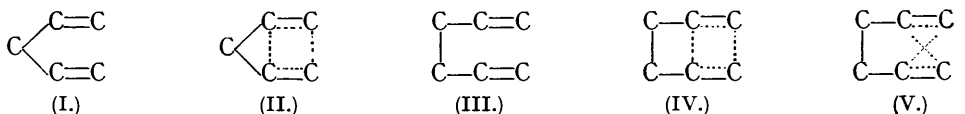


30. *On the Possibility of Ring-chain Mesomerism. Part II. Properties of  $\Delta^{ae}$ -Hexadiene- $\alpha\alpha\gamma\gamma\delta\delta\zeta\zeta$ -octacarboxylic Esters.*

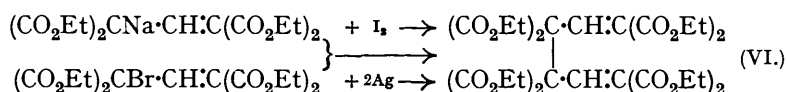
By CHRISTOPHER K. INGOLD, MUKUNDRAI M. PAREKH, and CHARLES W. SHOPPEE.

THIS paper records a continuation of our investigation into the evidence of intramolecular interaction between olefinic residues which are separated more widely than in an ordinary conjugated system. The simplest of the systems we have hitherto contemplated contains the form (I), and in the previous part (J., 1928, 365) we reported an examination of certain compounds of this type. These were derivatives of phorone. It was shown that whilst some, including phorone itself, have all the physical and chemical characteristics of open-chain diolefins, others undoubtedly possess an isomeric ring structure, and yet others display a character which makes it difficult to decide to which class they belong. The last exhibit physical and chemical properties indicating greatly reduced unsaturation, and they show on the one hand a propensity for giving substitution products which are undeniable ring compounds, and on the other a capacity for yielding the derivatives to be expected from an open-chain structure. These properties suggest a form of "conjugation" implying interaction at both ends of the olefinic residues, and we expressed this conclusion

in a symbol (II), which is to be interpreted as signifying an appreciable probability of electron exchange along each of the tracks indicated. We observed that the effect described became marked only in the presence of substituents which should polarise the double bonds in a way calculated to cause them to attract each other.\*



We then turned to the consideration of the case in which two saturated carbon atoms separate the olefinic residues (III). The possible types of interaction are shown in formulæ (IV) and (V), and that represented by the latter formula seemed likely to be the easier to realise, since this formula contains only one four-membered quasi-ring, whereas the other contains two. We therefore planned to create the form of polarisation which should favour this mode of interaction by attaching electron-attracting groups to the ends of the six-carbon chain; and, as a practical step, we decided to investigate the properties of the compound which should be obtained by the action of iodine on ethyl sodiodicarboxyglutaconate. Then we found that Guthzeit and Hartmann had already carried out this condensation (*J. pr. Chem.*, 1910, **81**, 329), and on account of the unexpected properties of the product had reached some remarkable conclusions concerning its constitution :

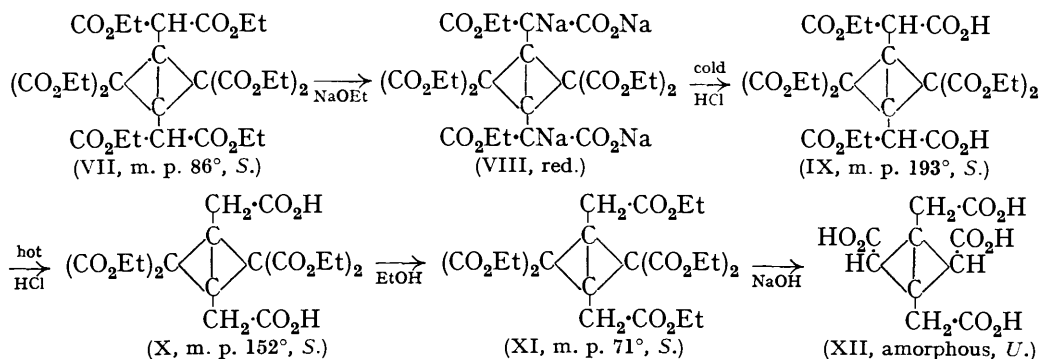


The product which should be (VI), a crystalline ester (m. p. 86°), may be obtained not only in the manner stated but also by several allied methods, including the action of silver on ethyl  $\alpha$ -bromodicarboxyglutaconate (Ingold and Shoppee, *J.*, 1930, 1619), and the action of the bromo-compound on the sodio-compound. All these methods point to structure (VI). However, as Guthzeit and Hartmann first observed, the substance is completely saturated to permanganate, chlorine, and bromine. These authors therefore rejected formula (VI) and regarded the substance as dicyclic. Their particular dicyclic formula (VII) involves a *bicyclobutane* nucleus, and they arrived at it on the basis of data and reasoning which it is necessary to summarise.

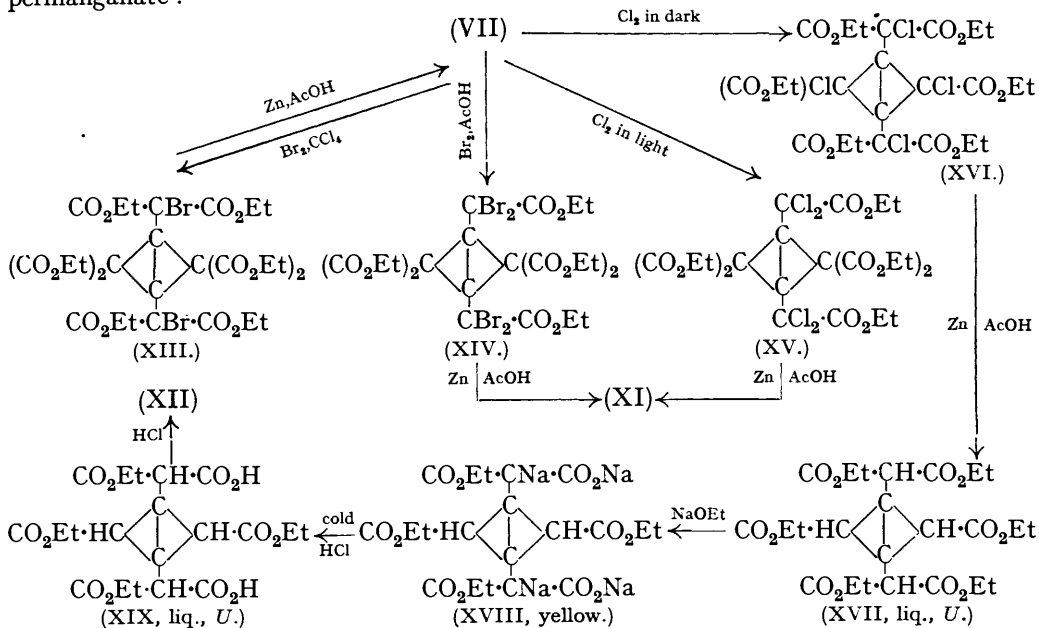
The data relate to three groups of reactions, of which we may first consider hydrolysis. On dissolution in cold sodium ethoxide the octa-ester, m. p. 86°, gave a red tetrasodium salt (VIII), which on acidification yielded a hexa-ester di-acid, m. p. 193° (IX), reconvertible into the octa-ester. Any of these compounds on hydrolysis with acids gave a tetra-ester di-acid, m. p. 152° (X), convertible by esterification into a hexa-ester, m. p. 71° (XI). The compounds (VII), (IX), (X), and (XI) were stable towards permanganate. Any of them on alkaline hydrolysis yielded an amorphous tetra-acid (XII), which, like its liquid

\* As Part I was published in 1928, it seems desirable to indicate the changes of theory and nomenclature which have taken place in the meantime. Employing the general conception then called "electronic strain," Ingold and Shoppee (*loc. cit.*, pp. 384—5) advocated the idea of a molecular state intermediate between those for which ordinary formulæ could be written—in contradistinction, for instance, to Sugden's suggestion (*ibid.*, p. 412) that separate isomerides corresponding to the ordinary formulæ were present in equilibrium. To Ingold and Shoppee's original view we still adhere. However, it was not until 1929 that the physical mechanism involved in the production of such an intermediate state was perceived by Burton and Ingold as an extrapolation of the exchange theory of the localised bond and therefore as a factor of molecular stability; thus no description of the intermediate state in terms of electron exchange or hybridised wave functions will be found in Part I. The difficulty of nomenclature, which incongruously led in 1928 to the use of the term "valency tautomerism" for something which was carefully explained to be nothing to do with tautomerides, was not cleared up until, in 1933, the word "mesomerism" was introduced, which is now used in the serial title (cf. *Proc. Leeds Phil. Soc.*, 1929, **1**, 421; *J.*, 1933, 1120; *Nature*, 1934, **133**, 946).

methyl and ethyl esters, was instantly oxidised by permanganate. In the following formulæ *S* signifies stable and *U* unstable towards permanganate :

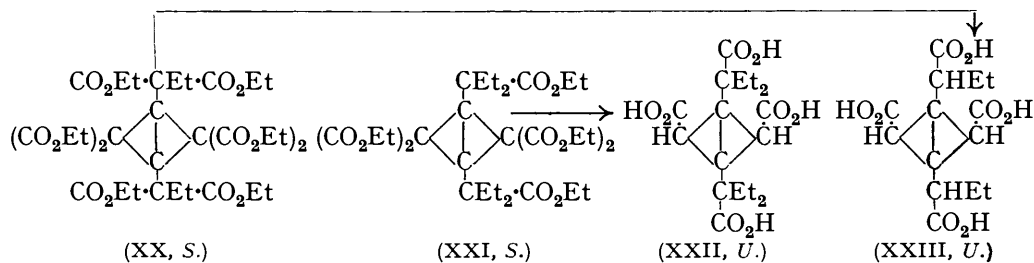


The second group of experiments relates to halogenation, which in every case is represented as a substitution process. Bromination of the octa-ester (VII) in carbon tetrachloride solution gave a dibromo-octa-ester (XIII), reducible by means of zinc and acetic acid to the original compound. Further bromination in acetic acid yielded a tetrabromo-hexa-ester (XIV), which on reduction with zinc and acetic acid gave the hexa-ester of m. p. 71° (XI). Chlorination in sunlight yielded a tetrachloro-hexa-ester (XV), which likewise on reduction gave the hexa-ester, m. p. 71°. On the other hand, chlorination in the dark produced an isomeric tetrachloro-hexa-ester (XVI), which was reduced by zinc and acetic acid to a liquid hexa-ester (XVII). This when treated with cold sodium ethoxide gave a yellow tetrasodium compound (XVIII), from which acids liberated a liquid tetra-ester di-acid (XIX), readily hydrolysable by means of acids to the amorphous tetra-acid (XII). The hexa-ester (XVII) and all compounds derived from it were instantly oxidised by permanganate :



The third series of observations relates to alkylation, which is stated to have been effected by the use of zinc and ethyl iodide. The product was a mixture of a diethylated octa-ester (XX) and a tetra-ethylated hexa-ester (XXI). These compounds were not

attacked by permanganate. By hydrolysis they were converted into the diethylated tetra-acid (XXIII) and the tetra-ethylated tetra-acid (XXII) respectively. These mixed acids, and likewise their esters, were instantly oxidised by permanganate.



These results and interpretations are those given by Guthzeit and Hartmann, and the general nature of their reasoning is as follows. As stated above, the necessity for some form of saturated bicyclic structure is assumed on account of the saturated nature of many of the substances. Three sets of observations, *viz.*, the formation of the coloured tetra-sodium salts, the course of the halogenation, and of the alkylation, all show that the original octa-ester contains two residues  $-\text{CH}(\text{CO}_2\text{Et})_2$ , each with replaceable hydrogen. This consideration rules out bicyclic formulæ such as (XXIV) and (XXV). Indeed it rules out all structural conceptions which require more than four carbon atoms for the construction of the bicyclic nucleus. Thus Guthzeit and Hartmann's formula is unequivocally indicated, and support for it is obtained from the circumstance that, when the scheme of inter-relations is worked out as shown above, a definite regularity is seen in the peculiar division of the compounds into those which are stable towards permanganate and those which are attacked (*cf.* the symbols *S* and *U*). The labile compounds are just those which have hydrogen directly linked to the  $\text{C}_4$ -nucleus. The assumption can therefore be made that hydrogen thus situated provides a necessary point of attack for the oxidising agent.



Dissatisfied with this interpretation but perceiving no flaw (except, of course, that the modes of formation of the octa-ester are unexplained), we commenced a repetition of the work, and also an examination of the corresponding methyl esters with a view to obtaining crystalline analogues of some of the substances which Guthzeit and Hartmann describe as liquids. The two investigations did not run entirely parallel, and we may describe our results for the ethyl series first, as they differ in many important respects from those recorded by Guthzeit and Hartmann. Our findings are as follows.

The octa-ester, *m. p.*  $86^\circ$ , is formed as Guthzeit and Hartmann describe; towards permanganate it has all the stability they attribute to it, and towards halogens more (see below).

The red tetrasodium salt of Guthzeit and Hartmann does not exist. It is possible by the action of sodium ethoxide to obtain a small quantity of an apparently red solid, but the colour is in the mother-liquor, and the solid does not contain half of the amount of sodium required by formula (VIII). The probable nature of this material is indicated by our work in the methyl ester series (see below).

The hexa-ester di-acid, *m. p.*  $193^\circ$ , can be obtained by acidification of a mixture of the octa-ester and alcoholic sodium ethoxide, but not by way of the solid compound as Guthzeit and Hartmann claim. It has the stability ascribed to it, and is a partial hydrolysis product of the octa-ester, into which it can be reconverted by esterification.

The tetra-ester di-acid, *m. p.*  $152^\circ$ , and the hexa-ester, *m. p.*  $71^\circ$ , both exist, but the empirical formulæ ascribed to them by Guthzeit and Hartmann are incorrect. Each has one molecule of water of constitution more than is represented in formulæ (X) and (XI). Guthzeit and Hartmann describe the acid as crystallising with  $1\text{H}_2\text{O}$  or  $3\text{H}_2\text{O}$ . We could

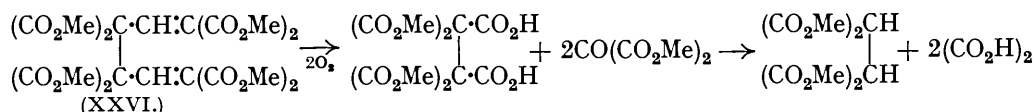
not prepare their trihydrate. The water of their monohydrate, however, cannot be removed from the acid. Furthermore, it is present in, and cannot be removed from, the dianilide. It is present also in the hexa-ethyl ester, even after distillation. The anhydrous salts and ester of Guthzeit and Hartmann's description have no real existence. Both the acid and the neutral ester are stable towards permanganate, and we have shown them to contain an alcoholic hydroxyl group.

The composition of the tetrabasic acid (which when pure has m. p. 193°) is also incorrectly given by Guthzeit and Hartmann, and so are those of its methyl and ethyl esters. Actually all these compounds contain an additional molecule of water of constitution. Guthzeit and Hartmann describe them all as causing instantaneous reduction of permanganate. We find, on the contrary, that they are stable towards permanganate. We have proved the presence of an alcoholic hydroxyl group.

We were for long completely misled by these numerous errors of composition. Guthzeit and Hartmann's paper records 40 analyses all in very good agreement with incorrect formulæ. Concerning Guthzeit and Hartmann's description of the halogenation and alkylation of the octa-ester, our experience in a prolonged investigation is simply that none of the reported reactions takes place. All these results are confirmed by our work on the methyl esters.

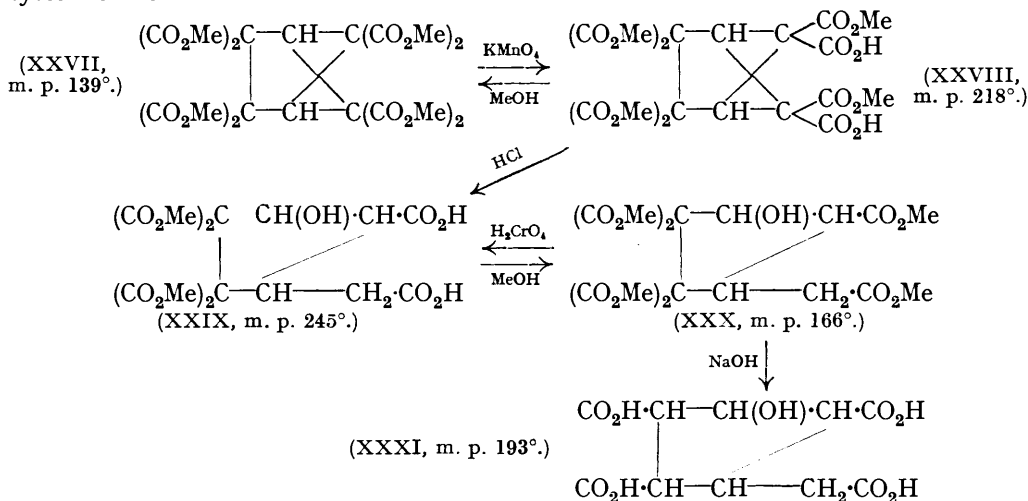
The foregoing observations destroy the foundations of the *bicyclobutane* formula, which is based primarily on the supposed presence in the octa-ester of two readily replaceable hydrogen atoms, and in an auxiliary manner on the alleged separation of derivatives of the octa-ester into the two classes characterised respectively by marked stability and marked instability towards permanganate. However, destruction of support is not proof of falsity, and the work thus far described does not show the *bicyclobutane* structure to be inapplicable to the octa-ester and the hexa-ester di-acid—the two compounds of the series which Guthzeit and Hartmann analysed correctly.

Our remaining evidence is derived from investigations in the series of methyl esters. The *octamethyl* ester, m. p. 139°, was prepared analogously to the ethyl ester. Its composition was normal, and it had the expected great stability towards permanganate. It was, however, broken down by means of ozone, and the products were methyl ethane-tetracarboxylate and oxalic acid. Subsequently a similar decomposition of the octa-ethyl ester was observed. This definitely disposes of the *bicyclobutane* structure, and shows that we must interpret the observations on the lines of formulæ such as (VI), (XXIV), and (XXV). For purposes of illustration we shall henceforth employ whichever of these alternatives appears most convenient in the case considered, reserving until later the discussion of apparent inconsistencies :

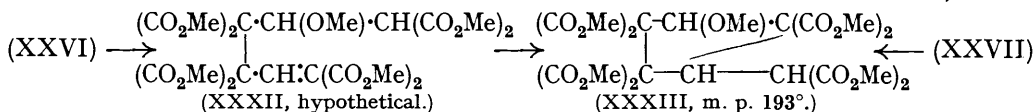


For a reason given below, it was not found possible to convert the octamethyl ester into a *hexamethyl ester di-acid* by the action of sodium methoxide. This ester-acid was, however, encountered during attempts to oxidise the octa-ester with alkaline permanganate and ferricyanide. Its composition was normal, and its relation to the octa-ester was confirmed by its reconversion into the latter (XXVII, XXVIII). Hydrolysis of either of these compounds with mineral acids gave the *tetramethyl ester di-acid* (XXIX), which contained the extra molecule of water of constitution, but was saturated towards oxidising agents. It could not be degraded even by means of ozone. The distilled *hexamethyl ester* (XXX), which, like its ethyl analogue, is crystalline, also contained this extra water molecule. It was unattacked by ozone, and attempts to oxidise it by means of hot chromic acid merely gave back the tetramethyl ester di-acid. The presence of an alcoholic hydroxyl group was proved. All four of these esters on hydrolysis with sodium hydroxide gave the tetrabasic acid (XXXI) already described. In formulating these transformations we assume hydrolysis to be initiated in those carbomethoxy-groups which may be presumed

to be the least sterically protected; they are also those most closely associated with the system concerned in addition of water :

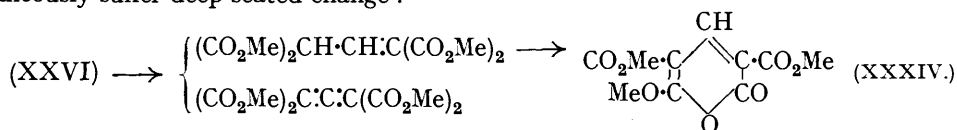


When the octamethyl ester, m. p. 139°, was dissolved in cold alcoholic sodium methoxide, and the solution acidified, the main product was an ester, m. p. 193°, having the composition of the original octa-ester plus a molecule of methyl alcohol. This is not solvent of crystallisation, because the compound can be distilled without decomposition; furthermore, the original octa-ester does not in fact take up methyl alcohol when crystallised from this solvent. The addition ester, m. p. 193°, was shown to contain nine methoxyl groups. It was formed very easily, although alkaline conditions appeared to be necessary: we obtained it from the octa-ester of m. p. 139°, not only as already described, but also by the action of cold methyl-alcoholic potassium hydroxide, and even methyl-alcoholic potassium cyanide, but we did not encounter it when esterifying the acid-ester of m. p. 218° with methyl alcohol and hydrogen chloride. It is probable that the sodium salt encountered in the experiments upon the ester ethyl is formed in a similar reaction, which, however, is overlaid in this case by much more rapid and extensive partial hydrolysis. The circumstance that addition of alcohol and hydrolysis were not observed to occur in the same molecule may be taken as an indication that the two processes are located in the same part of the molecular system. Two modes of formation of the addition ester, m. p. 193°, to which we ascribe formula (XXXIII), are represented below; one of them involves a hypothetical intermediate (XXXII):

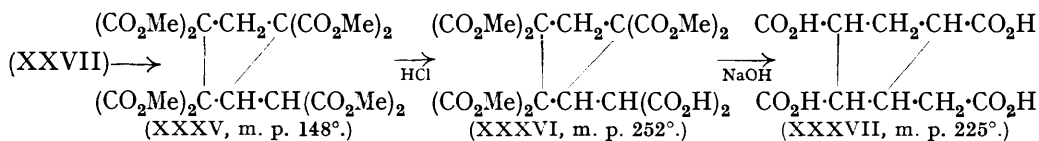


As contrast to what follows it is worth noting that not only this methoxy-ester, but all the neutral esters mentioned in this paper which have an extra molecule of water or alcohol of constitution, can be distilled without decomposition. Ingold and Shoppee have already recorded the decomposition by distillation of the octa-ethyl ester (m. p. 86°) (*loc. cit.*), but the observation was published for a reason which had nothing to do with the object of this paper, and its constitutional significance was not discussed. We now report the corresponding experiment with the octamethyl ester, m. p. 139°. In each case only half the original molecule appears in recognisable form, and this is a pyrone (*e.g.*, XXXIV). Its constitution reveals one of the two double links that can be ascribed to the original structure, and shows that a fission has occurred at the  $\gamma\gamma'$ -link which the ozonolytic experiment proved to be present. The pyrolysis may be illustrated as follows; it is known that the methyl dicarboxylglutaconate postulated as an intermediate would, if formed, undergo

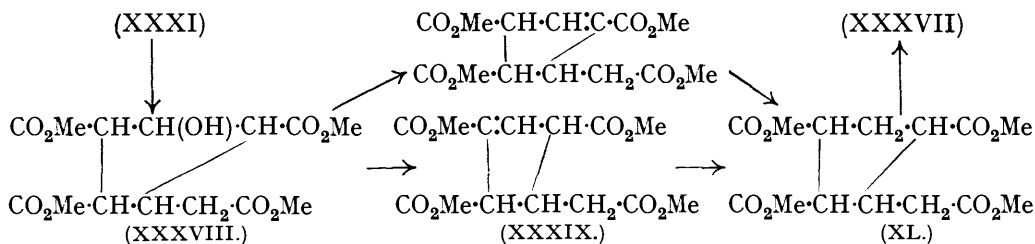
the reaction assumed, and it is supposed that allenetetracarboxylic ester would simultaneously suffer deep-seated change :



Although the octamethyl ester could not be reduced by zinc and acetic acid, nor yet by hydrogen at a platinum or palladium catalyst, it was successfully hydrogenated in acid solution by an electrolytic method. The product was a *dihydro-octa-ester*, m. p. 149°, which could be distilled without decomposition and appeared to be saturated. It was stable towards permanganate, and could not be further reduced by prolonged renewal of the treatment under which it was formed. On account of these properties we ascribe to it formula (XXXV). It was hydrolysed by means of hydrochloric acid to the *hexa-ester di-acid* (XXXVI), which in turn was completely hydrolysed by sodium hydroxide to the tetrabasic acid (XXXVII) :



We tried to prepare this acid from the hydroxy-tetrabasic acid (XXXI) by successive esterification, dehydration, hydrogenation and hydrolysis :



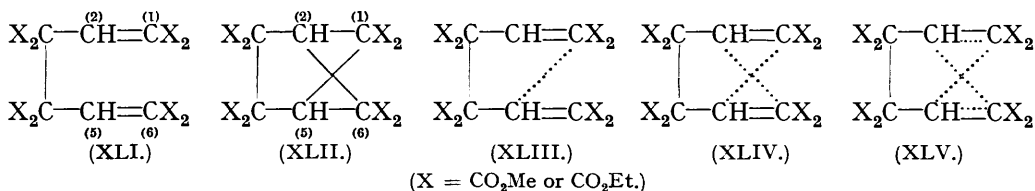
These reactions were realised : dehydration of the hydroxy-ester (XXXVIII) was effected by means of potassium hydrogen sulphate, and reduction of the unsaturated product by hydrogen in the presence of platinum. However, the final acid, for which there are a number of stereochemical possibilities, was a mixture which could not be separated.

With regard to halogenation and alkylation the methyl esters are in the same case as the ethyl esters. In particular the attack of halogens on the octamethyl ester, m. p. 139°, was very slow even with strong irradiation, and no definite product could be obtained. Alkylation of the octamethyl ester could not be effected either by Guthzeit and Hartmann's method, or by any other that we tried, including even the employment of sodamide.

These are the observations, and it remains now to consider what conclusions may be drawn concerning the structure to be ascribed to the original condensation products, the octa-esters of m. p. 86° and 139°. We have shown above that the types of structure which might possibly be considered in this connexion are confined to three alternatives. One of these, the structure with two fused *cyclobutane* rings, may forthwith be dismissed, as it does not account intelligibly for any of the additive transformations described above : we know that ditertiary alicyclic bonds, CH—CH, are never broken, even in highly strained *cyclopropane* derivatives, by additive reagents such as we have employed.

Decision between the other two structures is extremely difficult : the situation appears to be as follows. The decomposition with ozone indicates the unsaturated structure (XLI), but the great stability of the compounds to permanganate suggests the dicyclic structure (XLII) : it can be reconciled with formula (XLI) only if we import the supposition that the double bonds suppress each other's reactivity in some way not expressed in the formula

itself. The addition of methyl alcohol under alkaline conditions can be explained by means of either structure. The attack is evidently by the methoxide ion, and, employing the unsaturated structure (XLI), it may be supposed that methyl alcohol adds to one double bond by a process analogous to the Michael reaction, and that then a real Michael reaction closes the *cyclopentane* ring. The analogy permitting interpretation on the basis of the dicyclic structure (XLII) is the additive fission of suitably carboxylated strained rings by processes similar to the Michael reaction (*e.g.*, addition of ethyl cyanoacetate to ethyl *cyclopropane*-1 : 1-dicarboxylate) : the 1 : 1 : 6 : 6-carboxyl groups in the 1 : 2 : 6 : 5-*cyclobutane* ring are so disposed that an addition product of the correct constitution could be formed in one step. The addition of water in acidic media cannot, however, be interpreted by formula (XLI) on the lines suggested above, because the Michael reaction required to close the ring could not take place under such experimental conditions. The observation of this addition thus indicates formula (XLII) ; and we know analogies for the acid hydrolytic fission of strained rings where there is a bond rendered electrically dissymmetric by substitution (*e.g.*, conversion of caronic acid into terebic acid). As to the electrolytic reduction in acid solution, the doubly bonded structure (XLI) once again appears inadequate. Certainly it suggests that reduction might occur, but it does not explain why, after two atoms of hydrogen have been taken up, hydrogenation ceases and a ring is formed ; furthermore, it does not suggest how such a ring could be produced at that stage of the process under the experimental conditions obtaining. On the other hand, in the dicyclic structure (XLII) a ring has merely to be broken, and the disposition of carboxyl groups in the *cyclobutane* ring should confer on this ring a definite tendency to reductive fission, since the attacks of electrons and of nucleophilic anions (*e.g.*, methoxide) are analogous.



It seems that the only way of forcing an interpretation employing but one of these two formulæ to cover all known circumstances is to import *ad hoc* assumptions extraneous to the normal conceptual content of the formula adopted. We might, for example, adopt formula (XLI), and assume, further, (1) that the double bonds are "1 : 5-conjugated" in the sense that they allow 2 : 6-addition with 1 : 5-ring closure, which would be the analogue of  $\alpha\delta$ -addition with  $\beta\gamma$ -double bond formation in ordinary butadienoid conjugation ; and (2) that the two double bonds largely suppress each other's reactivity. The first assumption makes addition and ring closure mutually dependent and simultaneous, and thus it gets over the difficulty that ring closure would not take place as a separate act under the conditions of many of the observations. Formula (XLIII) expresses this idea. It does not, however, adequately represent the stability of the system : it implies reduced reactivity at atoms 1 and 5 but not at atoms 2 and 6, just as the conception of butadienoid conjugation implies suppressed reactivity in the middle of the chain but not at the free ends. For this reason we require the second assumption also ; and its introduction amounts to assuming that the "conjugation" is actually cyclic, affecting all the atoms 1, 2, 5, and 6. A confirmatory consideration is that the spatial symmetry of the system would have made it difficult to understand an association between atoms 1 and 5 without a similar association between atoms 2 and 6. The expression for this "conjugation" must therefore be changed to that of formula (XLIV).

It remains to be observed that, whether the properties of these compounds are expressed by the combination of ordinary formulæ (XLI and XLII) or by the single "conjugation" formula (XLIV), the implied physical idea is the same. Thus the physical significance of the "conjugation" formula is that part of the normal electron-content of the two double bonds is forming a charge cloud along the lines which mark the "conjugation" ;



or, to put it in another way, electron exchange is permitted in these directions as well as in the bonds. The electron conservation is better brought out by rewriting the "conjugation" formula as in (XLV). With regard to the pair of ordinary formulæ, (XLI) and (XLII), it is obvious that we must combine them as the canonical structures of a system in resonance, and not as independently existing, mutually convertible tautomerides, for our object is to explain a special stability. Their wave functions when mixed must give the wave function of (XLV), and their energies must be replaced by the smaller energy of (XLV). This is just the molecular condition we set out to seek, and although on many occasions the research has seemed to be leading in quite other directions, it appears to us when we review our results that the original object has been achieved.

#### EXPERIMENTAL.

*Methyl and Ethyl  $\Delta^{\alpha\epsilon}$ -Hexadiene- $\alpha\alpha\gamma\delta\delta\zeta\zeta$ -octacarboxylate* [*Methyl and Ethyl (1:1:2)-bicycloHexane-1:1:3:3:4:4:6:6-octacarboxylate*].—For the preparation of the methyl ester the starting points were methyl  $\alpha\alpha'$ -dicarboxylglutaconate, m. p. 43° (Found: C, 47.9; H, 5.0. Calc.: C, 48.2; H, 5.1%), its yellow sodio-derivative, m. p. 247—249°, its green copper salt, m. p. 246—248° (decomp.), and its  $\alpha$ -bromo-derivative (Found: Br, 22.8. Calc.: Br, 22.7%). The methyl ester named in the heading was prepared from the sodio-compound and iodine, from the bromo-compound and sodium or silver, from the copper compound and sulphur, and from the bromo-compound and the sodium compound, the methods being modelled on those given by Guthzeit and Hartmann or Ingold and Shoppee (*loc. cit.*). Crystallised from acetone, the octamethyl ester formed prisms, m. p. 139° (Found: C, 48.4, 48.5, 48.1; H, 4.8, 5.0, 4.8.  $C_{22}H_{26}O_{16}$  requires C, 48.4; H, 4.8%). The corresponding octa-ethyl ester is the compound described as having other constitutions by Guthzeit and Hartmann and by Faltis and his collaborators (references, see Ingold and Shoppee). Our preparation had m. p. 86° (Found: C, 54.7; H, 6.45. Calc.: C, 54.7; H, 6.4%).

*Hexamethyl Dihydrogen and Hexa-ethyl Dihydrogen  $\Delta^{\alpha\epsilon}$ -Hexadiene- $\alpha\alpha\gamma\delta\delta\zeta\zeta$ -octacarboxylate* [*Hexamethyl Dihydrogen and Hexa-ethyl Dihydrogen (1:1:2)-bicycloHexane-1:1:3:3:4:4:6:6-octacarboxylate*].—The former of these compounds was obtained as the product of an attempted oxidation of the octamethyl ester by the prolonged action of 2.5% permanganate in alkaline aqueous acetone. When worked up in the usual way, the crystalline acid ester separated after most of the acetone had been removed by distillation. The same acid ester was obtained also in the course of an attempted oxidation of the octamethyl ester by means of alkaline ferricyanide. The ester (1 g.) was heated on the steam-bath for 24 hours with a solution of potassium ferricyanide (2.5 g.) and potassium carbonate (0.7 g.) in water (80 c.c.). An ethereal extract of the neutralised solution, and an acetone extract of the precipitate which had been formed, both yielded the acid ester. (The octamethyl ester was, however, recovered unchanged after being boiled for 6 hours with chromic anhydride in glacial acetic acid.) Crystallised from acetone, the acid-ester had m. p. 218° (decomp.), but the product of thermal decomposition was a thick dark oil which could not be crystallised [Found: C, 46.0; H, 4.6; equiv. (titration), 258.  $C_{20}H_{22}O_{16}$  (dibasic) requires C, 46.3; H, 4.3%; equiv., 259]. A solution of the acid (2 g.) in methyl alcohol (25 c.c.) was saturated with hydrogen chloride, kept over-night, warmed for a short time, and evaporated. The product was the octamethyl ester, m. p. and mixed m. p. 139°. The hexa-ethyl dihydrogen ester (Guthzeit and Hartmann) had m. p. 193° (decomp.) after crystallisation from ethyl acetate containing ligroin (Found: C, 51.9; H, 5.7; OEt, 44.6. Calc.: C, 51.9; H, 5.7; OEt, 44.8%). The product of its thermal decomposition at 200° was a thick brown oil which could not be crystallised. The acid ester was treated with thionyl chloride on the steam-bath for 2 hours, and the excess of the reagent removed under reduced pressure. Desiccation of the product over potassium hydroxide yielded the crystalline *hexa-ethyl ester dichloride*,  $C_6H_2(CO_2Et)_6(COCl)_2$ , which after crystallisation from ether-ligroin had m. p. 65—66° (Found: C, 48.9; H, 5.1; Cl, 11.1.  $C_{26}H_{32}O_{14}Cl_2$  requires C, 48.8; H, 5.1; Cl, 11.1%). This compound was converted quantitatively into the octa-ethyl ester, m. p. and mixed m. p. 86°, by boiling with dry ethyl alcohol and evaporating the excess of the latter. Esterification of the acid ester, m. p. 193°, was also accomplished through the silver salt, which was soluble in water, and on concentration of its solution separated as a solidifying oil. The solid reacted readily with ethyl iodide, evolving heat and giving the octa-ethyl ester, m. p. and mixed m. p. 86°.

*Tetramethyl Dihydrogen and Tetra-ethyl Dihydrogen 3-Hydroxy-2:4:4:5:5-pentacarboxycyclopentane-1-acetate*.—The former *hydroxy-acid-ester* was prepared from the octamethyl ester

(10 g.) by boiling with 20% hydrochloric acid (100 g.) until solution was almost complete and the evolution of carbon dioxide ceased. The product, which separated in prisms on cooling, was crystallised from acetone. It became discoloured at 235° and had m. p. 245° (decomp.). It was unaffected by boiling with potassium dichromate and dilute sulphuric acid or with concentrated nitric acid, and by treatment in chloroform solution with ozone [Found : C, 45.9; H, 4.8; equiv. (titration), 208.4.  $C_{16}H_{20}O_{13}$  (dibasic) requires C, 45.7; H, 4.8%; equiv., 210]. The hexamethyl dihydrogen ester was used in place of the octamethyl ester, and 10% sulphuric acid in place of hydrochloric acid, in the above preparation. In each case a gummy by-product was obtained which could not be purified. The tetra-ethyl hydroxy-acid-ester was prepared but incorrectly formulated by Guthzeit and Hartmann, whose trihydrate we could not obtain. Our preparations, crystallised from ether-ligroin, had m. p. 152°. A sample was analysed after drying in a vacuum over sulphuric acid (Found : C, 50.5; H, 6.0. Calc. for  $C_{20}H_{28}O_{13}$  : C, 50.4; H, 5.9%). The same material was crystallised from hydrochloric acid and air-dried (Found : C, 50.4; H, 5.9%). By digestion with thionyl chloride for 1 hour on the steam-bath, removal of excess of the reagent by distillation, and treatment of the resulting chloride with aniline, a *dianilide* was obtained, which crystallised from ether-acetone in needles, m. p. 152° (Found : C, 61.1; H, 6.0; N, 4.4.  $C_{32}H_{38}O_{11}N_2$  requires C, 61.3; H, 6.1; N, 4.5%).

*Methyl and Ethyl 3-Hydroxy-2 : 4 : 4 : 5 : 5-pentacarboxycyclopentane-1-acetate*.—The above tetramethyl dihydrogen ester underwent considerable conversion into the *hexamethyl* ester when the attempt was made to crystallise the former from methyl alcohol. Quantitative conversion was effected by the Fischer-Speier method, or by the use of sulphuric acid as catalyst. The neutral ester separated from methyl alcohol in short needles, m. p. 168°, and could be distilled completely without decomposition at 5 mm. (m. p. again 168°, mixed m. p. the same) [Found (not distilled) : C, 47.9; H, 5.45. Found (distilled) : C, 48.0; H, 5.6.  $C_{18}H_{24}O_{13}$  requires C, 48.2; H, 5.4%]. On boiling with potassium dichromate and dilute sulphuric acid the hexamethyl ester was converted into the tetramethyl dihydrogen ester described above. After prolonged treatment with ozone in chloroform it was recovered unchanged. It did not appear to react with acetyl chloride, acetic anhydride, diazomethane or thionyl chloride, but Tschugaeff and Zerewitinoff's reagent yielded approximately the correct amount of methane (Found : OH, 3.6. Calc., 3.8%). The hexa-ethyl ester was prepared by Guthzeit and Hartmann but incorrectly analysed. Our material, obtained by the Fischer-Speier method, separated from ethyl acetate-ligroin in large prisms, m. p. 71°. It was completely distilled without decomposition, b. p. 250°/4 mm., and the distillate had again m. p. 71°, mixed m. p. the same [Found (undistilled) : C, 54.2; H, 6.8. Found (distilled) : C, 54.15; H, 6.8. Calc. for  $C_{24}H_{36}O_{13}$  : C, 54.1; H, 6.8. Calc. for  $C_{24}H_{34}O_{12}$  : C, 55.9; H, 6.5%. Guthzeit and Hartmann record C, 55.9; H, 6.5%, and four other closely agreeing analyses]. The ester was unaffected by phosphorus oxychloride, but reacted with phosphorus pentachloride in chloroform : we could not purify the chloro-compound. The hydroxy-ester also responded to the Tschugaeff-Zerewitinoff reagent.

*3-Hydroxy-2 : 4 : 5-tricarboxycyclopentane-1-acetate and its Methyl and Ethyl Esters*.—The acid was prepared by boiling either the octamethyl ester, the hexamethyl dihydrogen ester, the acid methyl hydroxy-ester, or the neutral methyl hydroxy-ester, or any of the corresponding ethyl esters with 10% aqueous-alcoholic potassium hydroxide. For example, the hydroxy-ester (10 g.) was boiled for 15 hours with a solution of potassium hydroxide (10 g.) in a mixture of methyl alcohol (34 c.c.) and water (66 c.c.). This acid was prepared by Guthzeit and Hartmann, although it and its silver salt and methyl and ethyl esters were all incorrectly analysed. The product was isolated as its silver salt by Guthzeit and Hartmann's method. The salt, suspended in dry ether, was decomposed by means of hydrogen sulphide, and the acid, part of which was obtained by evaporation of the ether and part by extracting the silver sulphide with ethyl acetate, was crystallised (3 g.) to constant m. p. from ethyl acetate containing acetone. It separated in small rectangular prisms, m. p. 193°. Guthzeit and Hartmann described this acid as amorphous and instantly oxidised by permanganate. The pure acid is stable towards permanganate, and is unaffected either by lead peroxide in glacial acetic acid at 100° or by chromic acid in acetic acid at 30°. It gives a yellow colour with ferric chloride [Found : C, 43.7, 43.8; H, 4.6, 4.7; *M* (Rast), 283, 299. Calc. for  $C_{10}H_{12}O_9$  : C, 43.5; H, 4.4%; *M*, 276. Calc. for  $C_{10}H_{10}O_8$  : C, 46.5; H, 3.9%; *M*, 258. Guthzeit and Hartmann record C, 46.4; H, 4.0%, and five other closely agreeing analyses. Found for the Ag salt : C, 16.75, 16.95; H, 1.4, 1.4; Ag, 59.4, 59.5. Calc. for  $C_{10}H_8O_8Ag_4$  : C, 17.0; H, 1.15; Ag, 61.4%. Calc. for  $C_{10}H_6O_8Ag_4$  : C, 17.5; H, 0.9; Ag, 62.9%. Guthzeit and Hartmann record C, 17.6; H, 1.0; Ag, 62.8%, and several other analyses closely agreeing]. The methyl ester was obtained from

the silver salt and methyl iodide as a viscous, pale yellow oil, b. p. 205°/3 mm., which did not decolorise permanganate in acetone (Found : C, 50·6; H, 5·9. Calc. for  $C_{14}H_{20}O_9$  : C, 50·6; H, 6·1%. Calc. for  $C_{14}H_{18}O_8$  : C, 53·5; H, 5·8%. Guthzeit and Hartmann record as found : C, 53·4; H, 5·9%). This compound could not be smoothly acetylated, but it reacted with the Tschugaeff-Zerewitinoff reagent, giving methane, as was proved by analysis of the gas (Found : OH, 4·5. Calc., 5·1%); the dehydration of the hydroxy-ester with potassium hydrogen sulphate is described later. The corresponding ethyl ester, b. p. 200°/about 1 mm., was similarly prepared and had similar properties (Found : C, 55·2; H, 7·35. Calc. for  $C_{18}H_{28}O_9$  : C, 55·6; H, 7·3%. Calc. for  $C_{18}H_{26}O_8$  : C, 58·35; H, 7·1%. Guthzeit and Hartmann record C, 58·0, 58·2; H, 7·4, 7·2%).

*Ozonolysis of Methyl and Ethyl  $\Delta^{\alpha}$ -Hexadiene- $\alpha\alpha\gamma\gamma\delta\delta\zeta\zeta$ -octacarboxylate [Methyl and Ethyl (1 : 1 : 2)-bicycloHexane-1 : 1 : 3 : 3 : 4 : 4 : 6 : 6-octacarboxylate].*—A solution of the methyl ester (5 g.) in chloroform (50 c.c.) at 0° was treated with ozonised oxygen for 24 hours. Some oxalic acid which had separated was collected, and the filtered chloroform solution was evaporated. The oily residue on boiling with water went almost completely into solution, but a turbidity appeared later and, on cooling, crystalline methyl ethanetetracarboxylate (0·9 g.) separated. Crystallised from acetone, it had m. p. 135°, and was identified first by analysis [Found : C, 45·8; H, 5·5; *M* (Rast), 262, 269. Calc. : C, 45·8; H, 5·4%; *M*, 262], and afterwards by its mixed m. p. with an authentic specimen, and by the products of its hydrolysis and decarboxylation. The mother-liquor from the decomposition with water yielded a further considerable quantity of oxalic acid, which was separated as calcium salt. It also yielded an oil, which on distillation gave a further quantity of crystalline methyl ethanetetracarboxylate. Similar results were obtained when the ozonide was reduced with zinc and acetic acid. The octa-ethyl ester was converted into ethyl ethanetetracarboxylate (m. p. and mixed m. p. 76°) and oxalic acid by the same method.

*Methyl 3-Methoxy-2 : 2 : 4 : 4 : 5 : 5-hexacarboxycyclopentane-1-malonate.*—The octamethyl ester (10 g.) was dissolved in a solution of sodium methoxide prepared from sodium (0·8 g.) and methyl alcohol (130 c.c.), and the product was precipitated by addition of dilute aqueous acid. Crystallised from acetone, the *methoxy*-compound had m. p. 193° (yield, 4 g.). The same compound was prepared from the octamethyl ester (0·5 g.) by treatment for 3 days with a cold solution of potassium hydroxide (0·5 g.) in methyl alcohol (50 c.c.). It was also obtained when the octamethyl ester (2 g.) was boiled for 3 hours with a solution of potassium cyanide (0·5 g.) in methyl alcohol (50 c.c.), but not when methyl alcohol alone was used as the reagent. Again it was obtained in attempts to methylate the octamethyl ester with methyl-alcoholic sodium methoxide and methyl iodide, but only the unchanged octamethyl ester was recovered when dry sodium methoxide and methyl iodide were employed with benzene as diluent. (Certain incidental observations of this kind are mentioned because no systematic account of the numerous negative experiments summarised in the introduction is included in this experimental account.) The methoxy-ester [Found : MeO (Zeisel), 47·5; C, 47·7, 47·6; H, 5·2, 5·0.  $C_{23}H_{30}O_{17}$  requires MeO, 48·3; C, 47·75; H, 5·2%] was unaffected on treatment with permanganate, bromine, boiling ordinary concentrated nitric acid, or cold concentrated sulphuric acid. It was attacked by prolonged treatment with ozone, but the products could not be recognised.

*Thermal Decomposition of Methyl  $\Delta^{\alpha}$ -Hexadiene- $\alpha\alpha\gamma\gamma\delta\delta\zeta\zeta$ -octacarboxylate [Methyl (1 : 1 : 2)-bicycloHexane-1 : 1 : 3 : 3 : 4 : 4 : 6 : 6-octacarboxylate].*—Decomposition set in above 200°, and a considerable quantity of the product distilled at 220—229°/18—20 mm. This was a viscous yellow oil, which partly solidified on keeping. The drained solid was crystallised from light petroleum, and identified as methyl 6-methoxy- $\alpha$ -pyrone-3 : 5-dicarboxylate, m. p. 129°, by comparison and mixed m. p. with an authentic specimen. As confirmation the pyrone was converted by means of ammonia into methyl hydrogen 6-methoxy-2-pyridone-3 : 5-dicarboxylate, m. p. 183° (Found : C, 47·7; H, 4·1; N, 6·2. Calc. : C, 47·6; H, 4·0; N, 6·2%).

*Methyl and Hexamethyl Dihydrogen 2 : 2 : 4 : 4 : 5 : 5-Hexacarboxycyclopentane-1-malonate.*—A solution of the octamethyl ester, m. p. 139°, (5 g.) and concentrated sulphuric acid (2 c.c.) in anhydrous methyl alcohol (200 c.c.) formed the catholyte, and dilute sulphuric acid formed the anolyte of an electrolytic cell. The solutions, each of which was kept cool by means of spiral tubes containing flowing water, were separated by a porous pot. The anode, a rod of lead, was placed inside the pot, and the cathode, a pool of mercury, outside. Electrolysis was effected with a current of 0·8—0·9 amp. passed for 24 hours, and the catholyte was then evaporated. The product was partly solid, and the drained crystals, after recrystallisation from methyl alcohol and acetone, yielded the *methyl dihydro-ester* in flat prisms, m. p. 149° [Found : C, 48·4;

H, 5.1; *M* (cryoscopic in benzene), 560, 570.  $C_{22}H_{28}O_{16}$  requires C, 48.2; H, 5.15%; *M*, 548]. The liquid product which accompanied this ester deposited further quantities of the crystalline substance on keeping, and was then distilled. It had b. p. 142—143°/0.45 mm., reduced cold permanganate, and did not give satisfactory analytical figures, but on keeping continued slowly to deposit crystals of the ester of m. p. 149°. The *hexamethyl acid-ester* was obtained by boiling the neutral dihydro-ester (1 g.) with 20% hydrochloric acid (30 c.c.); after about 1.5 hours the neutral ester went into solution and the acid-ester began to crystallise. Collected from the cooled solution and crystallised from acetone, it had m. p. 252° (decomp.) (Found: C, 46.4; H, 5.0.  $C_{20}H_{24}O_{16}$  requires C, 46.2; H, 4.65%).

2 : 4 : 5-*Tricarboxycyclopentane-1-acetic Acid*.—The above acid-ester (0.5 g.) was boiled with a 10% solution of potassium hydroxide in ethyl alcohol (10 c.c.) containing just enough water to cause complete solution. After 6 hours the solution was allowed to cool and kept over-night. Crystals of a potassium salt which then separated were collected, dissolved in water, and treated with hydrochloric acid, and the solution thus obtained was evaporated to dryness over sulphuric acid in a vacuum. The required *acid* was obtained from the residue by extraction with acetone and crystallisation from alcohol. It had m. p. 225°, and was stable towards alkaline permanganate (Found: C, 46.5; H, 5.0.  $C_{10}H_{12}O_8$  requires C, 46.2; H, 4.65%). The *silver* salt (Found: C, 17.6; H, 1.6; Ag, 58.6.  $C_{10}H_8O_8Ag_4$  requires C, 17.45; H, 1.2; Ag, 62.8%) was converted by means of methyl iodide into the methyl ester, and this by treatment with ammonia into the *amide*, which, crystallised from water, had m. p. 280° (decomp.) (Found: C, 46.2; H, 6.1; N, 21.3.  $C_{10}H_{16}O_4N_4$  requires C, 46.8; H, 6.3; N, 21.8%).

*Dehydration and Reduction of Methyl 3-Hydroxy-2 : 4 : 5-tricarboxycyclopentane-1-acetate*.—The ester (10 g.) was heated with dry, powdered potassium hydrogen sulphate (35 g.) for 20 hours at 180°. The product was lixiviated with ether, and the filtered extract was dried with potassium carbonate and evaporated. The residual oil was distilled under reduced pressure in order to remove coloured products, and the colourless distillate was fractionally distilled (1 mm.). The principal fractions had severally b. p. 175—185° (1.7 g.) (Found: C, 54.0; H, 5.6%), b. p. 185—195° (6.5 g.) (Found: C, 53.7; H, 6.0.  $C_{14}H_{18}O_8$  requires C, 53.5; H, 5.8%), b. p. 195—200° (0.5 g.) (Found: C, 53.4; H, 5.7%). All fractions instantly decolorised permanganate in acetone, and are assumed to consist essentially of mixtures of isomeric methyl 2 : 4 : 5-tricarboxycyclopentene-1-acetates. They absorbed about the correct amount of hydrogen on catalytic reduction. The large central fraction was hydrogenated with the aid of Adams's catalyst (1.5 g.) in methyl alcohol. Reduction was complete within 0.5 hour, and the product, which was stable to permanganate in acetone, was fractionated (2.5 mm.). The fractions had severally b. p. below 185° (0.3 g.), b. p. 185—187° (4.2 g.) (Found: C, 53.1; H, 6.6.  $C_{14}H_{20}O_8$  requires C, 53.15; H, 6.4%), b. p. 187—190° (0.5 g.) (Found: C, 53.2; H, 6.6%). The last two fractions were hydrolysed by means of aqueous methyl-alcoholic potassium hydroxide, but the main product was an intractable gum, which did not decolorise alkaline permanganate.

Throughout this experimental record duplicate analyses refer to independent preparations.

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