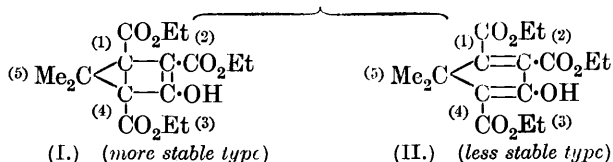


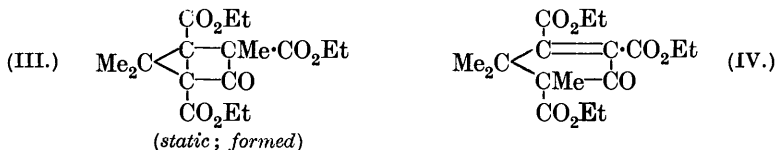
CCXV.—*The Chemistry of Polycyclic Structures in Relation to their Homocyclic Unsaturated Isomerides. Part VIII. The Differing Effects of the gem-Dimethyl and spirocycloHexane Groupings on the Direction of Blocking of an Intra-annular Tautomeric System by Substitution.*

By CHRISTOPHER KELK INGOLD and ERNEST ARTHUR SEELEY.
IN Parts I and II (Farmer and Ingold, J., 1920, **117**, 1362; Farmer, Ingold, and Thorpe, J., 1922, **121**, 128) proof was adduced that the bridged-ring ester (I), first prepared by Perkin and Thorpe (J.,

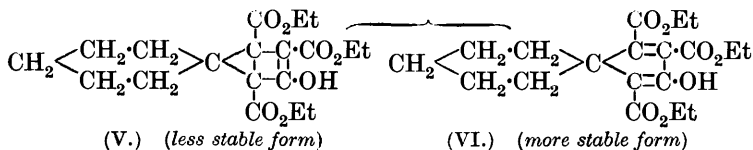
1901, 79, 729), behaved as though it also had the structure (II), and that its derivatives and hydrolysis products exhibited similar evidence of tautomeric behaviour.



It then became of interest to ascertain which of the two types of structure would be perpetuated when substitution converted the tautomeric parent into a static derivative. Thus the sodio-derivative of the above hydroxy-ester might methylate on carbon in position 2 through form (I) or in position 4 through form (II), giving, in the first case, a stable bridged ring, and, in the second, a stable monocyclic derivative. This question was answered in Part V (J., 1923, 123, 3303) where it was shown that the static methyl derivative possessed the bridged constitution (III) and not the monocyclic structure (IV) :



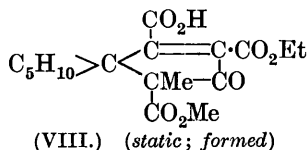
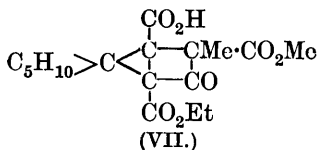
Part IV (J., 1923, 123, 853) recorded an investigation of the derivatives of a hydroxy-ester (V, VI) analogous to (I, II) but containing a *spirocyclohexane* ring in place of the *gem*-dialkyl group. Ingold and Thorpe (J., 1919, 115, 320) had adduced theoretical reasons for believing that the bridged structure in type (V) would be less stable than that in type (I); and it was subsequently found (Part IV, *loc. cit.*) that the reactions indicating the *cyclopentene* phase are actually more pronounced, and those indicating the bridged phase less pronounced, in the *cyclohexane* than in the *gem*-dimethyl series.



It therefore seemed possible that the blocking of the mobile intra-annular system by methylation might occur through the unbridged form in the *cyclohexane* series, the methyl group entering

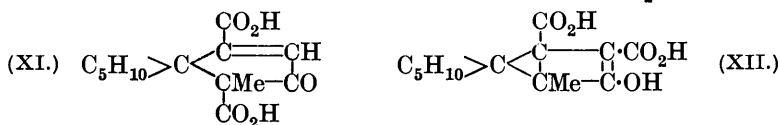
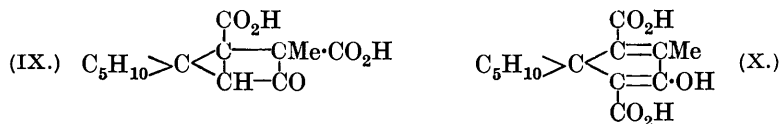
in position 4, in contrast to the established course of the reaction in the *gem*-dimethyl series.

When the methylation product obtained from the sodio-derivative of the *spirocyclohexane* ester (V, VI) is boiled with hydrochloric acid, a solid acid ester is obtained which may be formulated either as (VII) or as (VIII) according as the methyl group occupies position 2 or 4.



These formulæ assume that one of the carboxyl groups has been converted into a carbomethoxyl group during methylation; a partial conversion of this nature was established by Ingold and Thorpe (*loc. cit.*) and similar interchanges have frequently been recorded. The position given to the free carboxyl group is tentatively assigned on the grounds that the acid ester does not evolve carbon dioxide at its melting point. Any doubt which might be entertained on these points does not affect the substance of this argument. Either type of formula necessarily represents the acid ester as a substance in which intra-annular tautomerism has been suspended by substitution.

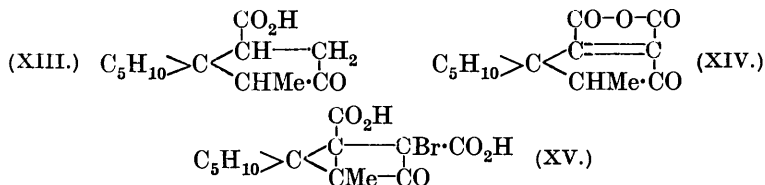
Hydrolysis of the acid ester with alcoholic potassium hydroxide leads to the production of a dibasic acid, $\text{C}_{13}\text{H}_{16}\text{O}_5$, the properties of which determine the position of the methyl group. The possible constitutions of an acid of this composition derived from an acid ester having formula (VII) are given by formulæ (IX) and (X); on the other hand, if the acid ester possessed the structure (VIII), the dibasic acid might be represented either by (XI) or by (XII).



Of these four formulæ, (XII) alone is consistent with the following properties of the isolated acid: (a) It gives a deep violet colour with ferric chloride, and is therefore a β -hydroxyacrylic acid. (b) It readily yields a stable cyclic anhydride, from which the original acid can be recovered after fission of the anhydride ring

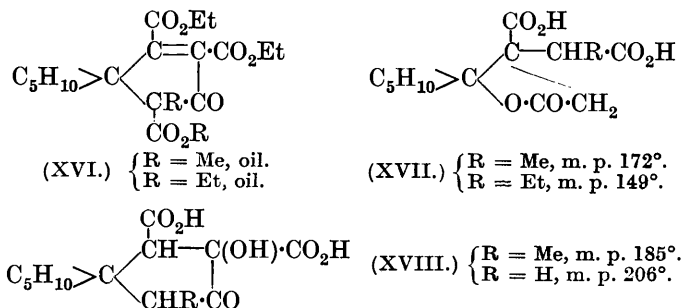
with hot alkali. (c) On treatment with a cold dilute solution of bromine in acetic acid, the dibasic acid undergoes nuclear substitution, one atom of hydrogen being replaced (compare Part IV, *loc. cit.*, pp. 857—862).

Formula (XII) connotes, of course, only one of the possible intra-annular tautomeric forms possessed by the dibasic acid $C_{13}H_{16}O_5$, and we regard formulæ (XIV) and (XV) as representing the most probable constitutions of its anhydride and bromo-derivative, respectively.



These observations show that the static methylation product (VIII) has a formula of the type assigned to it, the tautomerism of the *spirocyclohexane* five-carbon nucleus having been suppressed by methylation in a direction conforming to the general chemical differences between this series and the corresponding *gem*-dimethyl series of intra-annular tautomeric compounds.

These experiments necessitate a revision of the structures which Ingold and Thorpe (*loc. cit.*) assigned to certain derivatives of the mobile ester (V, VI) before the intra-annular tautomerism of the five-carbon nucleus was discovered. Thus the ester was assumed to methylate in position 2 by analogy with the methylation of the *gem*-dimethyl ester (I, II). The formula now suggested for the methylated product is XVI (R=Me), the probable structures of the fission products, m. p.'s 172° and 185° , being represented by XVII and XVIII (R=Me). Corresponding changes are necessary in the structures of the homologues (XVI, R=Et; XVII, R=Et; XVIII, R=H) and derivatives :



EXPERIMENTAL.

Methyl Ethyl Hydrogen 4-Methyl-5-cyclohexanespiro- Δ^1 -cyclopenten-3-one-1 : 2 : 4-tricarboxylate (VIII).—The yellow sodio-derivative (20 g.) of ethyl 5-cyclohexanespirodicyclopenten-3-ol-1 : 2 : 4-tricarboxylate was heated with a large excess of methyl iodide as described by Ingold and Thorpe (*loc. cit.*), and the crude methylation product (19 g.) was boiled for 12 hours with 20% hydrochloric acid. On extraction with ether a stiff gum was obtained which solidified after 2 months; the *acid ester* was then crystallised from ether-ligroin. It separated in prisms, m. p. 92—93° (Found : C, 60.9, 61.0; H, 6.7, 6.8; *M*, by titration, 339. $C_{17}H_{22}O_7$ requires C, 60.4; H, 6.6%; *M*, monobasic, 338).

4-Methyl-5-cyclohexanespiro-(0 : 1 : 2)-dicyclopenten-3-ol-1 : 2-dicarboxylic Acid [4-*Methyl-5-cyclohexanespiro-(0 : 1 : 2)-dicyclopentan-3-one-1 : 2-dicarboxylic Acid*] (XII).—The above acid ester was boiled with 2.2 parts of potassium hydroxide in 4*N*-solution in absolute methyl alcohol, and after 6 hours the precipitate was collected, dissolved in water, and decomposed by dilute hydrochloric acid (carbon dioxide was evolved). The aqueous solution was extracted thoroughly with ether, and the *acid* thus recovered was crystallised first from ether-ligroin and then from ether (Found : C, 61.8; H, 6.4; *M*, by titration, 126.3. $C_{13}H_{16}O_5$ requires C, 61.8; H, 6.4%; *M*, dibasic, 126.1).

The acid has m. p. 214—216°, and with an aqueous alcoholic solution of ferric chloride gives an intense violet coloration which after several minutes is replaced by a yellowish-brown precipitate. A dilute solution of permanganate was decolorised in about 1 minute. Oxidations with permanganate and with ferricyanide were tried on a larger scale under various conditions, but the products could not be crystallised.

The Anhydride (XIV).—The acid (0.4 g.) was heated for 20 minutes with 6 c.c. of acetyl chloride at 100°, and the residue obtained on evaporation was rubbed with aqueous sodium hydrogen carbonate and dried on porous porcelain. Subsequent treatment indicated the presence of a small amount of unchanged acid, which was difficult to remove by crystallisation, and the product was therefore again treated with acetyl chloride and the residue crystallised twice from ether-ligroin; large, pale green prisms, m. p. 95°, were then obtained (Found by microanalysis : C, 65.9, 66.3; H, 6.0, 6.6. $C_{13}H_{14}O_4$ requires C, 66.6; H, 6.0%). The green colour of this substance, which is absent from the acid, is similar to that of ketomalonic ester, which also contains a cross-conjugated system. The anhydride is affected only very slowly by boiling water, but is

hydrolysed by hot aqueous sodium hydroxide, yielding the sodium salt of the original acid, m. p. 214—216° (mixed m. p. the same). A solution of the anhydride in ether–ligroin gives precipitates with *p*-toluidine and *p*-chloroaniline which are soluble with effervescence in sodium hydrogen carbonate and are therefore presumably the substituted amic acids. The anhydride does not give a colour with ferric chloride, but rapidly decolorises permanganate.

The methyl-alcoholic filtrate from the potassium salt of the dibasic acid, on being worked up for organic acids, yielded a considerable amount of gum together with a small amount of a solid acid, which, after several crystallisations from benzene, had m. p. 102—105°, but still did not appear quite pure. The investigation of this had to be discontinued for lack of material.

2-Bromo-4-methyl-5-cyclohexanespiro-(0 : 1 : 2)-dicyclopentan-3-one-1 : 2-dicarboxylic Acid (XV).—The above dibasic acid (0.37 g.), dissolved in 10 c.c. of glacial acetic acid, was treated with 3 c.c. of a 10% solution of bromine in acetic acid (theory, 2.4 c.c.). After 4 hours, the bromine was nearly decolorised. On concentration of the acetic acid solution at the ordinary temperature, the *bromo-acid* readily crystallised. It separated from ether–benzene in small prisms, m. p. 197—198° (Found: Br, 23.6. $C_{13}H_{15}O_5Br$ requires Br, 24.1%).

4-Methyl-5-cyclohexanespirocyclopentan-3-one-1-carboxylic Acid (XIII).—The acid ester (VIII) was heated for 3 hours at 135—150° with constant-boiling hydriodic acid. The liquid was extracted with ether, and the iodine removed from the extract with aqueous sodium hydrogen sulphite. The product obtained on evaporation of the ether contained sulphur, but this was readily eliminated by crystallisation from ether–ligroin, which yielded the pure monobasic acid, m. p. 114—116° (Found: C, 68.4; H, 8.6. $C_{12}H_{18}O_3$ requires C, 68.5; H, 8.6%).

The *semicarbazone*, prepared from the acid, semicarbazide hydrochloride, and aqueous sodium acetate, has m. p. 223° (Found: C, 58.6; H, 8.2. $C_{13}H_{21}O_3N_3$ requires C, 58.8; H, 7.9%).

Gums which cannot be crystallised were obtained on attempting to oxidise this ketonic acid with permanganate and ferricyanide at 20—60°.

We desire to thank the Chemical Society for defraying part of the cost of this investigation.

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