LIV.—*On the Possibility of Ring-chain Valency Tautomerism and of a Type of Mobile-hydrogen Tautomerism analogous to the Wagner–Meerwein Re-arrangement. Part I. Some Derivatives of Phorone.*

By CHRISTOPHER KELK INGOLD and CHARLES WILLIAM SHOPPEE.

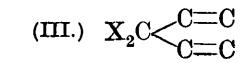
IT is now a commonly accepted view that whereas the stability and small additive power of certain ring systems containing several double linkings are to be attributed to some form of internal association of the centres of unsaturation, the numerous transformations which such systems undergo require the introduction of other phases into the general dynamic conception of their structure. Reasons for including a bridged ring in the dynamic scheme representing certain cyclic systems have recently been given. The phases (I) and (II), representing the *gem*-dialkyl*dicyclo*pentenes or *gem*-dialkyl*cyclo*pentadienes, express the dual chemistry of these substances, as, for instance, their oxidative fission to both ethylene and *cyclo*propane derivatives, and the fact that both static bridged-rings and static monocyclic compounds are formed on blocking the tautomeric system by substitution (Farmer and Ingold, J., 1920, **117**, 1362; Farmer, Ingold, and Thorpe, J., 1922, **121**, 128; Ingold, Grimwood, and Thorpe, J., 1923, **123**, 3303; Toivonen, *Ann. Acad. Sci. Fennicae*, 1927, *A*, **29**, No. 20; Ingold and Seeley, J., 1927, 1684). Further, the tautomeric substances of this series have been shown to exhibit many close analogies with aromatic compounds; and corresponding expressions representing transient forms of the aromatic nucleus have been proved possible by synthesis, and have been shown to furnish a consistent explanation of many aromatic phenomena, including the enhanced *meso*-dissociation of 9 : 10-diarylanthracenes * as compared with anthracene (Ingold, J., 1922, **121**, 1133, 1143; Ingold, Seeley, and Thorpe, J., 1923, **123**, 852; Challenor and Ingold, *ibid.*, p. 2066; Ingold and Marshall, J., 1926, 3080):

Excepting for the blocked systems referred to, the only bridged five-membered rings which have hitherto been studied are those

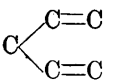
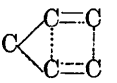
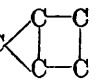
* The criticisms of Barnett, Cook, and Wiltshire (J., 1927, 1726) fail on the ground that it was not the *fact* of *meso*-dissociation but the *relative* exhibition of the phenomenon by 9 : 10-diarylanthracenes and by anthracene which was advanced as evidence of the existence of the bridged phase.

whose chemistry is complicated by their participation in an intra-annular tautomeric system. Nevertheless it is evident, in view of the situation outlined above, that considerable interest attaches to the conditions controlling the formation of static bridged-rings, and especially to instances of their preferential formation in reactions which might have been expected to yield unsaturated monocyclic or open-chain isomerides.

The reaction (I) ⟶ (II) clearly involves interaction between non-contiguous unsaturated carbon atoms. Using the term "conjugation" in a general sense to connote the yoking together of centres of unsaturation, not only when they are contiguous, but also when separated, the change implies conjugation through space and suggests the possibility of a similar conjugation between double bonds situated at a distance in open-chain olefinic compounds.* Thus a reaction such as (III) ⟶ (IV) appears possible; and, if it were reversible, it could appropriately be described as an instance of "ring-chain valency tautomerism":

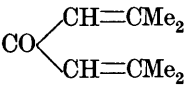
(III.)  (IV.)

That we have been in a position to examine both reversible and complete reactions which are apparently of this type is due to the kindness of Professor F. Francis, who suggested that we should continue the investigation of phorone derivatives commenced by himself and Mr. F. G. Willson in 1913 (J., **103**, 2238). Phorone is a $\Delta^{1:4}$-pentadiene and is obviously precluded by its structure from isomerisation to a butadiene derivative; hence, any direct conjugation between the ethylenic linkings must be through space. Assuming that such a tendency exists, then, since in substituted phorones it will presumably vary from case to case, it follows that in a sequence the extremes of which are represented by (V) and (VII) the physical and chemical properties should vary in a manner which can be specified theoretically. Thus on passing through the series (V) ⟶ (VI) ⟶ (VII), where (VI) is a general expression representing a gradation of intermediate states, one would expect to observe diminishing colour, decreasing refractivity, decreasing parachor, diminishing unsaturation, an increasing tendency to react in form (VII), and a decreasing tendency to react in form (V).

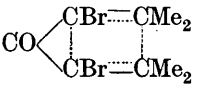
(V.)  (VI.)   (VII.)

* Certain olefinic terpenes, such as farnesene, which readily yield cyclic isomerides, could thus be regarded as possessing a conjugated structure.

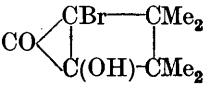
Francis and Willson have already accumulated evidence which favours the view that certain phorone derivatives behave in the manner indicated. Phorone itself is undoubtedly mainly of type (V); it is a bright yellow substance possessing a high refractivity (exaltation 3 units), and a nearly normal parachor (Sugden, following paper); it is also highly unsaturated, decolorising permanganate instantly, adding four atoms of chlorine and bromine and two molecules of hydrogen bromide, yielding di*iso*butyl ketone on reduction, and giving oxalic acid, acetone, and carbon dioxide on oxidation, all in accordance with formula (VIII).



(VIII.)



(IX.)



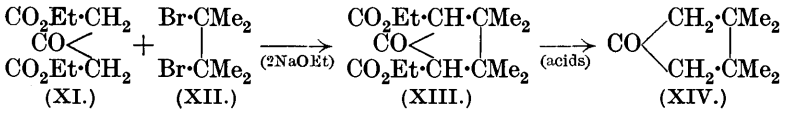
(X.)

An approach towards the saturated condition is, however, observed on passing from phorone to dibromophorone, which we regard as approximating to an intermediate condition which for the moment may be represented by formula (IX). This substance is only feebly coloured, its exaltation of refractivity is much smaller (Francis and Willson, *loc. cit.*,; see also p. 384), and its parachor abnormally low (Sugden, *loc. cit.*). Francis and Willson found it to be unattacked by mild oxidising agents, and either unaltered by reducing agents or converted in small amount into phorone; it was also unaffected by hydrogen bromide in acetic acid and by bromine in carbon disulphide. We have investigated the action of oxidising and reducing agents and find that little, if any, oxidation takes place in the presence of alkaline hydrogen peroxide, ferricyanide, or silver oxide, but that boiling alkaline permanganate causes oxidation to oxalic and acetic acids. Mild reducing agents also have no action, but vigorous reduction by Clemmensen's method yields small quantities of phorone and of deoxyphorone, a known reduction product of phorone (Claisen, *Annalen*, 1875, **180**, 6). On the other hand, Francis and Willson hydrolysed dibromophorone to a cyclic substance to which they assigned formula (X), and we have reduced it with phosphorus and hydriodic acid to a *cyclo*pentane ketone.

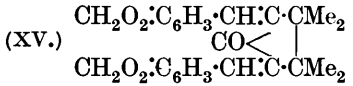
This ketone, which is a highly characteristic, crystalline, camphor-like substance, was previously obtained in a different way by Francis and Willson, who assigned to it formula (XIV). This is obviously in agreement with its formation from the dibromo-compound (IX); but, for reasons which will appear, it became of first importance during this investigation to make sure of the structure of the ketone and we have therefore been at pains to confirm it. Francis and Willson oxidised the substance to αααββ-tetramethylglutaric acid, and this, of course, agrees with the

suggested constitution, but does not dispose of the possible alternative structure in which the carbonyl group is next one of the CMe_2-groups. It will be shown in the sequel that the production by the reactions indicated of a ketone of the latter constitution is not inconceivable. The formation of alkylidene derivatives should decide the matter, but Francis and Willson experienced difficulty in obtaining definite condensation products with benzaldehyde and *o*- and *m*-nitrobenzaldehyde; we are, however, able to show that the ketone forms a *dipiperonylidene* derivative (XV), and a well-characterised *dioximino*-compound (XVI), which, with hydroxylamine, forms the *trioxime* (XVII) of a *substance* (XVIII) having the characteristics of a 1 : 2 : 3-triketone. These reactions, which were carried out in 1924, clearly establish formula (XIV), since the isomeric ketone could form only mono-alkylidene and mono-oximino-derivatives. Farmer and Kracovski have recently shown (J., 1927, 683) that ββ$\beta'\beta'$-tetramethyladipic anhydride, on heating, gives Francis and Willson's ketone, which proves the same point.

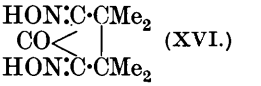
A satisfactory confirmation of the structure has also been obtained by the synthesis of the ketone from tetramethylethylene dibromide (XII) and ethyl acetonedicarboxylate (XI), by way of the cyclic ketonic ester (XIII).



(XI.) (XII.) (XIII.) (XIV.)

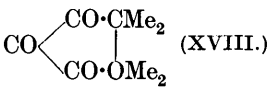


(XV.)



(XVI.)

(XVII.)



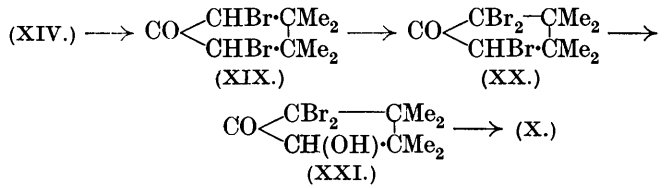
(XVIII.)

The above results may be summarised in the statement that dibromophorone (and dichlorophorone appears similar, although it was not investigated in the same detail) exhibits abnormal physical properties, *e.g.*, colour, refractivity, parachor; and, as compared with phorone, markedly diminished unsaturation. Further, it appears that, whereas on treatment with certain powerful reagents it undergoes reactions which, in so far as they indicate anything, point to a formula of the ordinary phorone type, its behaviour towards other reagents reveals a strong tendency to form closed rings. The effect of substituting phosphorus and concentrated hydriodic acid for zinc and concentrated hydrochloric acid in causing the formation of a cyclic instead of an open-chain reduction

product is noteworthy, and, along with the other physical and chemical evidence, suggests a condition intermediate between the open- and the closed-chain state.

A much more strongly marked approach towards the cyclic condition is apparent on passing to the bromohydroxy-derivative to which Francis and Willson assigned formula (X), and it is necessary now to consider the chemistry of this substance and its more immediate derivatives in some detail.

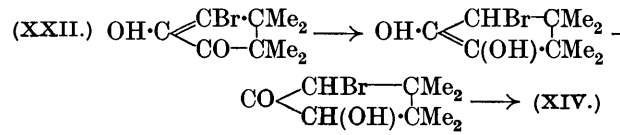
First, we have effected an independent synthesis of the bromohydroxy-compound from the ketone (XIV) by successive treatment with bromine and water. When the bromination is carried out in an anhydrous solvent, up to six atoms of bromine are absorbed and hydrogen bromide is evolved. During the process a crystalline bromide is produced and may separate, but our efforts to isolate and analyse it failed owing to the rapidity with which it decomposed into an oil containing between two and three atoms of combined bromine. We are not at present prepared to express any view as to the constitution of this intermediate product, beyond that it consists at least in part of a substance which, on treatment with water, gives the bromohydroxy-compound (X). When the bromination is incomplete (we suspect that it is affected by the fortuitous crystallisation of the solid bromide), as indicated by the smaller bromine-content of the residual oil, the change effected by water is also incomplete, and an unreactive compound containing two atoms of combined bromine remains. On further bromination this is converted into the precursor of the bromohydroxy-compound. Though modifications are possible, the following scheme is regarded as approximating to the observations, the compound (XIX) representing the unreactive, and (XX) the reactive, bromination product:



The elimination of hydrogen bromide from (XXI) is in accordance with analogy. Evidence of interaction between the α- and α′-positions of a cyclic ketone was encountered by Wallach (*Annalen*, 1917, **414**, 296) in the case of *cyclo*hexanone derivatives, and in the present instance the tendency to a reaction of this type would be expected to be increased by the accumulation of *gem*-dimethyl groups. The fact that, even where excess of bromine is employed,

only six and not eight atoms are involved is also in accordance with Wallach's observations on the halogenation of cyclic ketones (*Annalen*, 1905, **343**, 41), and may be compared with the difficulty often experienced in replacing this last available hydrogen atom in a keto-enol system (compare Dieckmann, *Ber.*, 1894, **27**, 954; 1897, **30**, 1471; Thorpe, numerous papers); it is also possible that higher bromination products are formed, but immediately bridge with the elimination of elemental bromine, as is suggested by the experiences of Guareschi (*Atti R. Accad. Sci. Torino*, 1910—1911, **46**, 662) and Meerwein (*J. pr. Chem.*, 1922, **104**, 161), thus giving a smaller net absorption. However this may be, it is evident that the process involves no re-arrangement of the carbon skeleton, since the bromohydroxy-compound on reduction both by acid and by alkaline reagents yields the original tetramethyl*cyclo*pentanone (XIV).

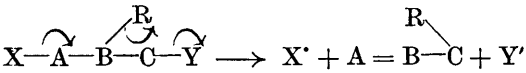
We have taken the view that this complete synthesis, even when taken together with Francis and Willson's degradation of the bromohydroxy-compound to tetramethylsuccinic acid, does not fully establish their formula for the compound; for although that formula certainly provides the simplest interpretation of the facts, the latter concern a field of organic chemistry in which subtle changes are possible, so that caution is necessary in drawing conclusions as to structure. We do, however, regard the following features as having been definitely diagnosed: (i) the presence of the *cyclo*pentane ring, (ii) the adjacent situation of the two *gem*-dimethyl groups, (iii) the unsymmetrical situation of the bromine atom with respect to the *gem*-groups, (iv) the symmetrical situation of one oxygen atom with respect to the *gem*-groups, (v) the presence of a hydroxyl group. In addition to formula (X), there is another formula which embraces all these conclusions, namely (XXII), and this can be brought into harmony with the reduction to the symmetrical *cyclo*pentane ketone (XIV), because preliminary 1 : 4-addition of hydrogen, followed by ketonisation and further reduction, could bring about the necessary alteration in the position of the carbonyl group:



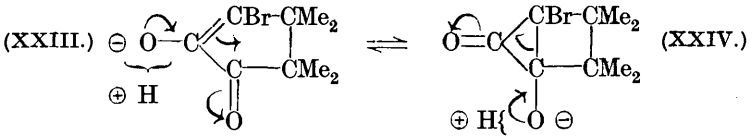
The scheme represented is illustrative, and its essentials are independent of any particular supposition regarding the stage at which the halogen is removed from the molecule. Further, formula (XXII) is not inconsistent with the evidence of synthesis; for the

two formulæ (X) and (XXII) are more closely related than appears at first sight, in that, although they are distinct in framework and differ in the position of a hydrogen atom, the latter is ionisable in either case, and hence potentially mobile, and the two carbon skeletons are related like those of the factor and product of a Wagner re-arrangement.

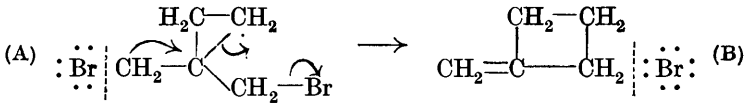
Considerations based on the electronic theory of valency lead us to formulate the pinacol–pinacolin, Wagner–Meerwein, and related transformations, such as the pinacolic deamination,* by the following general scheme :—



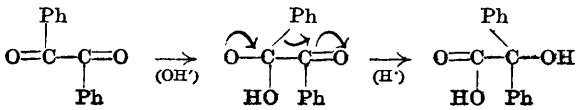
in which the tendency of X to part from, and Y to hold, electrons during ionisation or combination with a reagent supplies the driving force of the reaction. In the case under discussion, if we assume preliminary ionisation, the electron repulsion of the negative pole collaborating with the electron attraction of the neighbouring carbonyl group might provide the impetus necessary for the interconversion of the structures :



The postulated change in either direction may be compared with the formation of methylene*cyclo*butane (B) from ωω′-dibromo-1 : 1-dimethyl*cyclo*propane (A) and zinc (Ingold, J., 1923, **123**, 1756) on the supposition that an atom of metallic zinc first removes an atom of bromine with a sextet :

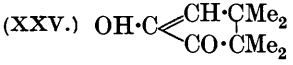


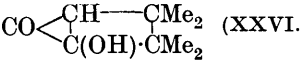
* Here the electron sink, Y, is presumably the positive pole of the diazonium ion formed by the action of nitrous acid (compare Baker, Cooper, and Ingold, this vol., p. 426). Similarly in the benzil-benzilic acid change the electron sink, X, is the negative pole formed by the addition of hydroxide ion :



Thus, tautomerism between the structures (XXIII) and (XXIV) is readily conceivable, and the problem of distinguishing between them becomes in the first instance that of ascertaining the position or positions occupied by each of the characteristic groups by the study of suitable derivatives.

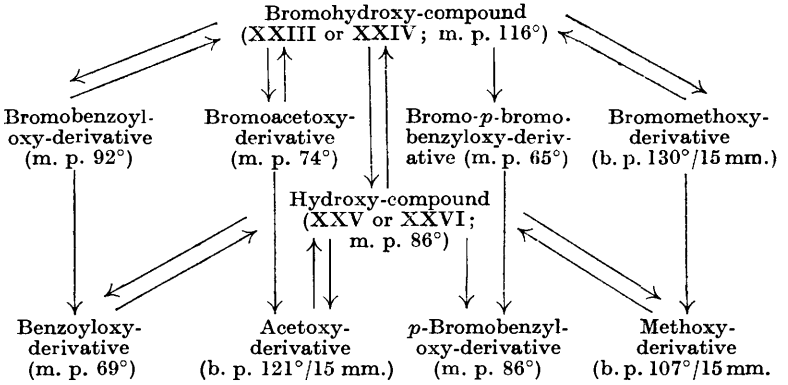
Francis and Willson found that when the bromohydroxy-compound was reduced with zinc dust and glacial acetic acid the bromine atom was replaced by hydrogen and a compound was formed which closely resembled the halogenated parent and evidently possessed a similar constitution. All our experiments confirm that conclusion; we have, for instance, regenerated the original bromohydroxy-compound by directly brominating the hydroxy-compound. Further, the derivatives formed by the bromohydroxy-compound resemble the corresponding derivatives of the hydroxy-compound; for instance, the latter, on acetylation, gave the same compound as that which Francis and Willson obtained by reduction of the acetyl derivative of the bromohydroxy-compound. Similarly, the bromobenzoyloxy-compound, the *bromomethoxy*-compound, and the *bromo*-p-*bromobenzyloxy*-compound, which were prepared directly from the bromohydroxy-compound, on reduction gave *benzoyloxy*-, *methoxy*-, and p-*bromobenzyloxy*-derivatives which were also obtained from the hydroxy-compound by acylation or alkylation. It is evident, then, that the constitutions of the halogen compounds are referable to those of the corresponding hydrogen derivatives (with the reservation mentioned on p. 379), and we have therefore concerned ourselves mainly with the bromine-free hydroxy-compound (XXV or XXVI) in the investigation, described below, regarding the respective functions of the two oxygen atoms contained in the complex :

(XXV.) 

 (XXVI.)

First, it should be stated that the alkyl and acyl compounds mentioned above are actually *O*-derivatives, and not *C*-derivatives, because the alkyl and acyl groups can readily be removed. For example, the bromoacetoxy- and bromobenzoyloxy-compounds are hydrolysed by acids, and the corresponding hydrogen derivatives by alkaline hydrolysing agents. The methyl group in the bromomethoxy-compound can be eliminated by the Zeisel method. The corresponding experiment was not tried with the bromo-*p*-bromobenzyl derivative, the same point having been proved for this compound at an early stage in the investigation through the observation that on ozonolysis the alkyl group appears in the form of *p*-bromo-

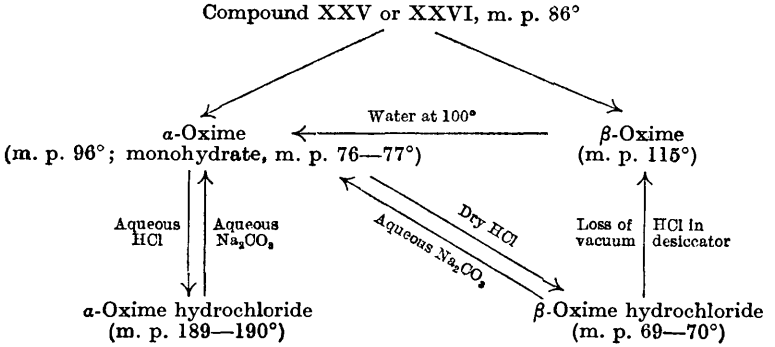
benzaldehyde. These relations are summarised in the following scheme :



In contrast with the close similarity between the bromohydroxy-compound and the bromine-free hydroxy-derivative in their hydroxylic reactions, these two substances differ notably in the degree to which they exhibit ketonic properties. In fact, neither Francis and Willson nor we have been able to obtain an oxime or semicarbazone of the bromohydroxy-derivative, and we have similarly failed in the case of all its derivatives in which a bromine atom is attached to the five-membered ring; yet on any probable view of the constitution of these substances a ring-bound carbonyl group must be present. On the other hand, the compounds of the reduced series all form oximes with moderate ease; indeed, from the parent hydroxy-derivative we obtained two *oximes* as well as a *semicarbazone*. In our view this remarkable difference is to be attributed, not to some fundamental difference of constitution, but to the inhibiting effect of the bromine atom. Oximation is a reaction notoriously sensitive to constitutional influences, and the strong inhibition (probably polar as well as steric) produced by bromine and chlorine in halogenated ketones is often such as to prevent oxime formation altogether. On the other hand, we are unwilling to employ the facts referred to as the basis of any constitutional argument regarding the relative positions of the bromine atom and carbonyl group in the bromo-compound (XXIV or XXIII), since the possibility of " short-cuts " for the transmission of polar influences in compact ring-structures cannot be disregarded.

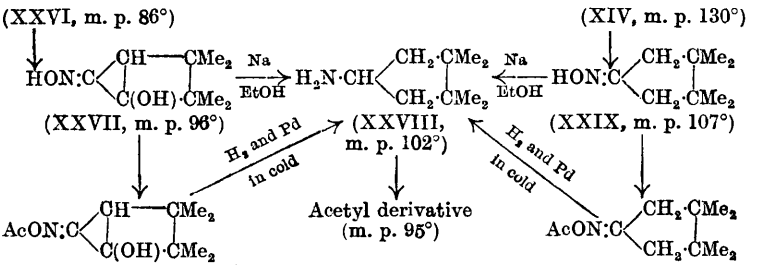
Our attention was first focussed on the two oximes in view of the possibility that they might be position-isomerides representing the two forms (XXV and XXVI) of the parent. This, however, was not the case, since the two oximes were found to be interconvertible

directly (β ⟶ α) and through the hydrochloride of one of them (α ⟶ β) in accordance with the following table:



Hence it appeared that the two compounds are stereoisomeric, and that the oximino-group is attached to the same nuclear carbon atom in each; it remained to determine which one.

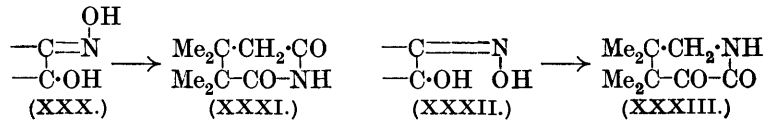
This was done by completely reducing the α-oxime (m. p. 96°) to a tetramethyl*cyclo*pentylamine. We found that sodium amalgam in boiling glacial acetic acid, and sodium in hot alcohol, effected the change smoothly, and that the same result could be obtained equally satisfactorily without the use of high temperatures by reducing the *acetyl* derivative of the oxime with gaseous hydrogen in the presence of colloidal palladium. The free *base* (XXVIII), a volatile crystalline solid, together with its *hydrochloride*, *picrate*, *chloroaurate*, and *acetyl* derivative, were identical, each to each, with the corresponding compounds prepared by applying the same three methods of reduction to the *oxime* (XXIX) (or its *acetate*) of the symmetrical ketone (XIV). Therefore, formula (XXVI) being adopted as a basis of representation, the reactions may be expressed as follows:



The orientation of the oximino-group in (XXVII), and of the amino-group in (XXVIII), thus depend on the constitution ascribed to the ketone (XIV), which was established in two independent ways

and is therefore beyond doubt. Although the experimental evidence is thus complete, the whole of it is further strengthened by the fact that, by methods described below, we have been able to prepare the isomeric unsymmetrical *ketone*, having its carbonyl group adjacent to one of the CMe_2-groups, its *oxime*, the corresponding unsymmetrical *amine* and its salts and *acetyl* derivative, all of which are easily identified crystalline compounds, as are the isomerides of the symmetrical series. We conclude that in the hydroxy-compound, m. p. 86°, the group exhibiting ketonic reactivity is that situated symmetrically with respect to the two *gem*-dimethyl groups in the carbon skeleton.

With regard to the space configurations of the two oximes (XXVII) we are able to advance the following evidence. On Meisenheimer's theory of *trans*-interchange, the two oximes might yield the following internal amides under the conditions of the Beckmann transformation :

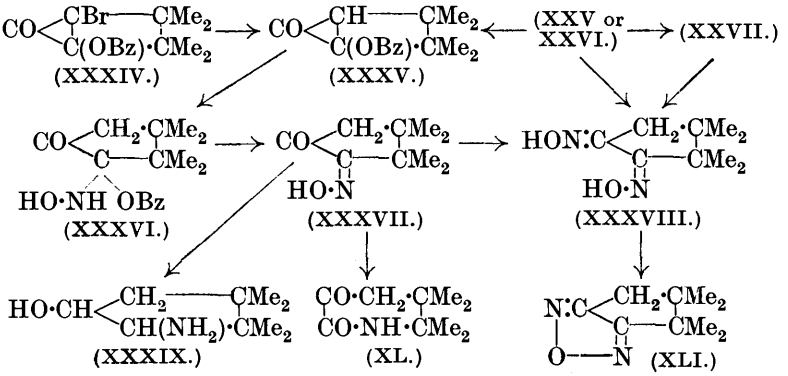


(XXX.) (XXXI.) (XXXII.) (XXXIII.)

Under the conditions in which we have effected a change of this type the α-oxime passes into its β-isomeride, and is therefore not available for the experiment. On the other hand, the β-isomeride, on treatment with excess of dry hydrogen chloride in a warm solvent, yields a re-arrangement *product* which apparently possesses formula (XXXIII). Its properties are in agreement with this constitution, and it is not the *imide* (XXXI), for we have prepared the latter by the action of gaseous ammonia on *ααββ-tetramethylglutaric anhydride*. If this interpretation is correct, it follows that the α-oxime, m. p. 96°, is to be regarded as having the configuration (XXX), and the β-oxime, m. p. 115°, is represented by (XXXII). It should be remarked that the β-oxime (but not the α-) gives a strongly coloured iron salt, in which the iron is conceivably chelated (compare formula XXXII).

Turning to the acyl derivatives of the bromohydroxy-compound and its halogen-free analogue, the benzoyl derivatives offered an attractive point of attack, since both are crystalline and possess all the characteristics of pure compounds. Both substances appear to be saturated. Thus neither responds to the Baeyer test for unsaturation, and neither absorbs bromine in chloroform. It is true that the bromobenzoyloxy-compound is attacked by zinc dust and acetic acid, but the reduction stops abruptly after the bromine atom has been replaced by hydrogen, the nucleus being unaffected.

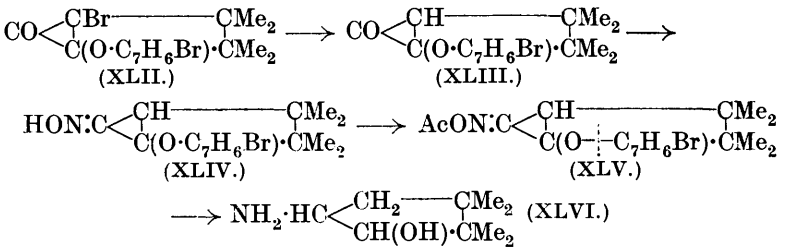
When the halogen-free benzoyl compound is treated with hydroxylamine, one molecule of this reagent is taken up and one of benzoic acid is simultaneously eliminated. This takes place in the cold under conditions which preclude ordinary hydrolysis of the acyl group, and we therefore infer that it is the hydroxylamine which has displaced the benzoyl radical. The compound formed (m. p. 115°) is isomeric with, and different from, the α- and β-oximes of the symmetrical series (mixed m. p. depressions), which were prepared from the parent hydroxy-compound without previous benzoylation, and is evidently the unsymmetrically oximinated analogue, since (*a*) it yields the original hydroxy-compound (m. p. 86°) on hydrolysis, and (*b*) on prolonged treatment with hydroxylamine it gives the same dioximino-compound as that prepared by further oximination of the symmetrical α-oxime. It is consistent with this interpretation that the new *monoxime* (XXXVII), on re-arrangement, gives an internal *amide* (XL) isomeric with the amide and imide mentioned above (XXXI and XXXIII) and that the *dioxime* (XXXVIII) readily yields a *furazan* (XLI). On reduction with sodium and boiling alcohol the new monoxime gives the *hydroxy-amine* (XXXIX). The whole series of observations corresponds with Francis and Willson's formulation of the bromo-hydroxy- and hydroxy-compounds, and may accordingly be represented as follows :



It must be pointed out that the above scheme for the orientation of the benzoyloxy-group in (XXXIV) and (XXXV) is dependent on the correctness of the inference that, because hydroxylamine displaces the benzoyl radical, the oximino-group therefore occupies that nuclear position from which the extruded group has been removed. Such a substitution of groups might take place through the reversible addition of hydroxylamine giving the addition product

(XXXVI), the subsequent irreversible decomposition of which is determined by the stability of the benzoate ion. We are not prepared to go further than to say that these assumptions seem to us plausible, and that we regard the orientation as tentative only.

The *p*-bromobenzyloxy-derivatives both of the bromohydroxy- and hydroxy-series are also crystalline, behaving in all respects as pure compounds, and closely resembling the benzoyl derivatives in their indications of saturated character. The bromo-*p*-bromobenzyloxy-compound (XLII) on reduction by zinc and acetic acid is converted into the *p*-bromobenzyloxy-derivative (XLIII), which is formed without by-products and appears to be incapable of further reduction by this method. It forms an *oxime* (XLIV), and, as might be expected, there is little or no tendency towards extrusion of the *alkyl* group. We have not yet succeeded in establishing satisfactory conditions for the reduction of the oxime itself, but its *acetyl* derivative (XLV), on reduction with sodium and boiling alcohol, yields a saturated *hydroxy-amine* (XLVI), isomeric with (XXXIX). These reactions may be formulated as follows, the interpretation being dependent on that applied to the benzoyl compounds :

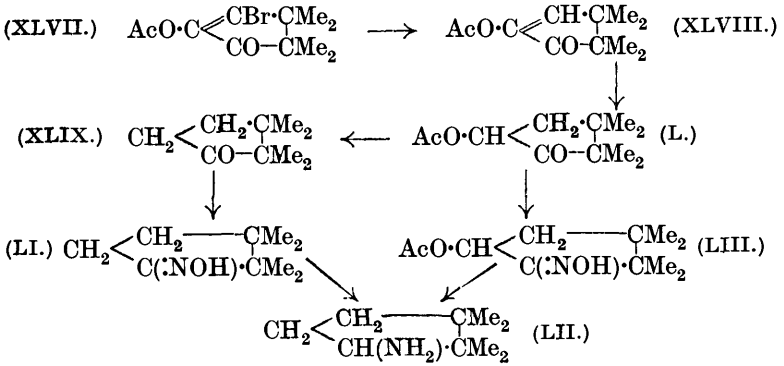


It is now necessary to consider some derivatives of the bromohydroxy- and hydroxy-compounds which exhibit some remarkable differences of behaviour as compared with the acyl and alkyl derivatives just mentioned. The group of compounds referred to includes the acetoxy-derivatives, the methoxy-derivatives, and probably also the liquid by-product which was obtained (see p. 388) along with the crystalline main product on alkylation of the bromohydroxy-compound with *p*-bromobenzyl bromide.

These compounds are conspicuously unsaturated. They are all oils, excepting the bromoacetoxy-derivative, which is crystalline; and for this reason we have examined the acetoxy-compounds in greater detail than the others. In illustration of the unsaturated character of these substances, the bromoacetoxy-compound rapidly reduces cold alkaline permanganate under conditions in which the bromobenzoyloxy-compound causes no perceptible reduction over

an extended period. The acetoxy-compound rapidly absorbs bromine in cold chloroform, in contrast with the benzoyloxy-compound, which remains unaffected under these conditions, and, even on boiling, is extremely slowly attacked. Again the acetoxy-compound is reduced by zinc dust and acetic acid to a *dihydro*-derivative, whereas the benzoyloxy-compound, as already mentioned, is unaffected by this treatment.

These contrasts suggest that the bromoacetoxy- and acetoxy-compounds may be derived from the unsaturated, monocyclic forms of their respective parents; and in support of this view we are able to advance the following experiments, which appear to orient the acetoxy-group in the symmetrical position with respect to the pair of *gem*-dimethyl groups. The bromoacetoxy-compound was reduced in the following stages with successive treatments with zinc or sodium amalgam in glacial acetic acid: bromoacetoxy-compound $\xrightarrow[(2H)]{}$ HBr + acetoxy-compound $\xrightarrow[(2H)]{}$ dihydroacetoxy-compound $\xrightarrow[(2H)]{}$ H·OAc + dihydro-compound. The final product, which is a saturated ketone, $C_9H_{16}O$, proved to be, not the symmetrical tetramethyl*cyclo*pentanone already described, but its unsymmetrical *isomeride* (XLIX) (*vide infra*). It was converted into its *oxime* (LI), which was reduced with sodium and alcohol to the unsymmetrical *tetramethyl*cyclo*pentylamine* (LII). Finally the *oxime* (LIII) of the dihydroacetoxy-compound (L) was completely reduced, and the product identified as the same tetramethyl*cyclo*pentylamine. If the monocyclic unsaturated formulæ (XLVII) and (XLVIII) be adopted for the bromoacetoxy- and acetoxy-compounds respectively, the above relationships are capable of explanation on the following lines:



The symmetrical and unsymmetrical ketones (XIV and XLIX) are superficially extremely similar (both have the appearance, odour, and large volatility of camphor), but are readily distinguished

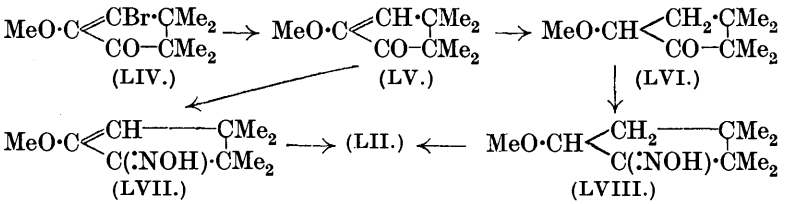
because they depress one another's m. p.'s, as do the derived oximes and semicarbazones. Both ketones, on oxidation with dilute nitric acid, yield αααββ-tetramethylglutaric acid, and this, taken in conjunction with the work already described on the symmetrical ketone, establishes the constitution of the unsymmetrical ketone. The two tetramethyl*cyclo*pentylamines are also crystalline, although on account of their volatility, we have, to conserve material, usually handled them in the form of their picrates or acetyl derivatives, which also give mixed m. p. depressions. The following comparison of m. p.'s illustrates the general similarity of the isomerides :

	Ketone.	Oxime.	Oxime hydrochloride.	Semicarbazone.	Amine.	Picrate.	Chloroaurate.	Acetyl derivative.
Symmetrical ...	130°	107°	119°	224°	100—102°	225°	230°	95°
Unsymmetrical	119	102	125	222	Not taken.	243	197 *ca.*	115

Although the ketone (XLIX) is undoubtedly the main product of the reduction represented in the scheme formulated above, it is usually accompanied by a small, but detectable, quantity of the isomeric symmetrical ketone (XIV) (for separation, see p. 397). In this connexion it may be remarked that, theoretically (and also practically), an essential condition for the preparation of the unsymmetrical ketone by the method outlined is that the acetyl group should remain attached to the molecule during the first two stages of the reduction; this follows from the tautomeric hypothesis relating to the cyclic hydroxy-ketones, for the formation by hydrolysis of a free hydroxyl group would liberate the mobile system, the reduction product of which is known to be the symmetrical ketone (XIV). It was for this reason that glacial acetic acid was employed as medium throughout the reductions, and that the intermediates (XLVIII) and (L) were purified and analysed in order to confirm the integrity of their ester groups. On the other hand, although the bromoacetoxy-compound appears to be a single individual, its reduction products (XLVIII) and (L) are liquids, and, despite their constant boiling points, it cannot be asserted that they do not contain isomerides. The migration of acyl groups is such a common experience that the possibility must be considered, but whether the appearance of the symmetrical ketone as a by-product is actually to be ascribed to tautomeric mobility of the acetyl groups under certain conditions, or to some undiscovered mechanism, cannot, we think, be decided on the evidence. We are likewise open-minded with regard to the possibility of the migration of *O*-alkyl groups during the reduction of the bromo-alkyloxy-compounds.

The bromomethoxy-compound (LIV) is unstable to permanganate

and, like the bromoacetoxy-derivative, can be reduced by zinc and acetic acid, not only to the halogen-free parent (LV), but also to the *dihydro*-derivative of the latter (LVI). The methoxy-group in the dihydro-compound cannot be eliminated by continued treatment, but since both the *oxime* (LVII) of the methoxy-compound and *that* (LVIII) of the dihydromethoxy-compound yield the unsymmetrical tetramethyl*cyclo*pentylamine (LII) on reduction with sodium in alcohol, we infer that the methyl and acetyl derivatives of the bromohydroxy- and hydroxy-compounds possess corresponding structures:



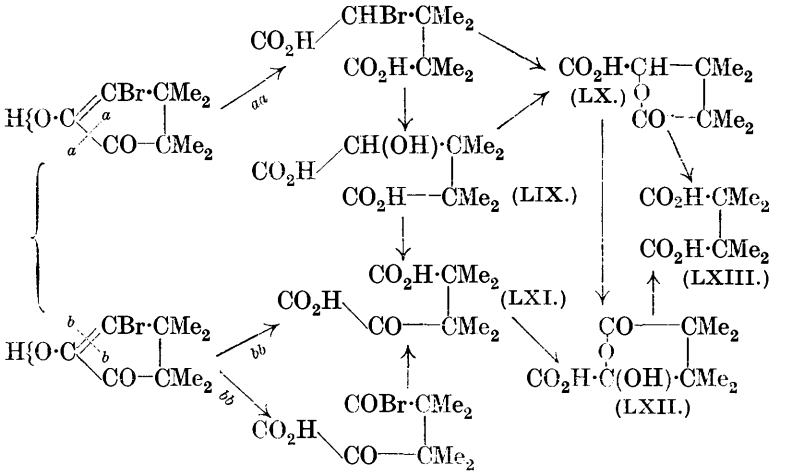
Summarising the above experiments on the substitution products of the bromohydroxy-compound, it appears that Francis and Willson's conception of that substance requires extension by the introduction of the alternative unsaturated formula (XXII).

Further evidence tending in this direction has been obtained by continuing the study, commenced by Francis and Willson, of the behaviour of the parent bromohydroxy-compound itself in the presence of reagents towards which it would be expected to reveal any unsaturated character it possessed.

The first series of experiments along these lines relates to oxidation. Francis and Willson used alkaline permanganate and obtained the lactonic acid (LXII) (compare Rothstein and Shoppee,* J., 1927, 531), formed by additive ring closure of the ketonic acid (LXI). We have obtained the same lactonic acid by employing also alkaline chlorate in the presence of osmium tetroxide, alkaline ferricyanide, and alkaline hydrogen peroxide. Using alkaline chlorate and osmium tetroxide, we have isolated, in addition, the lactonic acid (LX) of the dibasic hydroxy-acid (LIX). Oxidation with chromic anhydride or chromic acid (Francis and Willson) causes complete degradation to tetramethylsuccinic acid (LXIII).

* The opportunity may be taken to mention that in the light of observations recorded on p. 406, Rothstein and Shoppee now regard the compound, previously considered to be methyl γ-keto-$\alpha\alpha\beta\beta$-tetramethylglutarate, as the lactone of methyl hydrogen γ-hydroxy-γ-methoxy-$\alpha\alpha\beta\beta$-tetramethylglutarate, $\overset{\text{———O———}}{\text{CO·CMe}_2\text{·CMe}_2\text{·C(OMe)·CO}_2\text{Me}}$, a conclusion which further strengthens their case in favour of the cyclic constitution of the homologues of Balbiano's acid and its derivatives.

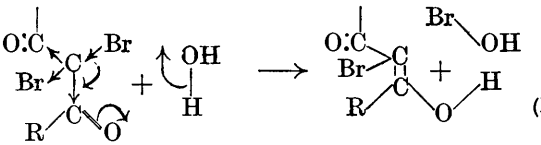
The interpretation of these results in terms of the unsaturated formula of the bromohydroxy-compound is not compulsory; nevertheless, we believe that this structure affords the more satisfactory basis for explanation, having regard to the sensitivity towards oxidising agents of the methyl and acetyl derivatives. Also, in view of the fact that the attack of mild oxidising agents usually proceeds much more smoothly in alkaline than in neutral solution, we suspect that degradation occurs most readily through the ion. These and other considerations relating to the observations lead us to advance the following general scheme for the oxidation of the bromohydroxy-compound :



It will be understood that this scheme is based partly on direct evidence and partly on indirect evidence or analogy. As an illustration of the use which has been made of the latter, the following point may be considered. When ozonised oxygen is passed into a chloroform solution of the bromomethoxy-compound, elementary bromine is eliminated, proving that the :CBr-group is involved in the attack; the product obtained on decomposing the ozonide is the hydroxy-lactonic acid (LXII). On the other hand, when the bromoacetoxy-compound is treated with ozone under similar conditions, the bromine atom remains attached to the molecule until the ozonide is reduced with zinc dust. Now the attack at the :CBr-group with fission at *bb* is probably dependent on the process $X\overset{\curvearrowright}{-}C\overset{\curvearrowright}{=}CBr$, the effectiveness of which should vary according to the value of X as an electron-source. The theoretical order, $O^{\ominus} > OMe > OAc$, being known, the inference, as regards the ion, is obvious.

We have further examined the behaviour of the bromohydroxy-compound towards halogens. Francis and Willson observed that on bromination in acetic acid a dibromo-compound is formed to which they ascribed formula (LXVI); since, however, one bromine atom (and only one) is readily removed by hydrolysis in the form of hypobromous acid, the original bromohydroxy-compounds being regenerated, they also recognised a possible tautomeric form represented by the alkyl hypobromite structure (LXIX); and having regard to our evidence in favour of the monocyclic formula of the bromohydroxy-compound, it is necessary to envisage the possibility (LXX) in addition.

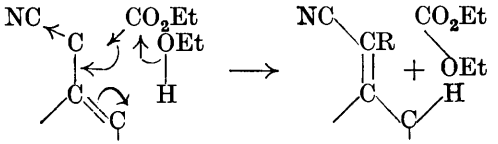
Lauer has recently shown that tribromophenol bromide and its congeners, which exhibit the same peculiarity in regard to hydrolysis, are actually aryl hypohalites (*J. Amer. Chem. Soc.*, 1926, **48**, 442), and not halogeno-quinone derivatives, as had previously been supposed (Thiele and Eichwede, *Ber.*, 1900, **33**, 673). On the other hand, Norris and Thorpe have proved (J., 1921, **119**, 1199) that the dihalogeno-derivatives of dihydroresorcinol homologues, which also exhibit the peculiarity, are not hypohalites but 2 : 2-dihalogeno-1 : 3-diketones. It follows that the exhaustive halogenation of ketones can give rise to both types of structure, and that the elimination of one atom of halogen as hypohalous acid on hydrolysis is not (contrast Vorländer, *Annalen*, 1897, **294**, 253), a criterion which will decide between them. The abnormal hydrolysis of the dihalogeno-diketones may be regarded as a six-cycle promoted by the electron affinity of the groups attached to the halogen-bearing carbon atom :

(LXIV.)  (LXV.)

Obviously the process cannot be repeated with the second bromine atom originally present in (LXIV), for it cannot occur with the enol (LXV), and, if this were ketonised, a repetition would merely enolise it again, since the forces operate to remove the atom (hydrogen) which most readily parts with electrons. This accounts for the dissimilar behaviour of the two bromine atoms, and expresses Norris and Thorpe's suggestion that the elimination of the halogen is fundamentally concerned with the tendency of the system to acquire a mobile hydrogen atom.* It also follows that, if two

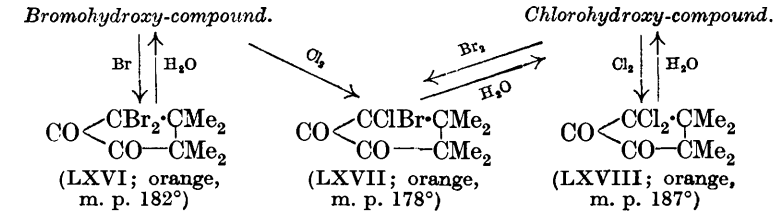
* [Added in proof] Soper and Smith's interesting experiments (this vol., p. 139) suggest that the hydrolysis of aromatic chloroamines may be analogous.

different halogen atoms are attached to the central carbon atom, the product of hydrolysis will retain that which has the greater affinity for electrons (F>Cl>Br>I). Obviously the water molecule might act as such or as H· and OH′ ions. A similar explanation may be given of the elimination of carbethoxyl as ethyl carbonate from cyano-esters (Rogerson and Thorpe, J., 1905, **87**, 1702; Ingold and Thorpe, J., 1919, **115**, 143)

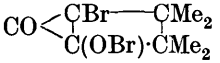
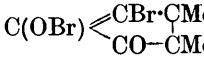


and this shows why the βγ-double bond is necessary, why the group R is necessary (since otherwise hydrogen would be removed), and why a βγ-unsaturated cyano-ester yields an αβ-unsaturated nitrile (Kon and Narayanan, J., 1927, 1536).

We find that Francis and Willson's dibromo-compound is actually the dibromo-diketone (LXVI), and is not an alkyl hypobromite (LXIX or LXX). For the derivative obtained by chlorinating the bromohydroxy-compound is identical with that prepared by brominating the chlorohydroxy-compound, which shows that the halogen atoms in the common *product* (LXVII) are in structurally equivalent positions; further, this derivative, the *dichloro*-compound (LXVIII), and the dibromo-compound, are so *very* closely similar (see table) that the same conclusion must, we think, be applied to the latter two. As would be expected, the chlorobromo-diketone, on hydrolysis, yields the chlorohydroxy-compound exclusively:

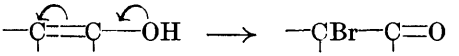


(LXVI; orange, m. p. 182°) (LXVII; orange, m. p. 178°) (LXVIII; orange, m. p. 187°)

(LXIX.)   (LXX.)

Here, as with oxidation, one is not compelled to interpret the reactions on the basis of the monocyclic unsaturated formula for the bromohydroxy-compound, but, nevertheless, there are good grounds for doing so. According to Orton, Hughes, and Watson (J., 1927, 2461), the bromination of a ketone takes place by direct

β-bromine-substitution of the enol, the product being necessarily ketonic :



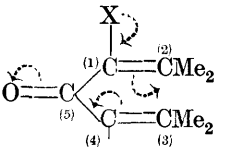
The reaction is assumed to occur on " activation " of the enol, and one form which activation might conceivably assume would be the ionisation of the hydroxyl group with the production of a strongly electron-repelling negative pole. This may be the significance of the observation that, whereas the dihalogeno-diketones are readily produced by halogenation in cold acetic acid (ionising solvent), they cannot be prepared in pure chloroform or carbon disulphide (non-ionising solvents) (compare Francis and Willson). Taking the view that in the bromination, as in the oxidation, of the bromohydroxy-compound, the reactive individual is probably the ion, and, accepting Orton, Watson, and Hughes's mechanism, the constitutions (LXVI—LXVIII) follow automatically.

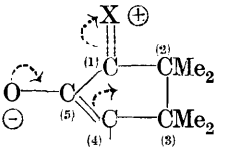
It is now possible to develop the suggestion made on p. 368 that dibromophorone represents a balanced example of ring-chain valency tautomerism. In its chemical properties it has much in common both with phorone and with its fully cyclised oxygenated derivatives. Sugden's parachor determinations provide interesting physical evidence pointing to an intermediate condition, and some additional confirmation from the physical side is provided by refractivity data :

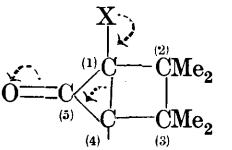
	Exaltation (λ 5893) for		
			
Phorone	3·04	4·77	5·32
Dibromo-derivative	1·37	3·10	3·65
Dichloro-derivative	0·30	2·03	2·57
Acetoxy-derivative	−1·52	0·21	0·76

The varying action of different substituents in favouring to different degrees the cyclic form of the phorone system arises, we believe, from their different electron-giving tendencies. An electron-giving group in position (1) (LXXI), collaborating with the elctron-attracting carbonyl group in position (5), will produce a series of mutually dependent displacements of the labile electrons of the double bonds (1—2) and (3—4), giving as the first stage of space-conjugation a partial valency between the carbon atoms (2) and (3) (LXXI). If the tendency to this change is sufficient, the molecule may reach or approximate to the dipolar condition, represented by (LXXII), in which the labile double-bond-electrons are now at (4—5), and are subject to simultaneous repulsion by the negative charge at (5) and attraction towards the positive charge at (1). This condition corresponds to a partial valency between (4) and (1),

and depolarisation in the direction of the potential gradient might establish the bond (4—1) (LXXIII). Formula (LXXII), then, may be taken to represent a whole range of states on either side of the dipolar condition; its equilibrium with (LXXI) exemplifies the conception of ring-chain valency tautomerism, and its equilibrium with (LXXIII) that of tautomerism corresponding with the Wagner re-arrangement. It is evident, also, that any mechanism for external depolarisation (*e.g.*, association with another ion) might obviate the necessity for internal re-adjustment.


(LXXI.)


(LXXII.)


(LXXIII.)

According to this view, the tendency of a substituted phorone to close up should run parallel with the basicity (tendency to become shared) of the unshared electrons in X; and, for the groups, X, examined, the order of the effect, as indicated, for instance, by *op*-directive power in aromatic substitution, should be OR> halogens>H, which agrees with the observations.

Experimental.

[*Note* : The analysis of many of the compounds described in this section gave difficulty until it was discovered that by the use of cuprous chloride (Haas, J., 1906, **89**, 570) the escape of unburnt methane and ethane could be avoided and correct results obtained. Most of the carbon and hydrogen estimations recorded below were carried out by Haas's method.]

αα-*Dibromophorone* (1 : 4-*Dibromo*-2 : 2 : 3 : 3-*tetramethyl*-[0,1,2]-dicyclo*pentanone*).—This was prepared in the manner recommended by Francis and Willson (yields 80—88%; m. p. 32°). It is necessary that the phorone tetrabromide (yields 80—90%; m. p. 88°) should be perfectly pure and our practice was to crystallise it three times from alcohol before conversion.

Care being taken to avoid accidental inoculation, dibromophorone, when fused and cooled to 20°, remains liquid long enough to enable its density and refractive index to be determined. We found $d_{4^\circ}^{20^\circ}$ 1·5727, and $n_{\mathrm{D}}^{20^\circ}$ 1·54766, whence $[R_L]_{\mathrm{D}} = 59{\cdot}74$. Francis and Willson, working at 37°, obtained $[R_L]_{\mathrm{D}} = 59{\cdot}77$. The exaltations recorded on p. 384 are calculated from Eisenlohr's (1910) atomic and structural constants and our observed value for $[R_L]_{\mathrm{D}}$.

Reduction of Dibromophorone to Phorone and Deoxyphorone.

Dibromophorone was reduced with amalgamated zinc and boiling concentrated hydrochloric acid (compare Clemmensen, *Ber.*, 1913, **46**, 1837). In the early stages of the process phorone distilled from the short condenser employed. After 2 hours the product was distilled in steam, the distillate extracted with ether, and the deoxyphorone thus obtained purified by washing with a little ligroin and crystallisation from alcohol; m. p. 190° (Found: C, 82·9; H, 10·7. Calc.: C, 83·0; H, 10·8%). The portion of the reduction product which did not distil in steam was a yellow, viscous oil, which decomposed on attempted distillation at 2 mm. It decolorised permanganate, but did not yield a semicarbazone or other crystalline derivative.

Reduction of Dibromophorone to 3 : 3 : 4 : 4-*Tetramethylcyclopentanone.*—Dibromophorone (25 g.), hydriodic acid (250 g.; *d* 1·7), and red phosphorus (30 g.) were boiled together under reflux for 4 hours and the product was distilled in steam. Owing to the volatility of tetramethyl*cyclo*pentanone in ether vapour, it was found advantageous to proceed with its isolation without the use of ether. The first 50 c.c. of distillate, which contained the bulk of the ketone, were therefore collected separately and saturated with ammonium sulphate; the oil was then removed, dried directly with calcium chloride, and distilled; b. p. 190—195°; m. p. 130° (Found: C, 76·7; H, 11·5. Calc.: C, 77·1; H, 11·4%) (compare Francis and Willson, *loc. cit.*). The aqueous liquid, on treatment with semicarbazide acetate, yielded the semicarbazone of the same ketone; m. p. 224° (Found: C, 60·7; H, 9·6. Calc.: C, 60·9; H, 9·6%) (compare Francis and Willson).

1 - *Bromo* - 2 : 2 : 3 : 3 - *tetramethyl* - [0,1,2] - dicyclo*pentan* - 4 - *ol*-5-*one* (1-*Bromo*-2 : 2 : 3 : 3-*tetramethyl*-Δ^5-cyclo*penten*-5-*ol*-4-*one*).—This compound (yield nearly quantitative; m. p. 116°. Found: C, 46·4; H, 5·6. Calc.: C, 46·3; H, 5·6%), its acetyl derivative (m. p. 74°. Found: C, 48·2; H, 5·6. Calc.: C, 48·0; H, 5·5%), and benzoyl derivative (m. p. 92°. Found: C, 56·8; H, 5·3. Calc.: C, 57·0; H, 5·0%), we have prepared by the methods of Francis and Willson. The free hydroxy-compound gives a wine-red colour with aqueous-alcoholic ferric chloride. Since the benzoyl derivative provides the most convenient route to the reduced compounds mentioned below, the following details of its preparation may be given. The hydroxy-compound (12 g.) and benzoyl chloride (8 g.) were heated in pyridine solution on the steam-bath for 30 minutes. The ethereal extract obtained after the mixture had been poured into water was washed several times with dilute sulphuric acid and

with dilute sodium hydroxide solution, dried with calcium chloride, and evaporated. The solid residue was crystallised twice from aqueous alcohol, and obtained as colourless needles, m. p. 92°. Neither the acyl derivatives nor the hydroxy-compound appears to yield an oxime or semicarbazone. The d-*bromocamphorsulphonyl* derivative was prepared by boiling a xylene solution of *d*-bromocamphorsulphonyl chloride with the silver derivative of the bromohydroxy-compound. After distillation of the xylene, the product was extracted with ether and the extract was washed with aqueous sodium carbonate, dried, and evaporated. The residue crystallised from ligroin or alcohol in pearly plates, m. p. 150° (Found: C, 43·2; H, 5·2. $C_{19}H_{26}O_5Br_2S$ requires C, 43·3; H, 5·0%). The compound decolorises permanganate in cold acetone with moderate rapidity, and does not appear to be capable of separation into optical isomerides by fractional crystallisation.

The *methyl* derivative was prepared by the action of an excess of methyl iodide on the solution obtained by adding the bromohydroxy-compound to an exact equivalent of alcoholic sodium ethoxide. After heating for 1 hour on the steam-bath, the mixture was poured into water and extracted with ether. The extract was washed with water, dilute sodium hydroxide solution and water, dried with calcium chloride, and evaporated. Distillation yielded the product as a colourless oil, which gave no colour with aqueous alcoholic ferric chloride. As it did not appear to form an oxime or semicarbazone, we have not been able to characterise it by means of crystalline derivatives, and there is therefore no proof that it is not a mixture of isomerides. If this is the case, however, the principal constituent is an unsaturated *O*-methyl ether, because the oil readily reduces cold permanganate in the presence of sodium hydrogen carbonate in aqueous acetone, and on hydrolysis by hydriodic acid yields the original bromohydroxy-compound. The refractive indices of different preparations do not agree very closely: $n_D^{20-21°}$ 1·5131—1·5147; the following densities have been observed: $d_4^{17°}$ 1·3203, $d_4^{20°}$ 1·3159, $d_4^{21°}$ 1·3162; and the following uncorrected b. p.'s: 95°/3 mm., 120°/14 mm., 130°/20 mm., 133°/25 mm. (Found: C, 48·3; H, 5·9. $C_{10}H_{15}O_2Br$ requires C, 48·6; H, 6·1%). A substance having substantially identical properties can be obtained, but less satisfactorily, by methylating the bromohydroxy-compound with twice the theoretical amount of methyl sulphate and excess of aqueous sodium hydroxide. The mixture was heated on the steam-bath for 1 hour, poured into water, and extracted with ether. A third method consists in allowing the silver salt of the bromohydroxy-compound to react with excess of methyl iodide in the cold; $d_4^{20°}$ 1·3167; $n_D^{20°}$ 1·5148.

The p-*bromobenzyl* derivative was prepared by means of *p*-bromobenzyl bromide and alcoholic sodium ethoxide, the mixture being heated on the steam-bath for 2 hours before being worked up as in the preceding example. The residue from the ethereal extract readily solidified and on crystallisation from dilute alcohol yielded iridescent plates, m. p. 65° (Found: C, 47·8; H, 4·4. $C_{16}H_{18}O_2Br_2$ requires C, 47·8; H, 4·5%). The same compound is obtained by allowing *p*-bromobenzyl bromide to react with the silver derivative of the bromohydroxy-compound in boiling ethereal-alcoholic solution. It forms no semicarbazone and does not give a colour with aqueous-alcoholic ferric chloride. It does not attack bromine in chloroform, does not form a semicarbazone, and is remarkably stable to dilute alkaline permanganate in aqueous acetone even at 65—70°. Part of the product of the action of *p*-bromobenzyl bromide on the sodio-derivative is an uncrystallisable oil, which is obtained from the ultimate mother-liquors in the crystallisation. It reduces permanganate but does not give a colour with ferric chloride; its behaviour on reduction is described below.

The p-*nitrobenzyl* derivative, similarly prepared, crystallises from alcohol in pearly plates, m. p. 111° (Found: C, 52·2; H, 5·1. $C_{16}H_{18}O_4NBr$ requires C, 52·2; H, 4·9%).

1-*Cyano*-2 : 2 : 3 : 3-*tetramethyl*-[0,1,2]-dicyclo*pentan*-4-*ol*-5-*one* (1-*Cyano*-2 : 2 : 3 : 3-*tetramethyl*-Δ^5-cyclo*penten*-5-*ol*-4-*one*).—This substance was obtained in poor yield both by heating the bromohydroxy-compound in 50% alcoholic solution containing an excess of potassium cyanide on the steam-bath for 3 hours, and by boiling a solution of the bromohydroxy-compound in ligroin (b. p. 100—120°) with silver cyanide for 6 hours. After several crystallisations from ligroin, it was obtained as colourless needles, m. p. 172—173° (Found: N, 8·0. $C_{10}H_{13}O_2N$ requires N, 7·8%).

2 : 2 : 3 : 3-*Tetramethyl*-[0,1,2]-dicyclo*pentan*-4-*ol*-5-*one* (2 : 2 : 3 : 3-*Tetramethyl*-Δ^5-cyclo*penten*-5-*ol*-4-*one*).—This was prepared, as described by Francis and Willson, both by reduction of the bromohydroxy-compound with zinc dust and glacial acetic acid, and by reduction of the bromoacetoxy-derivative with the same reagents and subsequent saponification with aqueous sodium hydroxide. Even by the latter method, however, we were unable to obtain more than an approximately 70% yield (contrast Francis and Willson), owing, as it subsequently appeared, to the fact that under our conditions part of the unsaturated halogen-free acetoxy-compound undergoes further reduction to a dihydro-derivative (*vide infra*). The free hydroxy-compound gives a dull red colour with aqueous alcoholic ferric chloride. The *acetyl* derivative, when purified by distillation after preparation in the manner indicated, or when

prepared by acetylation of the halogen-free crystalline hydroxy-compound by boiling for 1 hour with excess of acetic anhydride, is a colourless oil, b. p. 120°/15—16 mm. (Found: C, 67·0; H, 8·7. $C_{11}H_{16}O_3$ requires C, 67·2; H, 8·2%). It readily absorbs bromine in chloroform, and decolorises a cold aqueous acetone solution of potassium permanganate and sodium hydrogen carbonate; it gives no colour with aqueous-alcoholic ferric chloride. For the density and refractive index we find $d_{4^\circ}^{20^\circ}$ 1·0190 and $n_D^{20^\circ}$ 1·4549, whence $[R_L]_D = 52·21$. The exaltations given on p. 384 are calculated from Eisenlohr's (1910) constants. The benzoyl compound was prepared by Francis and Willson by benzoylation of the hydroxy-derivative. We have prepared it in considerable quantities by reducing the bromobenzoyloxy-compound with half its weight of zinc dust in boiling glacial acetic acid for about 2·5 hours. The mixture is then cooled, the liquid decanted from the zinc and zinc acetate into water, the solid washed with fresh acetic acid, and the precipitated oil extracted with ether. The extract was washed with cold 10% sodium hydroxide solution, dried, and evaporated. The product separates from dilute alcohol in glistening plates, m. p. 68° (after two crystallisations), and is identical with the material prepared by Francis and Willson's method (Found: C, 74·25; H, 7·1. Calc.: C, 74·4; H, 7·0%). It gives no colour with aqueous-alcoholic ferric chloride, and permanganate in aqueous acetone containing sodium hydrogen carbonate remains coloured for many hours. It is also unaffected by bromine in chloroform, and does not appear to undergo further reduction by prolonged treatment with excess of zinc dust in boiling glacial acetic acid. It is not easily hydrolysed by aqueous sodium hydroxide, but hydrolysis can be effected by heating on the steam-bath for 1 hour with 10% aqueous-alcoholic potassium hydroxide. The mixture is then evaporated to expel most of the alcohol, acidified, and extracted with ether, and the benzoic acid is removed from the ethereal solution by washing with aqueous sodium hydrogen carbonate. This provides the most satisfactory method for the preparation of the free hydroxy-compound.

The *methyl* derivative has been prepared by the following three methods: (1) The halogen-free hydroxy-compound was warmed on the steam-bath for 2 hours with methyl sulphate and 10% aqueous sodium hydroxide. After decomposition of the excess of methyl sulphate the methylation product was extracted with ether. In one experiment we obtained an oil, which, on strong cooling, yielded well-formed needles, m. p. 37° (Found: C, 71·2; H, 9·6. $C_{10}H_{16}O_2$ requires C, 71·4; H, 9·5%). The quantity obtained was small and was almost all used for the analysis. Unfortunately,

despite many attempts, we have not since succeeded in reproducing this result, and are therefore unable to describe the properties of this solid derivative. On all other occasions the product has been a colourless oil, b. p. 112—115°/21 mm., $n_D^{19°}$ 1·4687 (Found: C, 70·2; H, 9·3; OMe, 18·1. Calc.: OMe, 18·5%), which rapidly decolorises cold alkaline permanganate, and absorbs bromine in chloroform. It gives no colour with ferric chloride. (2) The hydroxy-compound was heated for 2 hours on the steam-bath with a methyl-alcoholic solution of sodium methoxide (1 mol.) and excess of methyl iodide. The product was poured into water and extracted with ether, and the extract dried and distilled. The distillate, b. p. 108—112°/18 mm., $n_D^{19°}$ 1·4687, OMe 18·1%, has properties identical with those of the product obtained by method (1). (3) The bromomethoxy-compound was reduced by the method already described for the reduction of the bromoacetoxy-compound. The methoxy-compound so obtained was purified by distillation, controlled by b. p. and refractive-index determinations (*vide* the dihydro-derivative). Since the liquid methoxy-compound gives an oily oxime, and we have not been able to prepare a crystalline derivative, there is no proof that it is not a mixture of isomerides; but if this is so, the principal constituent is 5-methoxy-2 : 2 : 3 : 3-tetramethyl-Δ^5-*cyclo*-penten-4-one, as is shown by its behaviour on further reduction (below). The Zeisel determinations show that it cannot contain a substantial proportion of any *C*-methylation product. The oxime has b. p. 140—150°/22 mm.

The p-*bromobenzyl* derivative was prepared by reducing the bromo-*p*-bromobenzyloxy-compound with glacial acetic acid and excess of zinc. After boiling for 3 hours, the acetic acid solution was poured into water and extracted with ether. The ethereal extract was washed with cold alkali, dried, and evaporated. The crystalline residue separated from ligroin in long, colourless prisms, m. p. 86° (Found: C, 59·2; H, 5·9. $C_{16}H_{19}O_2Br$ requires C, 59·3; H, 5·9%). The same substance was obtained by heating the hydroxy-compound (1·0 g.) with methyl-alcoholic sodium methoxide (prepared from 0·16 g. of sodium) and *p*-bromobenzyl bromide (1·7 g.) on the steam-bath for 1 hour (yield, 90%). The compound gives no colour with aqueous-alcoholic ferric chloride. It slowly decolorises permanganate in acetone, and does not appear to absorb bromine in cold chloroform, although on warming bromine disappears and hydrogen bromide is evolved, showing that substitution has taken place. It forms a crystalline oxime (p. 403).

3 : 3 : 4 : 4-*Tetramethylcyclopentanone*.—Francis and Willson obtained this substance from the bromohydroxy-compound by reduction with sodium amalgam, which is a convenient reagent for

the preparation of small quantities. For larger amounts the Clemmensen method is preferable. The reduction is complete in 1 hour and the ketone is then removed from the water-cooled trap employed to collect it. A further small quantity is obtainable from hydrochloric acid solution by distillation in steam (total yield, 75%). We have also prepared the ketone by the action of sodium amalgam on a hot aqueous solution of the bromine-free hydroxy-compound, and by the action of hydriodic acid at 140° on its methyl and *p*-bromobenzyl derivatives, as well as by the methods described elsewhere in this paper.

The *dipiperonylidene* derivative was obtained by boiling under reflux a solution of the ketone (0·5 g.), piperonaldehyde (1·5 g.), and potassium hydroxide (1·5 g.) in 80% alcohol (30 c.c.) for 1 hour. The cooled solution was diluted with water, and the product, which was precipitated as a slowly solidifying oil, was drained, washed with ligroin, and crystallised from methyl alcohol, from which it separated in yellow, rhombic prisms, m. p. 125° (Found : C, 74·0; H, 6·0. $C_{25}H_{24}O_5$ requires C, 74·2; H, 6·0%).

The *αα'-dioximino*-derivative (1 : 3-*dioxime* of 4 : 4 : 5 : 5-tetramethyl*cyclo*pentanetrione) was prepared by treating the ketone (0·7 g.) with *iso*amyl nitrite (1·2 g.) in ethyl alcohol (1·0 c.c.) containing 10 drops of concentrated hydrochloric acid. After being kept for 30 minutes, during which the temperature rose to 40°, the solution was basified with sodium hydroxide and extracted with ether, then acidified, and again extracted with ether. The second extract was washed with sodium hydrogen carbonate solution, dried, and evaporated, and the residue was washed with ether and chloroform (yield, 60%). The same substance was obtained from the ketone (0·7 g.), *iso*amyl nitrite (1·2 g.), and 0·5 c.c. of a solution of sodium methoxide prepared by dissolving 0·12 g. of sodium in 2 c.c. of methyl alcohol. The mixture was kept at 40° for 20 minutes, cooled, diluted with water, mixed with aqueous sodium hydroxide, and extracted with ether. The aqueous solution was then saturated with carbon dioxide and again extracted. Another method which has been used consists in passing nitrosyl chloride into a solution of the ketone in chloroform, ether, or ligroin. The dioxime separates from alcohol in pale yellow needles, m. p. 223° (decomp.) (Found : C, 54·1; H, 7·0. $C_9H_{14}O_3N_2$ requires C, 54·5; H, 7·1%). On hydrolysis with hydrochloric acid in the presence of formaldehyde (Perkin's method) it yielded a nitrogen-free oil which reduced Fehling's solution and stained the skin purple just as does 1 : 2 : 3-triketohydrindene. This evidently consisted of tetramethyl-*cyclo*pentanetrione or its hydrate, since on treatment with excess of hydroxylamine acetate in boiling 90% alcohol, it was converted

into a crystalline 1 : 2 : 3-*trioxime*, which was isolated by evaporating the alcohol and extracting the residue with chloroform. The same trioxime was obtained directly from the 1 : 3-dioxime by treatment with hydroxylamine acetate under the conditions described. It separates from chloroform–ether in colourless needles, m. p. 168—169° (Found: N, 19·5. $C_9H_{15}O_3N_3$ requires N, 19·7%), and gives a strong purple colour with aqueous-alcoholic ferric chloride.

The oxime was prepared by heating tetramethyl*cyclo*pentanone with an excess of aqueous-alcoholic hydroxylamine acetate for some hours on the steam-bath. The partly evaporated solution was extracted with ether, and the dried and concentrated ethereal solution was treated with dry hydrogen chloride, which precipitated the *hydrochloride* of the oxime, m. p. 119° (Found: Cl, 18·4. $C_9H_{17}ON,HCl$ requires Cl, 18·5%). The solution of this in aqueous sodium carbonate yielded the pure *oxime*, m. p. 107°, on extraction with ether (Found: N, 9·1. $C_9H_{17}ON$ requires N, 9·0%). The oxime is very soluble in most organic solvents, but can be crystallised from ligroin. It is volatile in steam. It reduces Fehling's solution and gives a green colour with bromine in aqueous pyridine (Piloty, *Ber.*, 1898, **31**, 454).

Formation of 3 : 3 : 4 : 4-*Tetramethyl*cyclo*pentanone from Pinacol and Ethyl Acetonedicarboxylate.*—Pinacol was converted into βγ-dibromo-βγ-dimethylbutane (m. p. 173°; compare Centurier, *Ann. Chim. Phys.*, 1892, **26**, 444) by treatment with the theoretical amount of phosphorus tribromide. Ethyl acetonedicarboxylate (20·2 g.), the dibromide (24·4 g.), and alcoholic sodium ethoxide prepared from 4·6 g. of sodium and 50 g. of ethyl alcohol were heated together for 4 hours on the steam-bath. The product was worked up into fractions insoluble in alkali, insoluble in sodium hydrogen carbonate but soluble in sodium hydroxide, and soluble in carbonate, but difficulty was experienced in the purification of these, and they were therefore hydrolysed by boiling with 20% hydrochloric acid under an efficient condenser. On distillation in steam the eliminated alcohol and the ketone passed over in the first runnings, from which the ketone was collected in the form of its semicarbazone, m. p. 224°, after addition of semicarbazide acetate.

Conversion of 3 : 3 : 4 : 4-*Tetramethyl*cyclo*pentanone into the Bromohydroxy-compound.*—A general description of these experiments is given in the introduction (p. 369), and it need be added only that the product was identified by m. p., mixed m. p., and analysis, and by the m. p. and mixed m. p. of its acetyl derivative.

3 : 3 : 4 : 4-*Tetramethyl*cyclo*pentylamine.*—(1) A solution of 3 : 3 : 4 : 4-tetramethyl*cyclo*pentanone oxime (2·0 g.) in alcohol was heated to 50—60° while 2·5% sodium amalgam (50 g.) and hot

glacial acetic acid were gradually added. The solution was cooled, separated from the mercury, diluted with water, and extracted with ether to remove any unchanged oxime. After basification with sodium hydroxide, the amine was extracted with ether, and the extract was dried with potassium carbonate and distilled through a fractionating column.

(2) A boiling solution of the oxime (2·0 g.) in absolute alcohol (50 g.) was slowly poured on sodium wire (5 g.), contained in a flask fitted with an efficient reflux condenser. After addition of an excess of aqueous acetic acid, the solution was evaporated to drive off most of the alcohol, extracted with ether, basified, and again extracted, the ether being finally removed through a column.

(3) The oxime (1·0 g.) was first converted into its acetyl derivative by mixing a solution in dry pyridine with acetyl chloride (0·5 g.) with external cooling. The product was isolated by pouring into dilute sulphuric acid and extracted with ether. The extract, after being washed with dilute acid, dried, and evaporated, gave a colourless oil, which yielded no precipitate when its solution in dry ether was treated with dry hydrogen chloride. The acetate was dissolved in 75 c.c. of glacial acetic acid, and treated with 10 g. of palladised barium sulphate (corresponding to 0·5 g. of palladium), and hydrogen at the ordinary temperature and 1·5 atmospheres pressure, with shaking, until the requisite amount of hydrogen had been absorbed (usually less than 1 hour). The mixture was then decanted into water, and the precipitate washed by decantation with fresh acetic acid; the diluted acid solution was then extracted with ether, basified with sodium hydroxide, and again extracted, the second extract yielding the amine.

The base obtained by these methods forms colourless needles, m. p. 100—102°, having a characteristic odour. Owing to its volatility, and great solubility in the usual solvents, we did not recrystallise it, but characterised it by means of its salts and acetyl derivative. The *picrate* was precipitated in alcoholic solution and crystallised twice from alcohol, from which it separated in bright yellow needles, m. p. 255° (decomp.) (Found: C, 48·1; H, 6·0. $C_{15}H_{22}O_7N_4$ requires C, 48·6; H, 6·0%). The *chloroaurate*, obtained by addition of chloroauric acid to a hydrochloric acid solution of the base, separated from 15% hydrochloric acid in orange-yellow needles, m. p. 230° (decomp.) (Found: C, 22·6; H, 4·6; Au, 39·9. $C_9H_{20}NCl_4Au$ requires C, 22·4; H, 4·2; Au, 40·1%). The *hydrochloride*, precipitated from ethereal solution by dry hydrogen chloride, had m. p. 308° (decomp.) and was very deliquescent. The *acetyl* derivative was prepared by boiling the picrate (0·5 g.) for 2 hours with excess of acetic anhydride in the presence of

anhydrous sodium acetate (0·5 g.). The product was poured into water, and, after decomposition of the acetic anhydride, extracted with ether. The acetic acid and picric acid were removed by washing with 5% aqueous sodium hydroxide, and the extract was dried with potassium carbonate and evaporated. The oil solidified while still hot (yield, 0·20 g.; m. p. 95°, unpurified), and crystallisation from ligroin yielded felted needles, m. p. 95° (Found: C, 71·9; H, 11·4. $C_{11}H_{21}ON$ requires C, 72·1; H, 11·4%).

2 : 2 : 3 : 3-*Tetramethyl*-[0,1,2]-dicyclo*pentan*-4-*ol*-5-*one Oximes*.—A solution of the hydroxy-ketone (0·5 g.), hydroxylamine hydrochloride (0·23 g.), and sodium acetate (0·27 g.) in 3 c.c. of 10% aqueous sodium hydroxide was kept at 40° for 40 hours; the precipitate was then collected, and washed with a little water, alcohol, and ether. This substance, m. p. 200° (decomp.), contained sodium and was evidently the *sodium* salt of an oxime. Its solution in water, on treatment with carbon dioxide, yielded the *monohydrate* of the α-oxime, m. p. 75°, as pearly plates, which after a further crystallisation from water had m. p. 76—77° (Found: H_2O, 9·6. $C_9H_{15}O_2N,H_2O$ requires H_2O, 9·7%). On desiccation in a vacuum the hydrate became converted into the anhydrous *α-oxime*, m. p. 96° (Found: N, 8·5. $C_9H_{15}O_2N$ requires N, 8·3%), which crystallised from carbon tetrachloride–ligroin in long prisms having the same m. p. The filtrate from the oxime hydrate was acidified with hydrochloric acid at 0° and extracted with ether; a gum was then obtained which, on desiccation, set to a slowly crystallising glass. On crystallisation from carbon tetrachloride–ligroin, this yielded pearly leaflets, m. p. 174—175°, which gave the reactions of a hydrochloride and contained solvent of crystallisation. On heating at 100° a loss in weight amounting to 38% (theory for 1 mol. of CCl_4, 43%) occurred, and the product then had m. p. 189—190° (Found: C, 53·5; H, 8·2. $C_9H_{16}O_2NCl$ requires C, 52·5; H, 8·2%). This is apparently the *hydrochloride* of the α-oxime, since its solution in water is acid, contains chloride ions, and on basification yields the α-oxime. This was obtained by extraction with ether after addition of sodium carbonate, and dehydration in ethereal solution with anhydrous potassium carbonate. The product was identified with the oxime, m. p. 96° (mixed m. p.), and then crystallised from water, the monohydrate, m. p. 76—77°, being obtained. The carbon tetrachloride–ligroin mother-liquors, on concentration, deposited crystals of the same oxime hydrate. In another experiment in which 5 g. of the hydroxy-ketone were condensed with hydroxylamine acetate, precipitation of the sodium salt of the oxime did not occur, and the whole yield of oxime was isolated by way of the hydrochloride in the manner indicated by the preliminary

investigation described. The *benzoyl* derivative of the oxime crystallised from dilute alcohol in colourless needles, m. p. 134—135° (Found: C, 70·0; H, 7·4. $C_{16}H_{19}O_3N$ requires C, 70·3; H, 7·0%).

When the α-oxime is treated with dry hydrogen chloride in cold ethereal solution, a new *hydrochloride*, m. p. 69—70°, is precipitated. On basification of its solution with sodium carbonate the hydrate of the α-oxime is precipitated, and the mother-liquors on concentration yield further crops of the same substance. However, on desiccation in a vacuum over potassium hydroxide the β-hydrochloride loses hydrogen chloride and gives the *β-oxime*, m. p. 114—115°, which on crystallisation from chloroform–ligroin forms rhombic prisms, m. p. 115° (Found: C, 64·1; H, 9·1. $C_9H_{15}O_2N$ requires C 63·9; H, 8·9%). On two occasions the β-oxime was obtained directly from the hydroxy-ketone and hydroxylamine, but we have not determined the exact conditions in which it is produced in place of the α-oxime. The second of these experiments was conducted as follows. A solution of the hydroxy-ketone (1 mol.), hydroxylamine hydrochloride (1 mol.), and sodium acetate (excess) in aqueous methyl alcohol was warmed at 40° for a short time and kept overnight. The solution was then made strongly acid with 15% hydrochloric acid, extracted with ether to remove the unchanged ketone, carefully neutralised with sodium hydrogen carbonate, made alkaline with sodium carbonate (1 mol.), and immediately extracted with ether. The residue from the ether was an oil, which solidified on rubbing, and after being washed with ligroin and crystallised, was identified as the β-oxime, m. p. 115°.

On boiling with water the β-oxime is converted into the hydrate of the α-oxime. A mixture of the α- and β-oximes melted at about 60°. Both oximes reduce Fehling's solution, but the α-oxime forms no colour with ferric chloride, whereas the β-oxime gives a red-purple colour.

When the β-hydrochloride was treated with hydrogen chloride in boiling ethereal solution, a red oil was obtained which subsequently solidified. The drained crystals were crystallised first from carbon tetrachloride–ligroin, and then from water (charcoal) which removed the red colour and yielded needles, m. p. 113° (a mixture with the β-oxime melted below 80°) (Found: C, 63·7; H, 8·9. $C_9H_{15}O_2N$ requires C, 63·9; H, 8·9%). The substance is not soluble in cold aqueous sodium carbonate, but in 10% potassium hydroxide it forms a pale yellow solution which, on acidification, becomes colourless. On account of its non-identity with ααββ-tetramethylglutarimide, we provisionally assign to this substance the formula of the *lactam* of *δ-amino-α-keto-ββγγ-tetramethylvaleric acid*.

αααββ-*Tetramethylglutaric anhydride*, which was prepared from the acid and acetic anhydride in the usual way, has m. p. 184°. On heating in a stream of dry gaseous ammonia, it is converted into the *imide*, which after sublimation has m. p. 200—202° (Found: N, 8·8. $C_9H_{15}O_2N$ requires N, 8·3%). The imide gives no colour with ferric chloride.

The hydroxy-ketone, or its α-monoxime, m. p. 96°, was heated for 2 hours on the steam-bath in ethyl-alcoholic solution with an excess of hydroxylamine hydrochloride, and anhydrous sodium acetate. The solution was filtered while hot, and mixed with ice-cold water, and the precipitated *dioxime* of 3 : 3 : 4 : 4-*tetramethyl*-cyclo*pentane*-1 : 2-*dione* purified by crystallisation from dilute alcohol. It forms rhombic prisms, m. p. 211° (decomp.) (Found: C, 58·8; H, 8·6. $C_9H_{16}O_2N_2$ requires C, 58·7; H, 8·8%). Its formulation as a 1 : 2-dioxime was confirmed by conversion into the furazan. For this purpose, the dioxime (0·5 g.) was heated with 3 c.c. of concentrated aqueous ammonia in a closed tube at 160—170° for 5 hours. The *furazan*, which crystallised on cooling, was dried and crystallised from a large volume of ligroin (b. p. 100—120°), from which it separated in flattened prisms, m. p. 209° (Found: C, 64·9; H, 8·8. $C_9H_{14}ON_2$ requires C, 65·0; H, 8·5%). The furazan is insoluble in cold 10% aqueous potassium hydroxide. The same dioxime and furazan can be prepared by starting with the α-oxime, m. p. 96°, in place of the hydroxy-ketone.

The hydroxy-ketone and *o*-phenylenediamine in equimolecular proportion were boiled in glacial acetic acid solution. The *condensation product*, which separated, after cooling, on addition of water, crystallised from dilute alcohol in golden-yellow needles, m. p. 100° (Found: C, 78·8; H, 8·1. $C_{15}H_{18}N_2$ requires C, 79·5; H, 8·0%).

The *semicarbazone* of the hydroxy-ketone was prepared by the usual method; it crystallised from dilute alcohol in colourless plates, m. p. 211—213° (decomp.) (Found: C, 56·8; H, 8·4. $C_{10}H_{17}O_2N_3$ requires C, 56·9; H, 8·1%).

The *anil* of the hydroxy-ketone, which was obtained by heating the latter (0·5 g.) with aniline (0·3 g.) at 100° for 1 hour, separated from ligroin in rhombic prisms, m. p. 104° (Found: C, 78·3; H, 8·4. $C_{15}H_{19}ON$ requires C, 78·6; H, 8·4%). The p-*dimethylaminoanil*, similarly prepared and purified, formed yellow needles, m. p. 90° (Found: C, 75·4; H, 8·8. $C_{17}H_{24}ON_2$ requires C, 75·0; H, 8·8%). These anils do not react easily with hydroxylamine, but when heated for 30 hours in alcoholic solution with hydroxylamine hydrochloride (6 mols.) and anhydrous sodium acetate (excess), yield the dioxime, m. p. 211°, and unidentified substances.

Reduction of the α-Oxime (m. p. 96°) to 3 : 3 : 4 : 4-Tetramethyl-cyclopentylamine.—This was effected by the three methods mentioned on p. 392, the oxime being acetylated before reduction by method 3. The identity of the base with that obtained from 3 : 3 : 4 : 4-tetramethylcyclopentanone oxime (m. p. 107°) was established by the following comparisons of m. p.'s and mixed m. p.'s :—

	Base.	Picrate.	Dichloro-aurate.	Hydro-chloride.	Acetyl derivative.
From 96°-oxime ...	100—102°	254°	229°	305°	94°
,, 107°-oxime ...	100—102	255	230	308	95
Mixed m. p.	100—102	254—255	229—230	306	94

Reduction of the Acetyl Derivative of the Hydroxy-ketone.—A boiling solution of the acetyl derivative (7·5 g.) in glacial acetic acid (100 c.c.) was treated with 10 g. of zinc dust, which was added gradually during 6 hours. The cooled solution was filtered, the solid residue washed by decantation with fresh acetic acid, and the combined filtrates mixed with water and extracted with ether. The extract was washed with aqueous sodium carbonate solution, dried, and evaporated. The oily residue on fractional distillation yielded a small quantity of unchanged substance (b. p. 120°/15—16 mm.; 1·2 g.) and a main fraction (3·4 g.), b. p. 127°/15—16 mm. This substance is shown in the sequel to be *5-acetoxy-2 : 2 : 3 : 3-tetramethylcyclopentanone* (Found : C, 66·2; H, 9·3. $C_{11}H_{18}O_3$ requires C, 66·6; H, 9·2%). On hydrolysis it gives a hydroxy-ketone, $C_9H_{16}O_2$, m. p. 140°, which is being investigated. These substances are more conveniently prepared directly from the acetyl derivative (m. p. 74°) of the bromohydroxy-compound by reduction under the conditions described above.

2 : 2 : 3 : 3-Tetramethylcyclopentanone.—A boiling glacial acetic acid solution of the acetoxytetramethylcyclopentanone was treated during 0·5 hour with 100 g. of 2·5% sodium amalgam. The cooled and diluted solution was extracted with ether, and the extract washed with dilute sodium carbonate solution, dried, and distilled (column). The oily residue, which had a strong odour resembling that of camphor, was distilled; *2 : 2 : 3 : 3-tetramethylcyclopentanone* was then obtained as a wax-like solid, b. p. 100°/16 mm., m. p. 119° (mixed m. p. with 3 : 3 : 4 : 4-tetramethylcyclopentanone, 105°), together with a less volatile fraction, b. p. 127°/16 mm., consisting of the unaltered acetoxy-ketone. The 2 : 2 : 3 : 3-tetramethylcyclopentanone obtained by this method is liable to be contaminated with traces of the 3 : 3 : 4 : 4-isomeride, which may be removed by taking advantage of the fact that it combines with semicarbazide much more rapidly than the 2 : 2 : 3 : 3-compound. For this purpose the crude ketone is treated with aqueous-alcoholic semi-

carbazide acetate at 18° for 30 minutes, and any precipitate which is formed is removed by filtration. From this the semicarbazide of the 3 : 3 : 4 : 4-ketone has been isolated by crystallisation. The 2 : 2 : 3 : 3-ketone is recovered from the filtrate by largely diluting it and extracting it with ether, and is finally purified by distillation. For the preparation of 2 : 2 : 3 : 3-tetramethyl*cyclo*pentanone in quantity it is convenient to employ, in place of the saturated acetoxy-ketone, the mixture of reduction products obtained by the action of zinc and acetic acid on the bromoacetoxy-compound, the precaution being taken of removing any 3 : 3 : 4 : 4-ketone in the manner described. It is also possible to obtain the ketone directly from the bromoacetoxy-compound by reduction with glacial acetic acid and a larger proportion of sodium amalgam.

The *semicarbazone* separates in the course of 24 hours when the ketone is left in contact with aqueous-alcoholic semicarbazide acetate at the ordinary temperature. It crystallises from dilute alcohol in needles, m. p. 222° (decomp.) (mixed m. p. with the semicarbazone, m. p. 224°, of 3 : 3 : 4 : 4-tetramethyl*cyclo*pentanone, 200—205°) (Found: C, 60·9; H, 9·9. $C_{10}H_{19}ON_3$ requires C, 60·9; H, 9·6%).

The *oxime* was prepared by boiling an alcoholic solution of the ketone for 18 hours with a slight excess of hydroxylamine hydrochloride and anhydrous sodium acetate. After dilution with water, the oxime was extracted with ether, and the extract washed with aqueous sodium carbonate, dried with calcium chloride, and concentrated to a small bulk. Dry hydrogen chloride was then passed in, and the *oxime hydrochloride*, m. p. 125° (Found: Cl, 18·6. $C_9H_{17}ON,HCl$ requires Cl, 18·5%), collected and washed with ether. The free oxime, liberated by means of sodium carbonate and isolated by extraction with ether, had m. p. 101—102°. It is extremely soluble in the usual organic solvents.

2 : 2 : 3 : 3-*Tetramethyl*cyclo*pentylamine*.—This was prepared from the oxime by reduction with sodium and alcohol as described on p. 392. The base is crystalline (needles) at the ordinary temperature, and is closely similar in odour and volatility to 3 : 3 : 4 : 4-tetramethyl*cyclo*pentylamine; but, apart from noting these points, we have not investigated the free amine owing to the rapidity with which it disappears. Its *picrate* separates from methyl alcohol–ligroin in yellow needles, m. p. 242—243° (decomp.). Found: C, 48·9; H, 5·9. $C_{15}H_{22}O_7N_4$ requires C, 48·6; H, 6·0%). It is closely similar in appearance to the picrate (m. p. 255°) of the isomeric base, but a mixture of the two melted at 235—236°. The *acetyl* derivative, obtained from the picrate by boiling with acetic anhydride and sodium acetate, separated from ligroin in prisms, m. p. 115° (Found:

C, 71·9; H, 11·4. $C_{11}H_{21}ON$ requires C, 72·1; H, 11·4%). A mixture with the acetyl derivative of the isomeric base had m. p. 83—85°.

Reduction of the Oxime of 5-Acetoxy-2 : 2 : 3 : 3-tetramethylcyclopentanone.—The oxime was prepared in the usual way, but it could not be crystallised and therefore was reduced, without purification, by means of sodium and alcohol. The product was identified as 2 : 2 : 3 : 3-tetramethyl*cyclo*pentylamine.

Action of Hydroxylamine on the Benzoyl Derivative of the Hydroxy-ketone.—(1) The benzoyloxy-compound was dissolved in a cold ethyl-alcoholic solution of hydroxylamine hydrochloride (1 mol.) containing dry sodium hydrogen carbonate (1 mol.) in suspension. After being kept at the ordinary temperature for 18 hours, the product was poured into water and extracted with ether, and the extract was washed with dilute sodium carbonate solution, dried, and evaporated. The *oxime* thus obtained in excellent yield separated from hot water or from chloroform–ligroin in well-developed prisms, m. p. 115° (Found : C, 63·8; H, 8·8. $C_9H_{15}O_2N$ requires C, 63·9; H, 8·9%). The sodium carbonate solution on acidification yielded benzoic acid. The new oxime, which may be distinguished by the prefix γ-, gives a pale red-brown colour with ferric chloride. It is soluble in sodium hydroxide and concentrated hydrochloric acid, and can be recovered from each solution unchanged, in the former case by neutralisation, and in the latter by dilution. A mixture with the β-oxime (m. p. 115°), described on p. 395, melted at about 100°, and a mixture with the isomeric lactam (m. p. 113°) (p. 395) melted at 85°. The same oxime was obtained by various modifications of the method described above, as, for instance, heating an alcoholic solution of the hydroxy-ketone with anhydrous sodium acetate (excess) and hydroxylamine hydrochloride (1 mol.) for 3 hours on the steam-bath. On boiling with dilute hydrochloric acid, the oxime is hydrolysed to the original hydroxy-ketone, which may crystallise from the solution on cooling or can be extracted with ether. When, however, hot concentrated hydrochloric acid is used in attempted hydrolysis, deep-seated changes take place and an intractable oil is produced.

(2) An alcoholic solution of the benzoyloxy-compound (2·5 g.) was boiled for 2 hours with hydroxylamine hydrochloride (3·5 g.) and anhydrous sodium acetate (4·0 g.). On working up the product, as in the preceding experiment, the dioxime, m. p. 211° (decomp.), was obtained together with benzoic acid. The same dioxime is obtained when the monoxime is further oximated under the same conditions.

Re-arrangement of the γ-Oxime.—The monoxime was heated in

a closed tube at 100° for 30 minutes with a chloroform solution of nitrosyl chloride. On evaporation an oil remained which soon became semi-solid. The crystals were drained, washed with ligroin and with xylene, and crystallised from carbon tetrachloride–ligroin, from which colourless octahedra separated, m. p. 200° (Found: C, 63·5; H, 8·5. $C_9H_{15}O_2N$ requires C, 63·9; H, 8·9%). The substance is soluble in cold 10% potassium hydroxide solution, and gives a faint red colour with ferric chloride. It is provisionally regarded as the *lactam* of *δ-amino-α-keto-γγ-dimethylisoheptoic acid*.

Reduction of the γ-Oxime.—The oxime was reduced with excess of sodium in boiling alcohol, as described on p. 392, and the base isolated and converted into its picrate. The latter was much more soluble in alcohol than the picrates of the tetramethyl*cyclo*pentylamines, and was therefore precipitated from ethereal solution. In the crude state it had m. p. 220—221°, and separated from alcohol–ligroin in yellow needles, m. p. 221° (Found: C, 46·8, 46·9; H, 5·7, 5·8; N, 14·9. $C_{15}H_{22}O_8N_4$ requires C, 46·6; H, 5·7; N, 14·5%). The substance thus appears to be the *picrate* of *5-hydroxy-2 : 2 : 3 : 3-tetramethyl*cyclo*pentylamine*.

*Action of Amyl Nitrite and Sodium Methoxide on 3 : 3 : 4 : 4-Tetramethyl*cyclo*pentanone*.—Unless special precautions are taken, the sole product obtained from the reaction indicated is the αα′-dioximino-compound described on p. 391. By carefully regulating the conditions, however, we have obtained, although in very small yield, a mono-oximino-derivative which appears to be identical with the γ-oxime obtained from the benzoyloxy-compound (above). The ketone (6 g.) and *iso*amyl nitrite (5 g.) were mixed at 0° with a solution of sodium methoxide prepared from 0·12 g. of sodium and 2 c.c. of methyl alcohol. The mixture was slowly warmed to 35—38° and maintained at this temperature for 20—30 minutes. (The limiting conditions of success in this experiment are very narrow; for example, in a similar experiment in which the mixture was kept at 32° oximination did not take place, and another experiment at 40° yielded mainly the dioximino-derivative.) After addition of water, the mixture was shaken with 10% sodium hydroxide and ether, and the aqueous solution saturated with carbon dioxide and again extracted with ether. The second extract was washed once with sodium hydrogen carbonate solution, dried with sodium sulphate, and evaporated. The residue, after draining on porous porcelain, was washed with ligroin containing a little xylene to remove coloured impurities, and then extracted with hot ligroin, in which the dioximino-compound is only slightly soluble. The solution on cooling deposited colourless needles, m. p. about 105° (Found: N, 8·5. $C_9H_{15}O_2N$ requires N, 8·3%); these probably

contained traces of the dioximino-compound, which, with the small quantities at our disposal, we have been unable to eliminate. In its general reactions, however, this oxime closely resembles the γ-oxime described above: for instance, it gives a pale red-brown colour with ferric chloride, reduces Fehling's solution, and on hydrolysis by means of hydrochloric acid yields the hydroxy-ketone (m. p. 86°). Similar results have been obtained by using nitrosyl chloride in place of *iso*amyl nitrite and sodium methoxide, but here again we have been unsuccessful in establishing the conditions for a satisfactory preparation. On the two occasions in which the mono-oximino-compound was isolated, chloroform was employed as solvent, and in one case the temperature was 0°, and in the other 15°. Upwards of a dozen similar experiments, with ether, ligroin, or chloroform as solvent, and at temperatures ranging from −12° to +15°, yielded the dioximino-compound unaccompanied by any appreciable quantity of the mono-oximino-derivative.

An isomeric oximino-compound was obtained under the following conditions. A solution of the ketone (0·6 g.) in methyl-alcoholic sodium methoxide (0·5 c.c. of a solution prepared from 0·12 g. of sodium and 4 c.c. of methyl alcohol) was kept at 60—65° while *iso*amyl nitrite (0·5 g.) was added very slowly through a capillary tube. The *sodium* salt which separated during this treatment (0·15 g., m. p. 200°) was drained from the adhering mother-liquor, washed with ether and ligroin, and decomposed in aqueous solution by means of carbon dioxide. The *δ-oxime monohydrate* precipitated was crystallised from water and obtained as clusters of colourless needles, m. p. 83° (Found: C, 57·7, 57·9; H, 8·7, 8·9. $C_9H_{17}O_3N$ requires C, 57·8; H, 9·1%). On keeping it in a vacuum at 100° over phosphorus pentoxide, the anhydrous *δ-oxime* is obtained as a white powder, m. p. 170—172°, which, on crystallisation from carbon tetrachloride–ligroin, gives colourless needles, m. p. 172° (Found: N, 8·3. $C_9H_{15}O_2N$ requires N, 8·3%), and on crystallisation from water passes back into the monohydrate, m. p. 83°. This oxime gives a strong red colour with ferric chloride, a blue-green precipitate with cupric acetate, and reduces Fehling's solution. An attempt to hydrolyse the compound by boiling with concentrated hydrochloric acid and formaldehyde led to the production of ααββ-tetramethylglutaric acid (m. p. 144°; mixed m. p., the same). This may be explained on the assumption that a Beckmann change first takes place, producing tetramethylglutarimide, which is then hydrolysed; the explanation would accord with the supposition that the γ- and δ-oximes are stereoisomeric, since the γ-oxime on re-arrangement yields an isomeride of the glutarimide.

Reduction of the Methyl Derivative of the Hydroxy-ketone.—The

reduction product, 5-*methoxy*-2 : 2 : 3 : 3-*tetramethyl*cyclo*pentanone*, is obtained as a by-product in the preparation of 5-methoxy-2 : 2 : 3 : 3-tetramethyl-Δ^5-*cyclo*penten-4-one by reduction of its bromo-derivative with zinc dust and boiling glacial acetic acid, and it can be separated from the accompanying unsaturated ketone by fractional distillation. The unsaturated ketone can be reduced to the dihydro-derivative by the same method, but it is difficult to induce the reaction to proceed to completion, and hence fractional distillation is again necessary. The following method gives satisfactory results. The methoxytetramethyl*cyclo*pentanone is treated with 15 times its weight of 2·5% sodium amalgam in boiling glacial acetic acid, and the product is extracted with ether after being poured into water. The extract is washed with sodium carbonate solution and dried and the residue obtained on evaporation is distilled. The saturated methoxy-ketone is a colourless oil, b. p. 88—90°/10 mm., $n_D^{19°}$ 1·4580; b. p. 90°/11 mm.; b. p. 90—92°/13—14 mm., $n_D^{19°}$ 1·4574 (three different preparations) (Found: C, 70·2; H, 10·4; OMe, 18·0. $C_{10}H_{18}O_2$ requires C, 70·6; H, 10·6%. $C_9H_{15}O{\cdot}OMe$ requires OMe, 18·2%). The oxime is an oil which could not be crystallised, and it was not found possible to prepare a solid semicarbazone or phenylhydrazone.

Unlike 5-acetoxy-2 : 2 : 3 : 3-tetramethyl*cyclo*pentanone, the saturated methoxy-ketone shows little tendency to undergo further reduction to a tetramethyl*cyclo*pentanone on treatment with zinc or sodium amalgam in acetic acid solution, although we have observed the characteristic camphor-like odour in some experiments.

When the methyl derivative of the hydroxy-ketone is reduced by boiling with concentrated hydriodic acid, 3 : 3 : 4 : 4-tetramethyl*cyclo*pentanone is formed, which was identified directly and through its semicarbazone. Since methyl iodide is also produced, we assume that demethylation with the formation of the tautomeric hydroxy-ketone constitutes the first stage in the reaction.

Reduction of 5-*Methoxy*-2 : 2 : 3 : 3-*tetramethyl*-Δ^4-cyclo*pentenone Oxime*.—The oxime (p. 390) was reduced with 5 times its weight of sodium in boiling ethyl alcohol, and after acidification with dilute acetic acid and extraction with ether, the free base was liberated by addition of alkali and extracted. The product was similar in all respects to 2 : 2 : 3 : 3-tetramethyl*cyclo*pentylamine and was identified by the analysis and properties of the picrate and acetyl derivative and by mixed m. p. determinations with authentic specimens.

Reduction of 5-*Methoxy*-2 : 2 : 3 : 3-*tetramethyl*cyclo*pentanone Oxime*.—The oxime (above) prepared from the methoxy-ketone

(1·7 g.), hydroxylamine hydrochloride (1·4 g.), and anhydrous sodium acetate (1·65 g.) by boiling in alcoholic solution for 2 hours, was reduced with sodium (4 g.) in boiling ethyl alcohol. The product, 2 : 2 : 3 : 3-tetramethyl*cyclo*pentylamine, was isolated and identified as in the preceding experiment.

Action of Hydroxylamine on the p-*Bromobenzyl Derivative of the Hydroxy-ketone.*—The *p*-bromobenzyloxy-compound (0·8 g.), hydroxylamine hydrochloride (0·4 g.), and anhydrous sodium acetate (0·8 g.) were heated for 2 hours in absolute alcohol on the steam-bath. The solid precipitated from the filtered solution by addition of ice-water was collected, dried, dissolved in ether, and treated with hydrogen chloride. The *oxime hydrochloride*, m. p. 133° (decomp.) (Found, by estimation of hydrochloric acid in the aqueous solution: Cl, 9·3. $C_{16}H_{20}O_2NBr,HCl$ requires Cl, 9·5%), which rapidly crystallised, was collected, washed with ether, and dried in a vacuum (yield, 40—50%). The ethereal filtrate, on evaporation, gave a rapidly solidifying oil consisting of the unaltered *p*-bromobenzyloxy-ketone. The hydrochloride was basified with warm aqueous-alcoholic sodium carbonate, and when solution was complete the liquid was diluted with water and cooled to 0°. The *oxime* which separated (m. p. 170—172°) crystallised from dilute alcohol in colourless needles, m. p. 175° (Found: C, 57·3; H, 6·2; N, 4·0, 3·9. $C_{16}H_{20}O_2NBr$ requires C, 56·5; H, 6·2; N, 4·1%). It reduces Fehling's solution.

Reduction of the Oxime and its Acetyl Derivative.—We were unable to obtain satisfactory results on reducing the free oxime either by sodium wire and boiling alcohol or by sodium amalgam in boiling acetic acid. In each case very small amounts of basic material were isolated which gave an impure picrate, m. p. about 202—203°, and the reduction appeared to yield mainly non-basic substances which have not been identified.

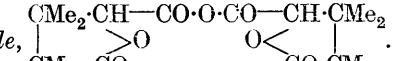
The oxime (1·6 g.) was therefore converted into its *acetyl* derivative by treatment with pure acetyl chloride (0·5 c.c.) in dry pyridine solution. The mixture was heated for a short time to complete the reaction, and then poured into water and extracted with ether. The extract was washed successively with water, dilute hydrochloric acid, dilute potassium hydroxide solution, and water, dried and evaporated. The residual oil solidified on being rubbed with ligroin; the product then crystallised from dilute alcohol as thin prisms, m. p. 84° (yield, 1·3 g.) (Found: C, 56·6; H, 6·1. $C_{18}H_{22}O_3NBr$ requires C, 56·8; H, 5·8%). This substance on reduction with sodium and boiling alcohol yielded a considerable amount of a non-basic product, which in the crude state had an odour of toluene, and on draining and crystallising from chloroform

yielded colourless needles, which melted at 161—162° and decomposed a few degrees higher. This substance seemed pure, but on analysis gave figures (C, 69·7, 69·5; H, 5·0, 4·7; N, 6·45, 6·5%) to which we can assign no simple formula. It gives no colour with ferric chloride, is insoluble in water and dilute acids and alkalis, and does not reduce Fehling's solution. Accompanying it in the crude neutral product is an oil which gives a deep crimson colour with ferric chloride. Besides these non-basic substances, an oily base was isolated, which yielded a picrate, m. p. 213° (decomp.) without purification, m. p. 215° (decomp.) after crystallisation from methyl alcohol–ether (Found: C, 46·9, 47·0; H, 5·9, 5·8; N, 14·6, 14·8. $C_{15}H_{22}O_8N_4$ requires C, 46·6; H, 5·7; N, 14·5%). The compound thus appears to be the *picrate* of 2-*hydroxy*-3 : 3 : 4 : 4-*tetramethyl*-cyclo*pentylamine*. A mixture with the isomeric picrate (p. 400) melted at about 195°.

Reduction of the p-*Bromobenzyl Derivative of the Hydroxy-ketone.*—On treatment with sodium amalgam in glacial acetic acid, under conditions in which the corresponding methyl compound is converted into its dihydro-derivative, no reduction occurs, the original substance being recovered unaltered (m. p. 85°. Found: C, 59·1; H, 5·8%). On reduction by means of boiling concentrated hydriodic acid 3 : 3 : 4 : 4-tetramethyl*cyclo*pentanone is formed (identified directly and through the semicarbazone), together with *p*-bromobenzyl iodide. We suppose that dealkylation constitutes the first stage of this reaction.

Examination of the Oily By-product obtained in the Alkylation of the Bromohydroxy-compound with p-*Bromobenzyl Bromide.*—This was reduced under the conditions used for the reduction of the crystalline bromo-*p*-bromobenzyl compound (p. 390), and the product, an oil, was converted into its oxime, also an oil which could not be purified. On reduction by means of sodium and boiling alcohol, this was moderately smoothly converted into 2 : 2 : 3 : 3-tetramethyl*cyclo*pentylamine, which was identified in the manner already described.

Action of Oxidising Agents on the Bromohydroxy-compound.—(1) *Sodium chlorate.* A solution of the bromohydroxy-compound (5 g.), sodium chlorate (13·0 g.), and osmium tetroxide (0·3 g.) in 150 c.c. of water containing a small excess of sodium hydroxide was kept at 40° in a thermostat for 72 hours; a considerable amount of chloride had then been formed. The solution was evaporated to a small bulk, cooled, filtered from the excess of sodium chlorate, acidified, and repeatedly extracted with ether. The residue, which readily solidified, was found to be separable by a prolonged series of fractional crystallisations from chloroform–ligroin into the lactonic

acid of $\gamma\gamma$-dihydroxy-$\alpha\alpha\beta\beta$-tetramethylglutaric acid and the lactonic acid of γ-hydroxy-$\alpha\alpha\beta\beta$-tetramethylglutaric acid. A more rapid method of proving the presence of these two substances is the following. The mixed acids were boiled for 1 hour with excess of acetic anhydride and the product was distilled under reduced pressure. After the excess of acetic anhydride had passed over, a small fraction was obtained, b. p. 150—200°/15 mm., and then the main bulk distilled at 220—245°/15 mm. The small fraction solidified, and after crystallisation was identified as the lactonic acid of the γ-hydroxy-γ-acetoxy-$\alpha\alpha\beta\beta$-tetramethylglutaric acid, m. p. 148°, described by Rothstein and Shoppee (*loc. cit.*). The main fraction, which also solidified, crystallised from benzene–ligroin in prisms, m. p. 177—178° (Found: C, 61·0; H, 7·7. $C_{18}H_{26}O_7$ requires C, 61·0; H, 7·4%). The compound is therefore the *dilactone anhydride*,  . On hydrolysis it yields the lactonic acid, m. p. 68°, of γ-hydroxy-$\alpha\alpha\beta\beta$-tetramethylglutaric acid.

(2) *Potassium permanganate.* The bromohydroxy-compound (2·2 g.) was treated with potassium permanganate (1·0 g.) in acetone solution at 0° in the presence of excess of carbon dioxide. After evaporation with water, filtration, and acidification, the acid product was extracted with ether and identified as the lactonic acid of $\alpha\alpha$-dihydroxy-$\alpha\alpha\beta\beta$-tetramethylglutaric acid (compare Francis and Willson, *loc. cit.*).

(3) *Potassium ferricyanide.* The bromohydroxy-compound (2·0 g.) was kept at 80° for 96 hours in an aqueous solution containing 18 g. of potassium ferricyanide and 4 g. of potassium carbonate. The product extracted with ether after acidification was the same lactonic acid.

(4) *Chromium trioxide.* Experiments were carried out with quantities of chromium trioxide corresponding with 1, 3, and 6 atoms of available oxygen, in glacial acetic acid solution. In each case, tetramethylsuccinic acid was obtained and no earlier product of oxidation could be recognised. The acid was isolated by distillation in steam, during which it probably passed over as its anhydride, which became rehydrated in the receiver. It was extracted from the distillate with ether, and crystallised from chloroform–ligroin containing only a very little alcohol (m. p. 190°).

(5) *Hydrogen peroxide.* The bromohydroxy-compound (2·4 g.) was dissolved in acetone and oxidised at the ordinary temperature with 6 c.c. of 6% aqueous hydrogen peroxide containing a little potassium carbonate. Acidification and extraction with ether

yielded only the lactonic acid of the αα-dihydroxytetramethylglutaric acid.

Action of Oxidising Agents on the Bromomethoxy-compound.—(1) *Ozone.* The methoxy-derivative (4·0 g.) was treated in chloroform solution with a stream of ozonised oxygen for 72 hours. Bromine was evolved, which the excess of oxygen carried over into a trap containing cooled chloroform, in which the bromine dissolved and was identified. The oily ozonides obtained after evaporation of the solvent in a vacuum were decomposed by shaking in ethereal solution (100 c.c.) with acetic acid (10 c.c.) and zinc dust (5 g.). The diluted and filtered solution was extracted with ether, and separated into neutral and acid fractions by means of aqueous sodium carbonate. The neutral portion on distillation yielded a fraction (1·5 g.), b. p. 155—165°/13 mm., which was shown by analysis and hydrolysis to consist essentially of the *lactone* of *methyl hydrogen γγ-dihydroxy-ααββ-tetramethylglutaric acid* (Found: C, 56·3; H, 7·3. $C_{10}H_{16}O_5$ requires C, 55·6; H, 7·5%), although it was probably impure, since we could not crystallise it. A fraction, b. p. 165—210°/13 mm., was also obtained, but its nature was not ascertained. The acid fraction yielded a small quantity of an oil which after some days partly solidified. The crystalline portion was identified by direct comparison and a mixed m. p. determination with the substance (m. p. 103°) described by Rothstein and Shoppee (*loc. cit.*) as dimethyl γ-keto-ααββ-tetramethylglutarate (Found: C, 57·3; H, 8·1. Calc.: C, 57·4; H, 7·9%). It is probably identical with the product, m. p. 93—97°, obtained by Francis and Willson (*loc. cit.*) by the action of diazomethane on the lactonic acid of γγ-dihydroxy-ααββ-tetramethylglutaric acid. Its formation in the reactions now described is very remarkable and suggests the implication of two molecules of the bromomethoxy-compound. Its appearance in the acid fraction may be explained by the supposition that its constitution is really that of the lactone of methyl hydrogen γ-hydroxy-γ-methoxy-ααββ-tetramethylglutarate, which would be soluble in alkali with ring fission, and, assuming its identity with Francis and Willson's methylation product, this structure corresponds with their method of preparation. It is readily soluble in cold 10% potassium hydroxide solution.

(2) *Potassium permanganate.* A solution of the bromomethoxy-compound (1·0 g.) in aqueous acetone containing sodium hydrogen carbonate was oxidised with potassium permanganate (0·38 g., = 1 atom of available oxygen), which was added gradually with stirring. The product, when worked up for organic acids in the usual way, yielded the lactonic acid of the dihydroxytetramethyl-glutaric acid.

*Ozonolysis of the Bromo-*p*-benzyloxy-compound.*—A solution of this substance (6·0 g.) in glacial acetic acid was treated with ozonised oxygen for several days. Bromine was liberated, and that carried over by the oxygen was caught in cooled chloroform and identified. The ozonides were decomposed by boiling with water, and the products were separated into a neutral and an acid fraction by means of ether and sodium carbonate. The neutral product was a yellow oil which, on treatment with semicarbazide acetate in aqueous alcohol, gave an immediate precipitate of p-*bromobenzaldehyde-semicarbazone*, which separated from alcohol in pearly plates, m. p. 232° (Found: C, 39·4; H, 3·3. $C_8H_8ON_3Br$ requires C, 39·7; H, 3·3%). The aqueous-alcoholic filtrate on dilution with water gave a small precipitate consisting of the unchanged bromo-*p*-benzyloxy-compound. The acid product contained two substances differing in solubility in water. The sparingly soluble compound was identified as *p*-bromobenzoic acid (leaflets from alcohol, m. p. 250°). A small amount of the same substance was collected from the chloroform solution of the ozonides. The soluble acid was obtained as an oil which became largely solid. The drained solid on crystallisation from chloroform–ligroin had m. p. 180—185° (decomp.), and was identified as tetramethylsuccinic acid by direct comparison with a specimen of this substance.

Action of Oxidising Agents on the Bromoacetoxy-compound.—(1) *Ozone.* The bromoacetoxy-compound (3·0 g.) was treated with ozonised oxygen in glacial acetic acid solution until no further absorption of ozone occurred. A yellow colour, which was not due to the liberation of bromine, was produced and disappeared on reduction of the ozonides with zinc dust after addition of ether. In another experiment the bromoacetoxy-compound was treated with ozone in chloroform solution, and here also no liberation of bromine took place. In this case, the ozonides were decomposed by boiling with water. Both experiments yielded tetramethylsuccinic acid (m. p. 190°. Found: C, 55·1; H, 8·4. Calc.: C, 55·1; H, 8·1%), and an acid gum the nature of which was not determined.

(2) *Potassium permanganate.* This experiment was carried out in the same way as the corresponding experiment with the bromomethoxy-compound. It yielded the same lactonic acid, which was obtained by crystallising the crude acid product from ethyl acetate–ligroin.

Oxidation of the Hydroxy-ketone.—Oxidation was effected by excess of 6% hydrogen peroxide in the presence of sodium carbonate at the ordinary temperature. The solution was extracted with ether, acidified, and again extracted. The residue from the second

extraction yielded αααββ-tetramethylglutaric acid, which was crystallised from ethyl acetate–ligroin (leaflets, m. p. 144°. Found: *M*, 190; C, 57·2; H, 8·4. Calc.: *M*, 188; C, 57·4; H, 8·5%).

Oxidation of 2 : 2 : 3 : 3-*Tetramethyl*cyclo*pentanone*.—Oxidation is not easily effected by means of cold neutral potassium permanganate in acetone, although αααββ-tetramethylglutaric acid can be obtained in this way in small yield. More satisfactory results were obtained by boiling the ketone under reflux with nitric acid (*d* 1·20) until oxides of nitrogen ceased to be evolved, the ketone which collected in the condenser being returned to the liquid from time to time. The nitric acid solution was extracted with a large volume of ether, and the extract was washed six times with small amounts of water, dried, and evaporated. The solid residue, after being washed with benzene and crystallised from ethyl acetate–ligroin, was identified as αααββ-tetramethylglutaric acid (m. p. 144°) by direct comparison and mixed m. p. determination. A further small quantity was obtained by evaporation of the aqueous washings.

Bromination of the Hydroxy-ketone.—(1) *In chloroform*. The hydroxy-ketone readily absorbs 2 atoms of bromine in cold chloroform, but an excess over this quantity is not decolorised. On removing the chloroform, hydrogen bromide and excess of bromine, the bromohydroxy-compound is obtained in an almost pure state (m. p. 115—116°; after purification, m. p. 116°).

(2) *In glacial acetic acid*. In this solvent 4 atoms of bromine are rapidly absorbed and the product is the orange dibromo-diketone (m. p. 182°) described by Francis and Willson.

Dichlorophorone (1 : 4-*Dichloro*-2 : 2 : 3 : 3-*tetramethyl*-[0,1,2]-dicyclo*pentanone*).—Phorone tetrachloride (m. p. 59°) and dichlorophorone (b. p. 115—117°/18 mm., $n_D^{24°}$ 1·5074, $d_4^{24°}$ 1·1661; compare Hellthaler, *Annalen*, 1919, **406**, 150) were obtained by methods similar to those used for the preparation of the bromine analogues.

1-*Chloro*-2 : 2 : 3 : 3-*tetramethyl*-[0,1,2]-dicyclo*pentan*-4-*ol*-5-*one* (1-*Chloro*-2 : 2 : 3 : 3-*tetramethyl*-Δ^5-cyclo*penten*-5-*ol*-4-*one*).—This was prepared by hydrolysis of dichlorophorone, following Francis and Willson's method for the corresponding bromine derivatives, and crystallised from dilute alcohol, from which it separated in well-formed, colourless needles, m. p. 116° (Found: C, 57·2; H, 6·9. $C_9H_{13}O_2Cl$ requires C, 57·2; H, 6·9%).

The *acetyl* derivative, prepared in the same way as its bromo-analogue, separates from dilute alcohol in prisms, m. p. 47° (Found: C, 57·3; H, 6·5. $C_{11}H_{15}O_3Cl$ requires C, 57·2; H, 6·5%).

1 : 1-*Dichloro*-2 : 2 : 3 : 3-*tetramethyl*cyclo*pentanedione*.—This substance was prepared from the chlorohydroxy-compound by treat-

ment with excess of chlorine in cold glacial acetic acid solution. It separates from alcohol in orange, foliated masses, m. p. 187° (Found : C, 48·6; H, 5·5. $C_9H_{12}O_2Cl_2$ requires C, 48·4; H, 5·4%).

On boiling in aqueous-alcoholic solution with addition of carbamide to destroy the hypochlorous acid, the chlorohydroxy-compound is formed.

1-*Chloro*-1-*bromo*-2 : 2 : 3 : 3-*tetramethyl*cyclo*pentanedione* was prepared by the action of bromine in acetic acid solution on the chlorohydroxy-compound, and crystallised from alcohol in orange, foliated masses, m. p. 178° (Found : C, 40·9; H, 4·8. $C_9H_{12}O_2ClBr$ requires C, 40·4; H, 4·5%). The same substance is formed when the bromohydroxy-compound is treated with chlorine in acetic acid, but in this case an unidentified colourless by-product, m. p. 197°, is also formed in small amount.

Reduction with boiling aqueous-alcoholic carbamide yields the chlorohydroxy-compound exclusively. Since the bromo- and chlorohydroxy-compounds melt at the same temperature and give somewhat small m. p. depressions in admixture, the reduction product was converted into its acetyl derivative (bromo-, m. p. 74°; chloro-, m. p. 47°) which was crystallised in fractions from dilute alcohol, in which the bromoacetoxy-compound is less soluble than its chloro-analogue; all the fractions had m. p. 47°.

1 : 1-*Dibromo*-2 : 2 : 3 : 3-*tetramethyl*cyclo*pentanedione*.—This substance (herring-bone-like clusters of orange rhomboids, m. p. 182°. Found : C, 34·6; H, 3·9. Calc. : C, 34·7; H, 3·8%), which Francis and Willson found to be reduced incompletely by boiling with water or alcohol, is, like its analogues, quantitatively converted into the halogenohydroxy-compound by boiling with aqueous-alcoholic carbamide.

This paper is published mainly in order to place on record the observations which have accumulated during the four years in which the work has been in progress; but it is realised that, in constitutional problems of this character, conclusions must necessarily be regarded as provisional, and accordingly further experiments on α-ketols and dialkylideneketones are in progress, which may help to resolve some of the issues raised. We would mention that the method of correlating the tautomeric substances, through their oximes or derivatives of their oximes, with the saturated cyclic amines, which has yielded illuminating results, was originally suggested to us by Mr. W. A. Wightman, and that on many occasions Dr. F. R. Goss has placed his time and great skill in micro-analytical technique at our service. Generous assistance in defraying the heavy cost of the investigation has been given by the Royal Society

and the Commissioners of the 1851 Exhibition, to whom our thanks are due. At one stage the continuity of the work was maintained by means of a valuable gift of the bromohydroxy-compound from Professor Francis.

THE UNIVERSITY, LEEDS. [*Received, December 17th*, 1927.]