonate. The solution was cooled and acidified, and the precipitate collected. It was identified as 2-carboxy-*trans*-hexahydrohydrindene-2-acetic acid, m. p. and mixed m. p. 202°.

Hydrolysis of the Bromo-lactonic Acid (XVII) with Sodium Carbonate.—The bromo-lactonic acid (2.2 g.) was dissolved in a solution of sodium carbonate (10 g.) in water (50 c.c.) and boiled for 6 hours. The solution was diluted, acidified, and shaken with ether, which extracted the keto-acid (XVIII), m. p. and mixed m. p. 164°.

trans-Hexahydrohydrindylidene-2-acetic Acid (XXI).—The small fraction of ester, b. p. 142—146°/10 mm., mentioned on p. 967 was hydrolysed with 15% aqueous-alcoholic potash at room temperature. The oily acid product isolated in the usual manner gradually deposited *trans*-hexahydrohydrindylidene-2-acetic acid, which crystallised from petrol (b. p. 60—80°) in prisms, m. p. 152—153°, and was identified by comparison with an authentic specimen.

Hydrolysis of the Dibromo-ester, (VII), with Methyl-alcoholic Potash.—The dibromo-ester (100 g.) was added as quickly as was consistent with safety to a boiling solution of potassium hydroxide (200 g.) in methyl alcohol, and the boiling continued for 20 minutes. The alcohol was then evaporated off entirely, and the residue was diluted with water and extracted once with ether to remove any neutral matter. The aqueous solution was acidified with hydrochloric acid and extracted four times with ether. The gummy residue obtained on evaporation of the ethereal solution was dried in a steam-oven for 1 hour and while hot kept in a vacuum desiccator. After about 12 hours, the whole mass frothed and hardened to a solid cake (50 g.). This was broken up and mixed with benzene (300 c.c.) and the clean white substance (m. p. 130—145°) (40 g.) thus obtained was collected. The residue obtained by evaporation of the benzene filtrate, when re-subjected to the above treatment, gave 3 g. of solid (m. p. 130—150°) and 6 g. of oil.

When the first solid (40 g.) was boiled with water (200 c.c.), a small quantity of it (2 g.) dissolved and the rest melted. The solution, decanted from the oil, deposited silky needles, m. p. 187° (decomp.), of *cis*-1 : 2-dicarboxy-1-hydroxycyclopropane-3(2')-spiro-*trans*-hexahydrohydrindene (XXIII) (Found: C, 61.3; H, 7.2;

equiv., by titration, 127.2. $C_{13}H_{18}O_5$ requires C, 61.4; H, 7.1%; equiv., 127).

The *anhydride* (XXIV) of this acid was obtained by heating the acid (1.5 g.) with acetyl chloride (5 c.c.) for 3 hours, evaporating the excess of acetyl chloride, and crystallising the viscous residue, after it had been kept over potassium hydroxide in a vacuum for 6 weeks, from petroleum (b. p. 60—80°); it formed small prisms, m. p. 110° (Found: C, 66.0; H, 7.1. $C_{13}H_{16}O_4$ requires C, 66.1; H, 6.8%).

cis- and trans-1 : 2-Dicarboxy-1-methoxycyclopropane-3(2')-spiro trans-hexahydrohydrindenes (XXVI and XXVII).—The mixture of acids (40 g.) was gently refluxed with acetyl chloride for 3 hours, the excess of acetyl chloride removed, and the residue kept over potash in a vacuum. It was dissolved in ether, repeatedly extracted with sodium bicarbonate solution, recovered, freed from oil by filtration after treatment with a small quantity of light petroleum, and crystallised from this solvent, the *anhydride* of the *cis-spiro-acid* (XXV) being obtained in thick regular hexagonal prisms, m. p. 91°. The oil, b. p. 214°/20 mm., solidified after distillation and was found to be identical with the above anhydride (Found: C, 67.1; H, 7.1. $C_{14}H_{18}O_4$ requires C, 67.2; H, 7.2%).

The *anilic acid* separated in long soft needles, m. p. 193°, when a benzene solution of the anhydride and aniline was kept for 24 hours (Found: C, 69.8; H, 7.2. $C_{20}H_{25}O_4N$ requires C, 69.9; H, 7.3%). The *anil* was obtained by heating the anilic acid above its melting point, freeing the product from acid by treatment with dilute aqueous ammonia, and crystallising it from dilute alcohol; it separated in prisms, m. p. 140° (Found: C, 73.7; H, 7.2. $C_{20}H_{23}O_3N$ requires C, 73.9; H, 7.1%).

cis-1 : 2-Dicarboxy-1-methoxycyclopropane-3(2')-spiro-trans-hexahydrohydrindene, obtained by decomposing the anhydride with hot water, formed long rods, m. p. 180° (decomp.), sparingly soluble in benzene but readily in chloroform and acetone (Found: C, 62.5; H, 7.7; equiv., by titration, 133.9. $C_{14}H_{20}O_5$ requires C, 62.7; H, 7.5%; equiv., 134). The *ethyl ester*, b. p. 195°/15 mm., was a thick viscous liquid which solidified after 1 month and crystallised from light petroleum (b. p. 60—80°) in plates, m. p. 80° (Found: C, 66.8; H, 8.6. $C_{18}H_{28}O_5$ requires C, 66.7; H, 8.6%).

The aqueous sodium carbonate extract in the above separation was acidified, the precipitated oil extracted with ether, recovered, and esterified with ethyl alcohol and sulphuric acid, and the product distilled. The main fraction, b. p. 190—192°/18 mm., was boiled with concentrated hydrochloric acid for 20 hours; the residue obtained by evaporation of the acid was dried at 100° and mixed

with benzene. After one hour, the precipitated solid (m. p. 130—140°) was collected and boiled with benzene. The insoluble portion was recrystallised from aqueous acetone, from which *trans*-1:2-dicarboxy-1-methoxycyclopropane-3(2')-spiro-*trans*-hexahydrohydrindene (XXVII) separated in needles, m. p. 185° (Found: C, 62.6; H, 7.3; equiv., by titration, 134. $C_{14}H_{20}O_5$ requires C, 62.7; H, 7.4%; equiv., 134); more was obtained on addition of light petroleum to the benzene solution. The filtrate on concentration deposited clusters of needles and plates, m. p. 127° (clearing at 164°), which could not be further purified as the quantity was too small.

The benzene filtrate obtained after the separation of the *cis*- and *trans*-methoxy-spiro-acids was evaporated to dryness, and the residue esterified with ethyl alcohol and sulphuric acid. The ester boiled at 198—199°/9 mm. (5 g.), a small fraction (0.5 g.) having distilled at 175—185°/9 mm. The ester, on hydrolysis with hydrochloric acid, gave a thick oil which partly solidified after 5 weeks. α -Hydroxy- α' -methoxy-*trans*-hexahydrohydrindene-2:2-diacetic acid (XXVIII) crystallised from benzene in plates, m. p. 171° (Found: C, 58.9; H, 7.9; equiv., 142.5. $C_{14}H_{22}O_6$ requires C, 58.7; H, 7.7%; equiv., 143).

Conversion of the cis- and trans-Methoxy-spiro-acids into 2-Carboxy-trans-hexahydrohydrindene-2-acetic Acid (XIX).—Either acid (0.5 g.) was boiled with hydrobromic acid (*d* 1.45; 15 c.c.) under reflux for 3 hours. The solution was diluted and extracted with ether. The viscous residue obtained on evaporation of the solvent solidified when rubbed with chloroform. It crystallised from water in plates, m. p. 203°, and was identified as 2-carboxy-*trans*-hexahydrohydrindene-2-acetic acid by comparison with a genuine specimen.

The keto-acid (XVIII) was converted into the same substance by similar treatment.

Hydrolysis of the Dibromo-ester, (VII), with Sodium Carbonate Solution.—The dibromo-ester (30 g.) was boiled with concentrated sodium carbonate solution (300 c.c.) for 40 hours. Unchanged ester having been removed with ether, the aqueous solution was acidified with concentrated hydrochloric acid and extracted thrice with ether. The residual syrup, which failed to solidify even after 10 weeks, was esterified with ethyl alcohol and hydrogen chloride. The ethyl esters produced were twice fractionally distilled, and two fractions obtained: (1) 200—210°/18 mm. (3 c.c.); (2) 214—218°/15 mm. (12 c.c.).

Hydrolysis of fraction (1) with hydrochloric acid gave an oil which deposited during several weeks a small quantity of solid, m. p. 163°, identified by means of a mixed melting point as the keto-acid (XVIII).

Fraction (2) was boiled with concentrated hydrochloric acid for 12 hours. When the solution was cooled a small quantity (2 g.) of the hydrolysis product crystallised as snow-white flakes, the rest (16 g.) separating as a thick viscid syrup. The solid was freed from traces of oily impurity by washing with benzene and crystallised from this solvent, the *trans*-lactone of α' -dihydroxy-*trans*-hexahydrohydrindene-2 : 2-diacetic acid (XXX) being obtained in clusters of plates, m. p. 212° (Found : C, 61.0; H, 7.2; equiv., by titration, 253.9. $C_{13}H_{18}O_5$ requires C, 61.4; H, 7.1%; equiv., 254).

The *aniline* salt, formed from the hydroxy-lactonic acid and aniline in benzene solution, crystallised in long silky needles, m. p. 130° (Found : C, 65.6; H, 7.2. $C_{19}H_{25}O_5N$ requires C, 65.7; H, 7.3%). The *acetyl* derivative, readily formed from the hydroxy-lactonic acid in boiling acetyl chloride, crystallised from benzene in clusters of flat needles, m. p. 205° (Found : C, 60.6; H, 6.7. $C_{15}H_{20}O_6$ requires C, 60.8; H, 6.7%).

The oily hydroxy-lactonic acid (above) was dried at 100° for 1 hour, kept over potash in a vacuum, and mixed with benzene-light petroleum (b. p. 60—80°). The solid which separated was collected and boiled with a small quantity of benzene. The *cis*-lactone of α' -dihydroxy-*trans*-hexahydrohydrindene-2 : 2-diacetic acid (XXXI) crystallised from chloroform-light petroleum (b. p. 60—80°) in laminae, m. p. 195° (mixed m. p. with the *trans*-lactonic acid, 175—180°) (Found : C, 61.2; H, 7.3%; equiv., 253.5).

The *aniline* salt crystallised from benzene in prisms, m. p. 126° (Found : C, 65.6; H, 7.4%).

The neutral fraction obtained after the hydrolysis of the dibrom-ester with sodium carbonate solution was distilled under reduced pressure. Ethyl bromide was eliminated and a syrupy liquid obtained, b. p. 195—200°/9 mm., which deposited a small amount of solid on standing. The syrupy liquid was mixed with benzene, and the solid collected. The *ethyl* ester of the *hydroxy-lactonic* acid crystallised from light petroleum in rhombic plates, m. p. 127° (Found : C, 63.7; H, 7.8. $C_{15}H_{22}O_5$ requires C, 63.8; H, 7.8%).

By the hydrolysis of the oily ester with concentrated hydrochloric acid, small amounts of the *trans*-lactonic acid (m. p. 212°) and the keto-acid (m. p. 164°) were obtained.

trans-Hexahydrohydrindylidene-2-acetone (XXXIX).—*trans*-Hexahydrohydrindene-2-acetic acid (18 g.) was treated with thionyl chloride (18 c.c.) at 50—60°, the excess of thionyl chloride removed under reduced pressure, and the residue distilled. *trans*-Hexahydrohydrindylidene-2-acetyl chloride passed over at 168°/18 mm. as a colourless mobile liquid. It was diluted with an equal volume of

dry toluene* and added dropwise to a well-cooled solution of zinc methyl iodide prepared from zinc-copper couple (13 g.), methyl iodide (6 c.c.), and ethyl acetate (3 c.c.) in toluene. The mixture was kept in ice for 1 hour and at room temperature for 2 hours and then decomposed with ice and dilute sulphuric acid. The filtered toluene solution was washed successively with dilute sulphuric acid, a saturated solution of ammonium sulphate, aqueous sodium bicarbonate, and water, dried, and fractionated in a vacuum : the *ketone* distilled at 142—144°/25 mm. (Found : C, 80.8; H, 10.0. $C_{12}H_{18}O$ requires C, 80.9; H, 10.1%). It readily formed a *semi-carbazone*, which crystallised from ethyl alcohol in cubes, m. p. 218° (Found : C, 66.5; H, 8.8. $C_{13}H_{21}ON_3$ requires C, 66.4; H, 8.9%).

Condensation of trans-Hexahydrohydrindene-2-acetone with Cyanoacetamide : 6-Hydroxy-2-keto-3-cyano-6-methylpiperidine-4(2')-spiro-trans-hexahydrohydrindene (XL).—The unsaturated ketone (9 g.) was mixed with a suspension of the sodio-derivative prepared by adding a solution of cyanoacetamide (4.2 g.) in hot absolute ethyl alcohol (15 c.c.) to a solution of sodium (1.2 g.) in ethyl alcohol, and heated on the steam-bath for 6 hours. A vigorous reaction ensued, during which the sodiocyanoacetamide partly dissolved and the sodio-derivative of the condensation product separated. There was slight evolution of ammonia during the early stages of the reaction. The crystalline solid (13 g.) which separated on dilution of the solution with water was collected and washed with a little alcohol. The mother-liquor when neutralised with dilute hydrochloric acid gave more (2 g.) of the same substance. The spiro-compound (XL) was insoluble in benzene, ether, or chloroform, appreciably soluble in dilute acids, and crystallised from methyl alcohol in sheaves of spear-shaped needles, m. p. 293° (decomp.) (Found : C, 68.4; H, 8.5. $C_{15}H_{22}O_2N_2$ requires C, 68.7; H, 8.4%).

Hydrolysis of the spiro-Compound (XL) with Concentrated Potassium Hydroxide Solution : Formation of 2-Acetyl-trans-hexahydrohydrindene-2-malonic Acid (XLI).—The preceding compound (12 g.) was heated with a solution of potassium hydroxide (15 g.) in water until the evolution of ammonia ceased (40 hours). The solution was then cooled, diluted with water, extracted with ether to remove any neutral product, and acidified. The precipitated oil was extracted with ether, washed, dried, and recovered. Dried in a vacuum desiccator, it completely solidified (9 g.) when treated with benzene. It crystallised from a large volume of benzene in lustrous short plates, m. p. 169° (decomp.) (Found : C, 63.5; H, 8.0; equiv., by titration, 141. $C_{15}H_{22}O_5$ requires C, 63.8; H, 7.8%; equiv., 141).

* The use of ether in place of toluene in the Blaise-Maire reaction considerably diminishes the yield of the ketone.

The *ethyl* ester prepared by means of ethyl-alcoholic hydrogen chloride, boiled at 214°/15 mm. and had $n_D^{18.2}$ 1.48025, $d_4^{18.2}$ 1.057, whence $[R_L]_D$ 89.3 (calc., 89.7) (Found : C, 67.2; H, 9.0. $C_{19}H_{30}O_5$ requires C, 67.4; H, 8.9%). It gave a *semicarbazone*, m. p. 130°, after repeated crystallisation from alcohol (Found : C, 60.9; H, 8.4. $C_{20}H_{33}O_5N_3$ requires C, 60.8; H, 8.4%).

Hydrolysis of the spiro-Compound (XL) with Concentrated Hydrochloric Acid. Formation of the Dilactone (XLIV).—The *spiro*-compound was boiled with concentrated hydrochloric acid for 6 hours. The crystalline product was separated from the diluted solution and recrystallised from alcohol, the *dilactone* being obtained in long prismatic needles, m. p. 154° (Found : C, 68.3; H, 7.7. $C_{15}H_{20}O_4$ requires C, 68.2; H, 7.5%).

Behaviour of 2-Acetyl-trans-hexahydrohydrindene-2-malonic Acid on Heating: Formation of the Dilactone (XLIV) and 2-Acetyl-trans-hexahydrohydrindene-2-acetic Acid (XLIII).—The acid (2.5 g.) was kept at 170—175° for 6 hours. The cooled melt was dissolved in ether and separated into acid and neutral fractions by means of dilute sodium carbonate solution. The dilactone thus obtained (0.5 g., representing 25% of the dibasic acid) melted at 154° and was identical with the compound (XLIV). The sodium carbonate extract on acidification gave a solid (1.6 g.) which separated in fern-like crystals, m. p. 87°, of 2-acetyl-*trans*-hexahydrohydrindene-2-acetic acid (described below), identified by comparison with a genuine specimen.

Synthesis of Ethyl 2-Acetyl-trans-hexahydrohydrindene-2-acetate (XLVII).—Ethyl hydrogen *trans*-hexahydrohydrindene-2 : 2-diacetate (14 g.), prepared as already described, was heated with thionyl chloride (15 c.c.) on the water-bath, and the excess of thionyl chloride removed under reduced pressure. The crude acid chloride, dissolved in toluene (30 c.c.), was added to a toluene solution of zinc methyl iodide (see p. 972). The keto-ester obtained gave a *semicarbazone*, m. p. 138° after recrystallisation from methyl alcohol (Found : C, 63.1; H, 9.2. $C_{17}H_{29}O_3N_3$ requires C, 63.2; H, 9.0%). *Ethyl 2-acetyl-trans-hexahydrohydrindene-2-acetate*, regenerated from the *semicarbazone*, boiled at 180°/15 mm. (Found : C, 71.8; H, 9.7. $C_{16}H_{26}O_3$ requires C, 72.2; H, 9.8%). This ester (2 g.), when heated with sodium (0.2 g.) in absolute alcohol (12 c.c.) for 5 hours on the steam-bath, was converted into *cyclohexane-3 : 5-dione-1(2')-spiro-trans-hexahydrohydrindene* (XLIX) (1.5 g.), which gave a crimson colour with alcoholic ferric chloride, dissolved in alkalis, and crystallised from alcohol in thick plates, m. p. 199° (Found : C, 76.0; H, 9.1. $C_{14}H_{20}O_2$ requires C, 76.4; H, 9.1%). The *methylene* compound crystallised from alcohol in needles, m. p.

275° (Found: C, 77.2; H, 8.9. $C_{29}H_{40}O_4$ requires C, 77.1; H, 8.9%).

2-Acetyl-trans-hexahydrohydrindene-2-acetic Acid (XLVIII).—The keto-ester (14 g.), mixed with a solution of potassium hydroxide (15 g.) in water (20 c.c.) and sufficient alcohol to give a clear solution, was boiled for 5 hours. The acid isolated in the usual way contained *2-acetyl-trans-hexahydrohydrindene-2-acetic acid* and a small amount of *trans-hexahydrohydrindene-2:2-diacetic acid*. Separation was effected by boiling the mixture with petroleum (b. p. 60—80°), in which the keto-acid alone was soluble. It crystallised from petroleum (b. p. 60—80°) in cubes, m. p. 87° (Found: C, 70.4; H, 9.5; equiv., by titration, 238. $C_{14}H_{22}O_3$ requires C, 70.6; H, 9.2%; equiv., 238). The *semicarbazone* crystallised in plates, m. p. 202° (Found: C, 61.2; H, 8.6. $C_{15}H_{25}O_3N_3$ requires C, 61.0; H, 8.5%).

Action of Acetic Anhydride on 2-Acetyl-trans-hexahydrohydrindene-2-acetic Acid.—A mixture of acetic anhydride and the acid (2 g.) was heated on the steam-bath for 6 hours. Acetic anhydride evaporated on keeping and the residue was treated with water and extracted with ether. The extract was washed with dilute sodium carbonate solution, and the solvent removed. The *unsaturated lactone* (XLV) slowly crystallised in needles, m. p. 58—59°, from light petroleum (b. p. 60—80°), in which it was extremely soluble. It readily combined with bromine in chloroform solution (Found: C, 72.6; H, 9.0. $C_{14}H_{20}O_2$ requires C, 76.4; H, 9.1%).

Condensation of Methyl trans-Hexahydrohydrindene-2:2-diacetate with Methyl Oxalate: Formation of 2:5-Dicarbomethoxycyclopentane-3:4-dione-1(2')-spiro-trans-hexahydrohydrindene (LII).—Methyl *trans-hexahydrohydrindene-2:2-diacetate* was gradually added with vigorous shaking to an ethereal suspension (200 c.c.) of the sodio-compound obtained from methyl oxalate (38 g.) and dry sodium ethoxide (prepared from 14.8 g. of sodium and 20.4 g. of absolute methyl alcohol). The vigorous reaction that ensued caused the ether to boil. After 10 hours, ether was distilled off on the steam-bath, and the residue heated at 110—120°. Alcohol (25 c.c.) having distilled off, the temperature was maintained at 130° for 6 hours. The powdered residue was treated with ice-cold sulphuric acid and the solid which separated was collected (18 g.). This contained the *spiro-compound* (LII) and *trans-hexahydrohydrindene-2:2-diacetic acid* in equal proportion. Separation was effected by hot petroleum (b. p. 60—80°), in which the former alone was soluble. This ester was easily soluble in all solvents, crystallised from petroleum in needles, m. p. 112°, dissolved in aqueous sodium bicarbonate and gave a red coloration with ferric chloride (Found: C, 63.1;

H, 6.7. $C_{17}H_{22}O_6$ requires C, 63.3; H, 6.8%). The *semicarbazone*, after crystallisation from alcohol, melted at 202° (decomp.) (Found: C, 56.8; H, 6.4. $C_{18}H_{25}O_6N_3$ requires C, 57.0; H, 6.6%).

cyclopentane-3 : 4-dione-1(2')-spiro-trans-hexahydrohydrindene (LIII).—The ketonic ester was hydrolysed by boiling for 2 hours with an excess of 20% sulphuric acid. The *diketone* which separated on cooling crystallised from petroleum (b. p. $60-80^\circ$) in fern-like needles, m. p. 111° . Its alcoholic solution gave a red coloration with ferric chloride (Found: C, 75.9; H, 8.6. $C_{13}H_{18}O_2$ requires C, 75.7; H, 8.7%). The *disemicarbazone* was purified by boiling with a large volume of alcohol, in which it was only sparingly soluble; it separated in micro-crystalline needles, m. p. 270° (Found: C, 55.9; H, 7.6. $C_{15}H_{24}O_2N_6$ requires C, 56.2; H, 7.5%).

Ethyl 2-Acetyl-trans-hexahydrohydrindene-2-acetate (LIV).—The crude acid ester (48 g.) was converted into the acid chloride with thionyl chloride (30 c.c.) in the usual way. The crude acid chloride, diluted with toluene, was slowly added to a cold toluene solution of zinc methyl iodide. After 3 hours, the product was worked up in the usual way. The keto-ester (LIV) distilled at $180-182^\circ/10$ mm. (yield, 30 g.).

2-Acetyl-trans-hexahydrohydrindene-2-acetic Acid.—The above keto-ester was hydrolysed by boiling aqueous-alcoholic potassium hydroxide. The oil precipitated on acidification of the solution after evaporation of the alcohol solidified on standing. It was a mixture of *2-acetyl-trans-hexahydrohydrindene-2-acetic acid* and *2-carboxy-trans-hexahydrohydrindene-2-acetic acid*. The separation of these two acids was effected by hot petroleum (b. p. $60-80^\circ$), in which only the former was soluble and from which it crystallised in colourless prisms, m. p. 123° (Found: C, 69.6; H, 9.1; equiv., 223.9. $C_{13}H_{20}O_3$ requires C, 69.6; H, 8.9%; equiv., 223.9).

The *ethyl ester*, prepared by means of ethyl alcohol and hydrogen chloride, boiled at $164^\circ/10$ mm. and had n_D^{25} 1.48142, d_4^{25} 1.030, whence $[R_L]_D$ 69.1 (calc., 68.7) (Found: C, 71.5; H, 9.6. $C_{15}H_{24}O_3$ requires C, 71.4; H, 9.5%).

cyclopentane-2 : 4-dione-1(2')-spiro-trans-hexahydrohydrindene (LV).—The keto-ester (LIV) (4 g.) was mixed with a suspension of sodium ethoxide in ether and warmed on the steam-bath. The mixture was cooled, diluted with water, and extracted with ether. The *diketone* was separated from the neutral material by extraction with sodium bicarbonate. The product, which solidified in contact with sodium-dried ether, crystallised from alcohol in plates, m. p. 190° (yield, 28–30%). It decolorised potassium permanganate and absorbed bromine (Found: C, 75.5; H, 8.8. $C_{13}H_{18}O_2$ requires C, 75.7; H, 8.7%).

In conclusion I desire to express my indebtedness to Professor J. F. Thorpe, C.B.E., F.R.S., for his interest during the progress of this investigation, and to the Chemical Society for **generous** grants towards its heavy cost.

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[*Received, February 19th, 1931*]
