XCII.—*The Chemistry of Polycyclic Structures in Relation to their Homocyclic Unsaturated Isomerides. Part VI. Some Reactions of* iso*Phorone.*

BY JOHN WILLIAM BAKER.

THE chemistry of homocyclic compounds is often complicated by reactions which find no simple explanation in the structure usually assigned to the compound (Farmer and Ingold, J., 1920, **117**, 1362, and subsequent papers), the ambiguity extending in one case even to the synthesis of the substance, syntheses which should yield respectively the acids (I) and (II) yielding the same acid (Farmer, Ingold, and Thorpe, J., 1922, **121**, 128).
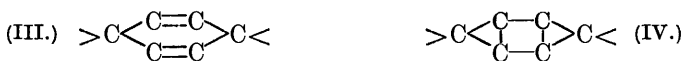
(I.) $Me_2C{<}^{C(CO_2H){\cdot}CH_2}_{CH\text{——}CO}$ $Me_2C{<}^{C(CO_2H){:}CH}_{CH_2\text{——}CO}$ (II.)

Such conflicting evidence was reconciled by the assumption of intra-annular tautomerism between the *bicyclo*pentene and the *cyclo*pentadiene systems, the two enolic forms being merely valency isomerides in accordance with the scheme :

$$Me_2C{<}^{C(CO_2H){:}CH}_{CH\text{====}C{\cdot}OH} \rightleftharpoons Me_2C{<}^{C(CO_2H){\cdot}CH}_{CH\text{——}C{\cdot}OH}$$
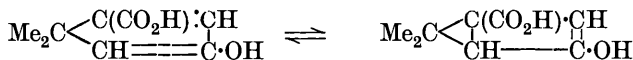
There is no *a priori* reason why such redistribution of residual affinity within the ring, extending from mere conjugation of affinity across the ring to the establishment of a real bridge bond, should be restricted to the *cyclo*pentadiene series : its extension to the

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heterocyclic rings thiophen and furan, and to benzene has already been developed (Ingold, J., 1922, **121**, 1133, and subsequent papers).

The present paper deals with the extension of such intra-annular tautomerism to the *cyclo*hexadiene series in accordance with the general scheme :

$$\text{(III.)} \quad >C<{\overset{\displaystyle C=C}{\underset{\displaystyle C=C}{}}>C< \qquad\qquad >C<{\overset{\displaystyle C-C}{\underset{\displaystyle C-C}{}}>C< \quad \text{(IV.)}$$

On first inspection it may be considered that the structure (IV) is improbable in view of the strain involved, but it must be understood that it is not intended to represent a stable individual substance, but merely a phase in the scheme of valency distribution which, under favourable conditions, may pass into a more stable, true bridged phase. Such favourable conditions may occur when one or both of the potential trimethylene rings are stabilised by the presence of a *gem*-dimethyl group, and, in this case, products containing a *cyclo*propane ring may result from the degradation of the molecule.

An example of this type of intra-annular tautomerism has, in the author's opinion, been established in the case of *iso*phorone. The generally accepted formula (V) for *iso*phorone has been established both by synthesis and by oxidation. Knoevenagel and Fischer (*Annalen*, 1897, **297**, 185) obtained it by the condensation of mesityl oxide and ethyl acetoacetate at 5° and hydrolysis of the *iso*phoronecarboxylic ester so produced. The structure was confirmed by Crossley and Gilling (J., 1909, **95**, 24), who obtained the ketone by the condensation of ethyl sodiomalonate with chlorodimethyl*cyclo*hexenone and hydrolysis of the ethyl dimethyl*cyclo*hexenoneacetate so obtained.

The oxidation of *iso*phorone was investigated by Bredt and Rubel (*Annalen*, 1898, **299**, 160), who obtained a whole series of acids intermediate between *iso*phorone and its final oxidation product, *as*-dimethylsuccinic acid. Formula (V) is also in good accord with most of the reactions of the ketone, *e.g.*, the formation of monobenzylidene-monopiperonylidene derivatives.

Kerp and Muller (*Annalen*, 1898, **299**, 193), however, found that this structure alone was not sufficient to represent all the reactions of *iso*phorone (obtained, in this case, by the condensation of acetone). *iso*Phorone condenses with another molecule of acetone to yield a higher condensation product, xylitone, which these investigators found also yields a monobenzylidene derivative, and hence must contain the group $CMe_2:C\cdot CO\cdot CH_2\cdot$; this necessarily involves the existence of the group $\cdot CH_2\cdot CO\cdot CH_2\cdot$ in the original *iso*phorone molecule. Hence, in this reaction at least, *iso*phorone

must be represented by the structure (VI) rather than (V), and these authors concluded that *iso*phorone obtained from acetone is a static mixture of the two isomerides (V and VI).

The interconversion of these two forms merely involves the well-known $\alpha\beta$–$\beta\gamma$ change across a three-carbon system, and the conflicting results would be readily explained if such a tautomeric system were assumed to exist in the *iso*phorone molecule. The enolic modification (VII) of the structure (VI) conforms to the *cyclo*hexadiene type mentioned above, and hence there is the possibility of a second kind of tautomeric change, *viz.*, intra-annular, a redistribution of affinity across the ring resulting, initially, in the tri*cyclo*hexane structure (VIII). It is not suggested that this form represents more than a transitory phase in the whole scheme, for only one of the potential three-membered rings is stabilised by the presence of a *gem*-dimethyl group, and it is to be expected that such a structure would immediately ketonise across the ring, thus destroying the unstabilised three-membered ring, to yield a bridged modification of the *iso*phorone molecule (IX). Finally, this could change in the usual manner to yield an enolic modification of a bridged form of *iso*phorone. The complete scheme is as follows :
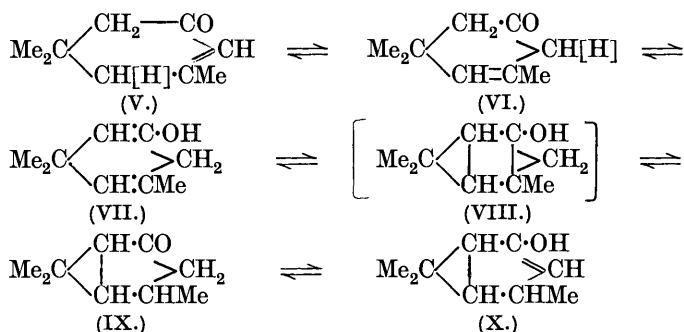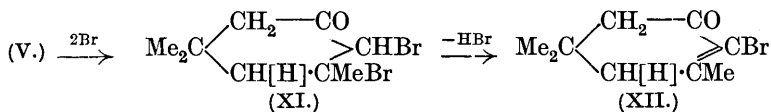

Thus in the *iso*phorone molecule three types of tautomerism are possible, each being superimposed on the other ; (*a*) three-carbon, $\alpha\beta$–$\beta\gamma$-change, (*b*) intra-annular, (*c*) keto-cyclol.

Evidence is submitted in this paper which, in the author's opinion, can be explained only by assuming such a scheme in connexion with the *iso*phorone molecule.

Kerp and Muller (*loc. cit.*) found that in ice-cold glacial acetic acid solution *iso*phorone forms an unstable dibromo-additive product which spontaneously evolves hydrogen bromide. Their analysis is 5% low for this compound. When, however, *iso*phorone in ice-cold carbon tetrachloride solution is treated with a standard

solution of bromine in the same solvent, absorption is rapid and a white, crystalline dibromo-compound (XI) separates, but no trace of hydrogen bromide is evolved until two atoms of bromine have been added. This additive compound is stable in the absence of moisture, but on exposure to air it immediately loses one molecule of hydrogen bromide to form monobromo*iso*phorone (XII). Although the possibility of bromine addition to the enolic double bond and subsequent loss of hydrogen bromide to yield a α-bromoketone cannot be excluded, it is considered more probable, in view of the degree of stability of the intermediate compound, that the addition of bromine occurs at the double bond in the three-carbon system, thus forming a blocked system, which therefore spontaneously liberates hydrogen bromide to reform a mobile system in accordance with the scheme :
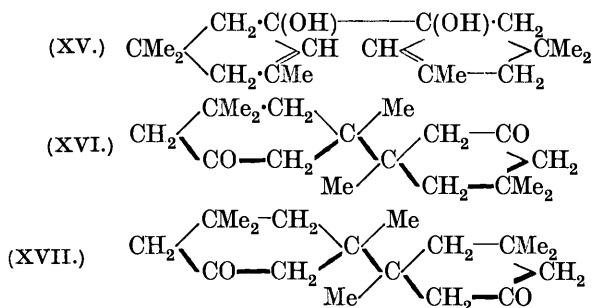
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(V.) \xrightarrow{2Br} \quad Me_2C\Big\langle{\begin{smallmatrix}CH_2\text{---}CO\\ \\ CH[H]\cdot CMeBr\end{smallmatrix}}\Big\rangle CHBr \xrightarrow{-HBr} Me_2C\Big\langle{\begin{smallmatrix}CH_2\text{---}CO\\ \\ CH[H]\cdot CMe\end{smallmatrix}}\Big\rangle CBr
$$

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(XI.) \qquad\qquad\qquad\qquad\qquad (XII.)
$$

Evidence of the bridged modification of *iso*phorone was obtained by a study of its reduction products. When *iso*phorone is reduced by the Clemmensen method, a solid hydrocarbon, $C_{18}H_{28}$, can be isolated in small yield from the product. This hydrocarbon is saturated, and therefore valency considerations necessitate the existence of the bridged structure (XIII). This structure is supported by the oxidation of the hydrocarbon with boiling potassium permanganate in sodium hydrogen carbonate suspension, the main product being *trans*-caronic acid. The formation of this hydrocarbon from the bridged, enolic modification of *iso*phorone (X) is represented by the following scheme, additive ring formation preceding the reduction :

$$
2(X) \longrightarrow Me_2C\Big\langle{\begin{smallmatrix}CH\cdot C(OH)\cdot C(OH)\cdot CH\\ | \qquad | \qquad\quad |\\ CH \; CH\text{---}CH \quad CH\\ \diagdown\diagup \qquad \diagdown\diagup\\ CHMe \qquad\quad CHMe\end{smallmatrix}}\Big\rangle CMe_2 \xrightarrow{4H}
$$

$$
Me_2C\Big\langle{\begin{smallmatrix}CH\cdot CH\cdot CH\cdot CH\\ | \quad | \quad | \quad |\\ CH \; CH\cdot CH \; CH\\ \diagdown\diagup \quad \diagdown\diagup\\ CHMe \; CHMe\end{smallmatrix}}\Big\rangle CMe_2
\qquad
Me_2C\Big\langle{\begin{smallmatrix}HO_2C \qquad CO_2H\\ CMe\text{-}C\text{---}C\text{---}CMe\\ | \quad | \quad | \quad |\\ CH\text{---}CH\text{---}CH\text{---}CH\end{smallmatrix}}\Big\rangle CMe_2
$$

(XIII.)   (XIV.)
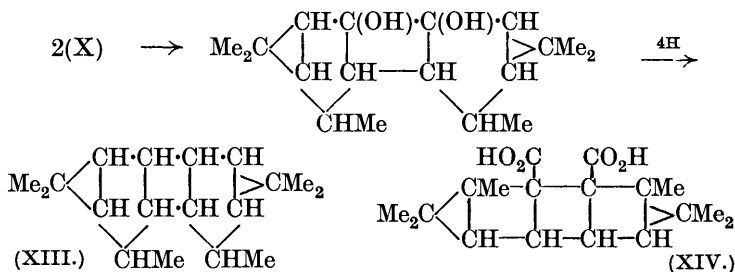
A similar constitution has been assigned to α-dicamphylic acid (XIV) obtained by the action of potash on sulphocamphylic acid (Perkin, J., 1903, **83**, 835).

Reduction of *iso*phorone with sodium and moist ether yields a

mixture of two isomerides, $C_{18}H_{30}O_2$, m. p. 126° and 162°, respectively. The latter is undoubtedly the product obtained by Hess and Munderloh (*Ber.*, 1916, **51**, 383) by the reduction of *iso*phorone with 2·5% sodium amalgam and methyl alcohol. These investigators, apparently merely on the analytical data, assigned the pinacol formula (XV) to this product. Such a constitution is, however, quite inconsistent with the properties of this reduction product. Both substances, m. p. 126° and 162°, are saturated and do not decolorise potassium permanganate in sodium hydrogen carbonate solution in the cold, both yield disemicarbazone derivatives, but neither will form an acetyl derivative on heating with acetic anhydride. They are probably derived from the unsaturated ring form of *iso*phorone (VII) by a reduction similar to that which occurs in the formation of deoxymesityl oxide and deoxyphorone, respectively, from mesityl oxide and phorone, two stereoisomerides (XVI and XVII) being produced.

$$\text{(XV.)} \quad CMe_2\!\!<\!\!\begin{array}{c}CH_2 \cdot C(OH)\!\!-\!\!\!-\!\!\!-\!\!C(OH)\cdot CH_2\\ >\!\!CH \quad CH\!\!<\\ CH_2\cdot CMe \quad\quad CMe\!\!-\!\!\!-CH_2\end{array}\!\!>\!\!CMe_2$$

$$\text{(XVI.)} \quad CH_2\!\!<\!\!\begin{array}{c}CMe_2\cdot CH_2\\ CO\!\!-\!\!CH_2\end{array}\!\!>\!\!C\!\!<\!\!\begin{array}{c}Me\\ \\ Me\end{array}\!\!>\!\!C\!\!<\!\!\begin{array}{c}CH_2\!\!-\!\!CO\\ \\ CH_2\!\!-\!\!CMe_2\end{array}\!\!>\!\!CH_2$$

$$\text{(XVII.)} \quad CH_2\!\!<\!\!\begin{array}{c}CMe_2\!\!-\!\!CH_2\\ CO\!\!-\!\!CH_2\end{array}\!\!>\!\!C\!\!<\!\!\begin{array}{c}Me\\ \\ Me\end{array}\!\!>\!\!C\!\!<\!\!\begin{array}{c}CH_2\!\!-\!\!CMe_2\\ \\ CH_2\!\!-\!\!CO\end{array}\!\!>\!\!CH_2$$

Thus the ambiguity of structure which had previously been noted in the *cyclo*pentadiene series would seem to be present also in other unsaturated cyclic systems, and may indeed be of much more frequent occurrence than is generally supposed.

EXPERIMENTAL.

The *iso*phorone employed was prepared by the condensation of mesityl oxide and ethyl acetoacetate (Knoevenagel and Fischer, *loc. cit.*), but at the temperature of the steam-bath for 4 hours, under which conditions the main portion of the *iso*phoronecarboxylic ester is converted into *iso*phorone. The fraction, b. p. 95—100°/14 mm., consisted of nearly pure *iso*phorone. In order to determine whether it was a single individual or a mixture of isomerides (compare Kerp and Muller, *loc. cit.*), its semicarbazone was submitted to a rigorous fractional crystallisation from alcohol. No trace of a second semicarbazone could be detected. The pure semicarbazone, crystallised from alcohol, has m. p. 199·5° (decomp.) (Crossley and

Gilling, *loc. cit.*, give 191°), and does not depress the melting point of a specimen prepared by the latter method (Found : C, 61·5; H, 8·8. Calc., C, 61·5; H, 8·8%). The ketone regenerated from the pure semicarbazone by steam distillation with oxalic acid had b. p. 99°/14 mm.; the oxime had m. p. 79·5° (Crossley and Gilling, *loc. cit.*, give 78°).

A *monopiperonylidene* derivative was obtained and after crystallisation from ethyl acetate had m. p. 145—146° (Found : C, 75·2; H, 7·0. $C_{17}H_{18}O_3$ requires C, 75·4; H, 6·7%).

Bromination of isoPhorone. Formation of the Unstable Dibromide (X).—A standard solution of dry bromine in dry carbon tetrachloride (1 c.c. = 0·1 g. Br) was added dropwise to a solution of 1 g. of dry *iso*phorone, in a little carbon tetrachloride cooled in ice, moisture being rigorously excluded. Decoloration was instantaneous, and when 2 c.c. had been added the crystalline dibromide began to separate. When 13 c.c. (1·3 g. Br) had been added, the solution became coloured with free bromine and a trace of hydrogen bromide could be detected. Addition of two atoms of bromine requires 1·2 g. of bromine. After traces of bromine and hydrogen bromide had been removed under diminished pressure, the product was broken into a large excess of water, and the liberated hydrobromic acid titrated with potassium hydroxide (Found : 0·56 g. of hydrogen bromide. Liberation of 1 mol. of hydrogen bromide requires 0·60 g.). In another experiment the solvent was removed by evaporation in a vacuum. The dibromide remained as a mass of short, thick prisms, m. p. about 40°, which on exposure to air immediately changed to a colourless oil with the evolution of hydrogen bromide.

Monobromoisophorone (XII).—The carbon tetrachloride solution of the unstable dibromide having been poured into water, the precipitated, colourless oil was extracted with pure ether and washed with very dilute alkali. The residue from the dried ethereal extract was left in an evacuated desiccator over potash for 24 hours, and since it could not be distilled without decomposition, was analysed in the crude state (Found : C, 50·4; H, 6·2. $C_9H_{18}OBr$ requires C, 49·8; H, 6·0%).

1 : 3 : 4 : 5(?)-*Tetrabromo*-3 : 3 : 5-*trimethyl*cyclo*hexan*-1-*one* is obtained by exhaustive bromination of *iso*phorone in carbon tetrachloride solution. After crystallisation from ethyl acetate–ligroin (b. p. 60—80°), it has m. p. 135° (Found : C, 24·0; H, 2·4; Br, 70·7. $C_9H_{12}OBr_4$ requires C, 23·7; H, 2·6; Br, 70·2%). The same compound is produced when an excess of bromine is added to *iso*phorone in ice-cold glacial acetic acid solution, and crystallises on keeping.

Attempts to prepare the tribromo-compound always resulted in the formation of an uncrystallisable gum.

Reduction of iso*Phorone.*—(1) *With sodium and moist ether. Formation of* 1 : 1′ : 3 : 3 : 3′ : 3′-*trimethyl*bicyclo*hexyl*-5 : 5′-*dione,* α *and* β *forms* (XVI *and* XVII). isoPhorone was dissolved in 20—30 times its volume of ether saturated with water, and sodium wire added in small successive portions. It seems to be essential to allow the first reaction to proceed as vigorously as possible. A flocculent solid separated, the liquid turning first yellow and finally deep red. The product was poured into water, acidified with hydrochloric acid, extracted with ether, and any acid fraction removed with sodium hydrogen carbonate solution. The neutral residue was a brown syrup which partly crystallised. The solid crystallised from ethyl acetate–ligroin had m. p. 162° (Found : C, 77·6; H, 10·8; M, cryoscopic in benzene, 268. $C_{18}H_{30}O_2$ requires C, 77·6; H, 10·8%; M, 280). It does not decolorise potassium permanganate in sodium hydrogen carbonate solution.

A *disemicarbazone* was obtained which after crystallisation from glacial acetic acid had m. p. 259—260° (decomp.) (Found : C, 61·0; H, 9·4. $C_{20}H_{36}O_2N_6$ requires C, 61·2; H, 9·3%).

The portion of the reduction product which had failed to solidify was fractionally distilled under reduced pressure. Low fractions consisting mainly of unchanged *iso*phorone were first obtained, and then a large, exceedingly viscous fraction distilled at 220—240°/20 mm., which immediately solidified when rubbed with low-boiling ligroin. The solid was crystallised from ethyl acetate–ligroin. It consists of the second isomeride, m. p. 126° (Found : C, 77·4; H, 10·7%). It does not decolorise potassium permanganate in sodium hydrogen carbonate solution in the cold, and only slowly on boiling. Careful fractional crystallisation of this substance failed to indicate the presence of any other product. A further quantity of this isomeride was obtained by a second fractional distillation of the gum obtained from the ligroin mother-liquors.

A *disemicarbazone* was obtained as before, but was precipitated from the alcoholic reaction mixture only on addition of water. After crystallising several times from about 90% methyl alcohol, it had m. p. 220° (decomp.) (Found : C, 61·2; H, 9·4%).

The same products were obtained when *iso*phorone was reduced with zinc and acetic acid, or with sodium amalgam and a boiling alkaline solution.

(2) *By the Clemmensen method. Formation of the hydrocarbon* (XIII). The ketone (10 g.) was refluxed with about 50 g. of amalgamated zinc and an excess of concentrated hydrochloric acid for 3 hours, small quantities of hydrochloric acid being occasionally

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added. The reaction mixture was steam distilled. The first portion of the distillate consisted of a very small quantity of a volatile oil, with a camphoraceous odour, which was not obtained in quantity sufficient for identification. The hydrocarbon then distilled and solidified in the receiver, cooled in ice. The yield was small, a large amount of resinous material, non-volatile in steam, being produced. The hydrocarbon was extracted with ether, and the residue from the dried extract rapidly solidified. It crystallised from dilute alcohol in fine needles, m. p. 112° (Found : C, 88·5; H, 11·5; M, cryoscopic in benzene, 231. $C_{18}H_{28}$ requires C, 88·5; H, 11·5%; M, 244). It is stable to potassium permanganate in sodium hydrogen carbonate solution in the cold, but decolorises bromine in carbon tetrachloride solution, probably owing to the destruction of two of the bridge bonds.

Oxidation of the Hydrocarbon XIII.—The hydrocarbon (0·42 g.), suspended in a solution of potassium permanganate and sodium hydrogen carbonate, was heated under reflux, successive quantities of permanganate being added until the reaction mixture remained pink (48 hours). The product was steam-distilled to remove traces of the hydrocarbon, and the alkaline liquor was worked up in the usual manner, acidified at 0° with dilute sulphuric acid, and the product extracted with pure ether. The residue from the dried, ethereal extract immediately solidified. Crystallised from pure ether, it had m. p. 212—213°, either alone or mixed with a genuine specimen of *trans*-caronic acid (Found, by micro-combustion : C, 52·6; H, 6·7. Calc., C, 53·1; H, 6·4%). The oxidation was repeated, with the same result, on a fresh quantity of the hydrocarbon obtained by the reduction of a different specimen of *iso*phorone.