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Autocondensation of Cyclic Ketones

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The reactions of cyclohexanone and 2-, 3-, and 4-methylcyclohexanones, cyclopentanone, and cycloheptanone, mainly under the action of acid and alkaline reagents, have been examined. The conditions governing the formation and the structures of the dimeric, trimeric, and polymeric autocondensation products—$\alpha\beta$-, $\beta\gamma$-, and other unsaturated ketones, hydroxyketones, compounds with furan or hydrogenated furan rings, dihydropyrans, hydrocarbons such as dodecahydrotriphenylene, and other compounds—have been discussed.
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I. INTRODUCTION

Cyclohexanone is the starting material in the manufacture of ϵ-caprolactam. Under the conditions of the synthesis[1] of cyclohexanone by catalytic dehydrogenation of cyclohexanol[2] or the oxidation of cyclohexane, and during storage[3], and in subsequent conversion of cyclohexanone into ϵ-caprolactam[4], side reactions occur, including autocondensation reactions. As a result impurities appear in the ϵ-caprolactam which impair its quality[5] as a monomer for the manufacture of polyamide resins. Moreover, cyclohexanone has found wide applications in organic synthesis as a solvent in the processing of polymers. Here too, when cyclohexanone is heated or comes into contact with various chemical reagents, side autocondensation reactions are possible.

The cyclohexanone autocondensation products have also found some applications. For example, it has been suggested that they be used for the stabilisation of poly(vinyl chloride)[6] and as intermediates[7] or starting materials[8] in the manufacture of plastics, herbicides[9,10], insecticides[11], and polystyrene plasticisers[12].

In the present review an attempt is made to give a general account of the conditions governing the formation and structure of the cyclohexanone autocondensation products. The autocondensation of other cyclic ketones, many of which have found practical application although on a more restricted scale than cyclohexanone, is also considered.

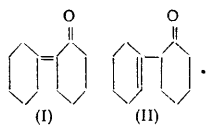
Among cycloalkanones, cyclohexanone is the most reactive, as can be seen, for example, from the rate of formation of oximes or cyanohydrins in the reactions of these cyclic ketones with hydroxylamine and hydrogen cyanide respectively. The differences in the reactivities of cycloalkanones with 5,6, and 7 carbon atoms are associated with their stereochemical structures. While cyclohexanone exists predominantly in the unstrained chair form, cyclopentanone and cycloheptanone molecules are extremely strained systems which in the case of rings with 7 and more members is due to the interaction between hydrogen atoms and the carbonyl oxygen (not linked directly) and in 5-membered rings there is classical (Baeyer) ring strain. The characteristics of the structure of cycloalkanones are reflected in their behaviour in autocondensation reactions. Indeed the autocondensation reactions of cyclohexanone are more varied than those of cyclopentanone and cycloheptanone. There are no literature data on the autocondensation of cyclic ketones with higher molecular weights.

II. DIMERIC AUTOCONDENSATION PRODUCTS

The autocondensation of cycloalkanones takes place predominantly under the influence of condensing agents. Those employed are substances with acid or basic properties.

I. Ketones

Cyclohexanone. In the autocondensation of cyclohexanone a liquid unsaturated product A with the composition $C_{12}H_{18}O$ is formed most readily. The unsaturated ketone A was obtained for the first time by Wallach[13] in 1896 by allowing cyclohexanone to stand for a long time with sodium ethoxide. Since the ketone A can have the structure of either 2-cyclohexylidenecyclohexanone (I) or 2-Δ^1-cyclohexenylcyclohexanone (II), the structure of the liquid ketone A began to be investigated from that time and a search was made for other methods of its synthesis.



(I) (II)

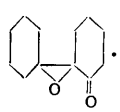
The liquid ketone A is obtained by the autocondensation of cyclohexanone in the presence of sodamide[14,15], by heating with potassium hydroxide[16-19], on prolonged standing with sodium methoxide in methanol[20], on refluxing with concentrated sulphuric acid[17,21] and *p*-toluenesulphonic acid, and by reaction with 60% sulphuric acid[22] or 70% perchloric acid[23]. It is also formed from cyclohexanone on prolonged refluxing[24], on heating under pressure[25], on heating with lithium phosphate[26], calcium hydride[27,28], zinc chloride[29], lead dioxide[30], alumina (under pressure)[31], aluminium chloride[32], boron chloride[33], boron trioxide[34], aluminium phenoxide[35], tri-isobutylaluminium[36], acetoxydi-isobutylaluminium[37], and phosphorus pentoxide[16], by interaction with titanium tetraisopropoxide[38], dibromogermane, or polymeric dichlorogermane[39], by heating with cyclohexanone azomethines[8] and ion-exchange resins[7,40-42],

by ultraviolet irradiation (in the presence or absence of hydrogen chloride) in monochloroacetone solution[43], etc.

The ketone A is also formed as a side product in various reactions of cyclohexanone, for example in the condensation with methanol[44], trichlorogermane[38], acrylonitrile[45], 4-vinyl pyridine[46], etc.

Either structure (I) or (II) has been attributed to the liquid ketone A or it was regarded as a mixture of ketones (I) and (II). Various reactions have been employed to establish the structure. In the hydrogenation in the presence of solid catalysts[47], reaction with benzaldehyde[29], condensation with ethyl sodiocyanoacetate[48], and in the Wolf–Kishner reaction[49], the liquid ketone A reacts as an $\alpha\beta$-unsaturated ketone (I). In the reaction with nascent hydrogen[47,50], in oxidation with ozone[48] or potassium permanganate[51], and in methylation with methyl iodide[48], the ketone A reacts as a $\beta\gamma$-unsaturated ketone (II). The absence of appreciable exaltation of molecular refraction[42,51] was regarded as proof of the endocyclic position of the double bond in the ketone.

In 1942 Reese[51] obtained a solid ketone B (m.p. 57°C) with the same composition as the liquid ketone A. There is no doubt about the position of the double bond in the $\alpha\beta$-position in the ketone B and therefore Reese believed that the liquid ketone A is a $\beta\gamma$-unsaturated compound; however, when the ketone A was oxidised with hydrogen peroxide, a small amount of compound (III), which is a product of the addition of oxygen to the exocyclic double bond, was isolated. The same compound is formed in a quantitative yield when the ketone B is oxidised with hydrogen peroxide[51]:



(III)

Kon and Nutland[48] showed that the products of the reaction of the liquid ketone A with semicarbazide is a mixture of two semicarbazones with high (main substance) and low (small amount) melting points, which they believe to differ in the position of the double bond. However, these investigators[48] did not succeed in obtaining the ketone in any one form from the high-melting semicarbazone: on reaction with semicarbazide, the regenerated liquid ketone again gave a mixture of semicarbazones. The product of the reaction of the liquid ketone A with 2,4-dinitrophenylhydrazine is also a mixture[52] of two hydrazones: orange (a colour characteristic of a ketone with an endocyclic double bond) and red (corresponding to an $\alpha\beta$-unsaturated carbonyl compound). When this mixture of hydrazones is allowed to stand with a solution of sodium hydroxide in methanol, the red form of the hydrazone is completely converted into the orange form.

Spectroscopic studies on the ketones A and B showed that their ultraviolet spectra have the same absorption maximum at 254.0–257.5 nm,[53-58] which is characteristic of $\alpha\beta\beta$-trisubstituted $\alpha\beta$-unsaturated carbonyl compounds[59]. However, the extinction coefficients of the two ketones differ—the value for the solid ketone B [56] is 6500 and that for the liquid ketone A is smaller[19,55,58], amounting to 680–800.

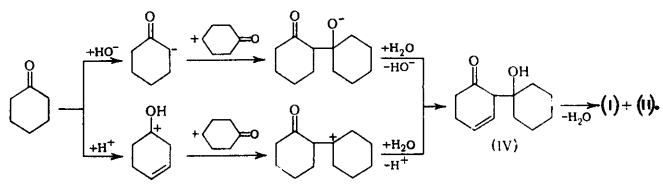
The infrared spectrum of the solid ketone B shows only one maximum[56,57] at 1670–1680 cm^{-1}, corresponding to the $\alpha\beta$-unsaturated ketone (I). At the same time the infrared spectrum[57] of the liquid ketone A has an intense band at 1710 cm^{-1}, characteristic of the $\beta\gamma$-unsaturated ketone (II), and a weak band at 1680 cm^{-1}.

The NMR study of the ketones A and B showed[57] that the spectrum of the solid ketone B contains no signals due to vinylic protons, which the spectrum of the liquid ketone A revealed the presence of a vinylic proton.

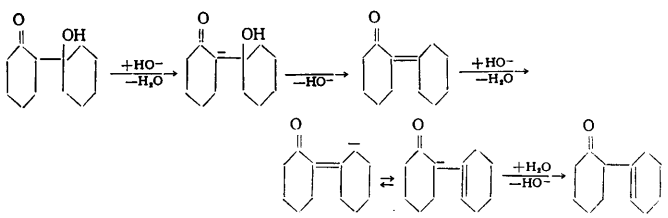
Thus the available data on the chemical and physicochemical properties of the liquid ketone A lead to the conclusion that it is a mixture not of two stereoisomers[54] but of two structural isomers with structures (I) and (II). The content of the solid ketone in this mixture is various—55% according to some data[52] and 7–20% according to others[19,57,60], which can be explained by the use of different methods of synthesis and identification. The variable composition of the liquid ketone A is evidently responsible for the wide variation of the published literature values of the constants for the product: b.p. [8,33], 142–150°C at 15 mmHg, refractive index[16,45] n_D^{20} = 1.5048–1.5112, and specific gravity[32,61] d_4^{20} = 1.0010–1.0072.

The fact that the liquid ketone A behaves in many reactions as a ketone with structures (I) or (II) can probably be accounted for by the migration of the double bond in the course of the reaction.

The formation of a mixture of ketones (I) and (II) in the autocondensation of cyclohexanone under the influence of bases and acids can be represented by the following mechanism:



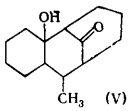
The $\alpha\beta$-unsaturated ketone (I) formed initially by the dehydration of the hydroxyketone (IV) isomerises[19] to the $\beta\gamma$-ketone (II):



Owing to the similarity of the boiling points of ketones (I) and (II), they cannot be separated by vacuum distillation. Bibo[19] subjected the liquid product A to low-temperature crystallisation and isolated a compound with m.p. 9°C and an ultraviolet absorption maximum at 291 nm (ϵ_{max} = 46), which is characteristic of an isolated C=O group. The ultraviolet spectrum of this compound did not show the presence of bands corresponding to the C=C–C=O group and the product is probably the pure $\beta\gamma$-unsaturated ketone (II).

The autocondensation of aliphatic ketones is known to give rise together with unsaturated carbonyl compounds also to stable hydroxyketones, for example, acetone gives the diacetone alcohol[62] and triacetone dialcohol[38], which can be readily converted into $\alpha\beta$-unsaturated ketones—mesityl oxide and phorone. It might have been expected that, under the cyclohexanone autocondensation conditions, the hydroxyketone (IV) forms as an intermediate in the synthesis of ketones (I) and (II). However, until recently the hydroxyketone (IV) could not be isolated from the

cyclohexanone autocondensation products. The first mention of the hydroxyketone (IV) appeared in 1934 when the reaction of cyclohexanone with Grignard reagents (phenylmethyl aminomagnesium bromide[63] and t-butylmagnesium bromide[64]) was achieved. The compound isolated from the reaction products melted at 56°C and on reaction with semicarbazide yielded the semicarbazone[63] of the hydroxyketone (IV) or the liquid product A. In 1952 Stanek[16] reported that, in the autocondensation of cyclohexanone in the presence of alcoholic potassium hydroxide, he isolated a solid hydroxyketone (m.p. 160°C)—2-(1-hydroxycyclohexyl)cyclohexanone (IV). However, Plešek and Munk[65] showed convincingly that this compound is in fact 2-hydroxy-4-methyl-2,3-cyclohexanobicyclo [1,3,3] nonan-9-one (V)--the product of the interaction of two cyclohexanone molecules with one acetaldehyde molecule formed from ethanol under the reaction conditions:

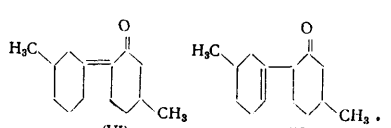


(V)

Bibo[19] isolated from the products of the reaction of cyclohexanone with powdered potassium hydroxide (20°C) a crystalline compound (m.p. 32–33°C) with the composition $C_{12}H_{20}O_2$, which may be vacuum-distilled (0.1 mmHg) almost without decomposition. An isolated carbonyl group (λ_{max} = 290 nm, ϵ_{max} = 21), a hydrogen-bonded OH group (3528 cm^{-1} band in the infrared spectrum), and a hydrogen-bonded C=O group (1695 cm^{-1} band) were found in this compound. On the basis of these data, the structure of the hydroxyketone (IV) was attributed to the compound $C_{12}H_{20}O_2$. In addition, Bibo[19] repeated the reaction of cyclohexanone with t-butylmagnesium bromide described by Ivanoff and Spassoff[64] and isolated from the reaction mixture a compound $C_{12}H_{20}O_2$ with m.p. 32–33°C, which did not depress the melting point when mixed with the compound having the same composition synthesised by the action of powdered potassium hydroxide on cyclohexanone.

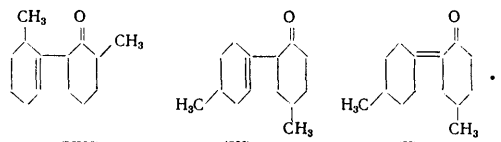
Bibo showed[19] by thin-layer chromatography that in the autocondensation of cyclohexanone in the presence of potassium hydroxide at 20°C the reaction mixture contained the hydroxyketone (IV), while in the autocondensation of cyclohexanone in the presence of the same condensing agent but in boiling toluene solution with continuous removal of the water formed in the reaction the hydroxyketone (IV) was already absent from the reaction product in the very early stages and only the ketones (I) and (II) could be detected.

Alkylcyclohexanones can also undergo autocondensation with formation of dimeric products. When 3-methylcyclohexanone was allowed to stand with sodium ethoxide, on heating with calcium hydride[27] and potassium hydroxide[66], and on irradiation of 3-methylcyclohexanone in the presence of hydrogen chloride in chloroacetone solution[43], a liquid ketone with the composition $C_{14}H_{22}O$ was obtained, to which the structure of either the $\alpha\beta$-unsaturated carbonyl compound (VI)[27,67] or the $\beta\gamma$-unsaturated carbonyl compound (VII)[51,66,68] was attributed. At the same time Reese[51] synthesised a solid (m.p. 71°C) ketone with the composition $C_{14}H_{20}O$, in which the carbon–carbon double bond is in the $\alpha\beta$-position relative to the carbonyl group [compound (VI)]:



(VI) (VII)

The corresponding liquid ketones, to which structures (VIII) and (IX) were attributed, were synthesised by heating 2-methylcyclohexanone with potassium hydroxide[66] and 4-methylcyclohexanone with barium hydroxide[66] or when the ketones were exposed to ultraviolet light and hydrogen chloride in monochloroacetone solution[43]:

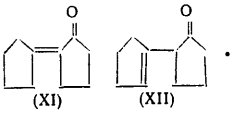


(VIII) (IX) (X)

It has been stated[36] that the dimeric product of the autocondensation of 4-methylcyclohexanone has the structure of the $\alpha\beta$-unsaturated ketone (X). However, it should be noted that the liquid dimeric products of the autocondensation of 2-, 3-, and 4-methylcyclohexanones as well as the liquid product A of the autocondensation of cyclohexanone are mixtures of ketones with $\alpha\beta$- and $\beta\gamma$-double bonds. The infrared spectra of these compounds have bands at 1718–1720 and 1692–1695 cm^{-1} characteristic of the C=O and C=C–C=O groups respectively.

Cyclopentanone. One dimeric product of the autocondensation of the ketone is known. The liquid dimeric autocondensation product C with the composition $C_{10}H_{14}O$ is formed from cyclopentanone on heating under the conditions of its synthesis from adipic acid[69], in the presence of sodium ethoxide[13,70,71] and methoxide[72], potassium t-butoxide[73,74], potassium hydroxide[16,71,75–77], and alcoholic potassium hydroxide[16], on prolonged standing with sodium hydroxide[78], on reaction with aqueous alcoholic sodium hydroxide[79], on heating with a complex of n-butyllithium and trimethylboron[72], on saturating cyclopentanone with hydrogen chloride[71,80], on heating with sulphuric acid[81], calcium hydride[27] or carbide[27,82], lithium phosphate[26], and tri-isobutylaluminium[36], and on passing cyclopentanone vapour over alumina[75,77]. The liquid product C is obtained also by the reaction of cyclopentanone with aluminium chloride[83], t-butylmagnesium chloride[84], isopropylmagnesium halides[85,86], aluminium and magnesium amalgam[87], phosphorus pentoxide or polyphosphoric acid[70], etc. The product C is formed when cyclopentanone is reduced with aluminium isopropoxide[88], under the conditions of the reaction with acetone[89], etc.

The exaltation of the molar refraction of the liquid product C, calculated for 2-cyclopentylidenecyclopentanone (XI)[48,82] has the normal value. Nevertheless on ethylation the product C behaves as a $\beta\gamma$-unsaturated carbonyl compound (XII),[48] while the reaction with ethyl sodiocyanoacetate and oxidation with oxone lead to the formation of compounds characteristic of the $\alpha\beta$-unsaturated ketone (XI):[48]



(XI) (XII)

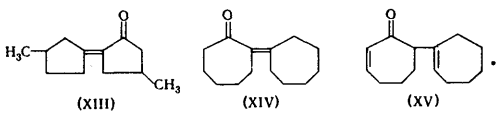
Moreover, Kon and Nutland[48] showed that, when the product C interacts with semicarbazide, a mixture of high-melting and low-melting semicarbazones in proportions of 20:1 is formed, and they suggest that the semicarbazones differ in the position of the double bond. The liquid carbonyl compound isolated from the high-melting semicarbazone was converted on treatment with semicarbazide into the same mixture of semicarbazones in the same proportions.

The ultraviolet spectrum of the liquid product C has an absorption maximum (at 254–259 nm)[53,56,79], characteristic of $\alpha\beta\beta$-trisubstituted $\alpha\beta$-unsaturated carbonyl compounds[59]. The extinction coefficient is high[53,56,79] (ϵ_{max} = 10700–12600) and corresponds to $\alpha\beta$-unsaturated ketones[59]. The infrared spectrum shows an intense band[56] (1700 cm^{-1}) due to an $\alpha\beta$-unsaturated ketone. At the same time the literature values of the specific gravity[75,76] d_4^{20} vary in the range 1.0172–1.0217 and the refractive indices[75,76] n_D^{20} vary in the range 1.5098–1.5211.

With rare exceptions[26], the structure of 2-cyclopentylidenecyclopentanone (XI) is attributed to product C. However, on the basis of the data quoted one cannot exclude the possibility that it contains also a small amount of 2-Δ′-cyclopentenylcyclopentanone (XII).

It has been stated that in the interaction of cyclopentanones with phenylmethyl aminomagnesium bromide[63], t-butylmagnesium bromide, or isopropylmagnesium bromide[64], the primary autocondensation product is a dimeric hydroxyketone. However, there are no reliable analytical data confirming the structure of this hydroxyketone.

Under the action of hydrochloric acid[13] or on heating with calcium hydride[27], 3-methylcyclopentanone is converted into the unsaturated ketone (XIII):

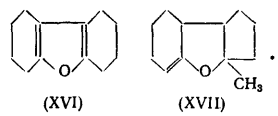


(XIII) (XIV) (XV)

When cycloheptanone is heated with lithium phosphate[26], potassium t-butoxide[73], or potassium hydroxide[90], an autocondensation product with the composition $C_{14}H_{22}O$ is obtained, which is regarded as a mixture of 2-cycloheptylidenecycloheptanone (XIV) and 2-Δ′-cycloheptenylcycloheptanone (XV), since the infrared spectrum showed absorption bands at frequencies of 1720 and 1692 cm^{-1} (see p. 555).

2. Oxygen-containing Heterocyclic Compounds

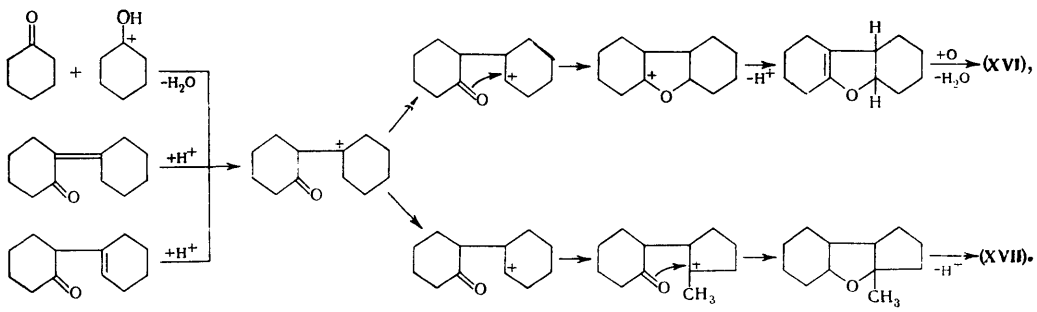
In 1964 Svetozarskii et al.[90] showed that oxygen-containing heterocycles may be formed in the autocondensation of cyclohexanone. 1,2,3,4,5,6,7,8-Octahydrodibenzofuran (XVI) and 2-methyl-2,3-cyclopentano-4,5-cyclohexeno-(Δ⁵)-2,3,4,5-tetrahydrofuran (XVII) were isolated from the products of the reactions of cyclohexanone, the ketone (I),[91] or the liquid mixture[66] of the ketones (I) and (II) (product A) with a large amount of concentrated sulphuric acid in the absence of a solvent[90] or in the presence of benzene[66]:



(XVI) (XVII)

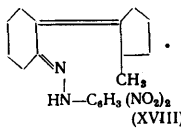
The substituted tetrahydrofuran (XVII) and octahydrodibenzofuran (XVI) are formed in small amounts as side products under conditions of the Beckmann rearrangement of cyclohexanone oxime under the influence of oleum and when the product of the rearrangement comes into contact subsequently with cyclohexanone[4]. Compound (XVI) is obtained in small amounts[92] also when a mixture of the $\alpha\beta$- and $\beta\gamma$-unsaturated ketones (I) and (II) is passed over a zinc–iron catalyst at 450°C.

The formation of compounds (XVI) and (XVII) under the conditions of the autocondensation of cyclohexanone under the influence of concentrated sulphuric acid can be explained by the following mechanism[90,91]:



In this reaction the oxidising agent is probably sulphuric acid.

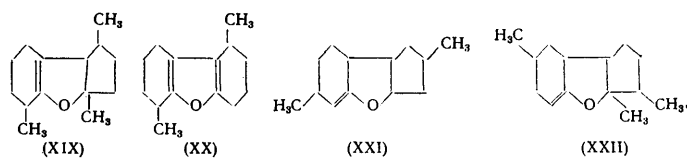
On reaction with 2,4-dinitrophenylhydrazine, compound (XVII) gives rise[90] to the hydrazone of an $\alpha\beta$-unsaturated ketone (XVIII):



(XVIII)

When an attempt was made to regenerate the $\alpha\beta$-unsaturated ketone from this 2,4-dinitrophenylhydrazone (XVIII), only the initial substituted tetrahydrofuran (XVII) was isolated[90]. Probably the steric positions of the groups in 2-(2-methylcyclopentylidene)cyclohexanone are so unfavourable that ring closure to the more stable tetrahydrofuran derivative (XVII) takes place readily. The instability of this ketone is in all probability due to the powerful interaction of the carbonyl oxygen with the methyl group, which entails a considerable deformation of the $\pi-\pi$ conjugated system leading to the migration of the double bond with simultaneous cyclisation to the substituted tetrahydrofuran (XVII).

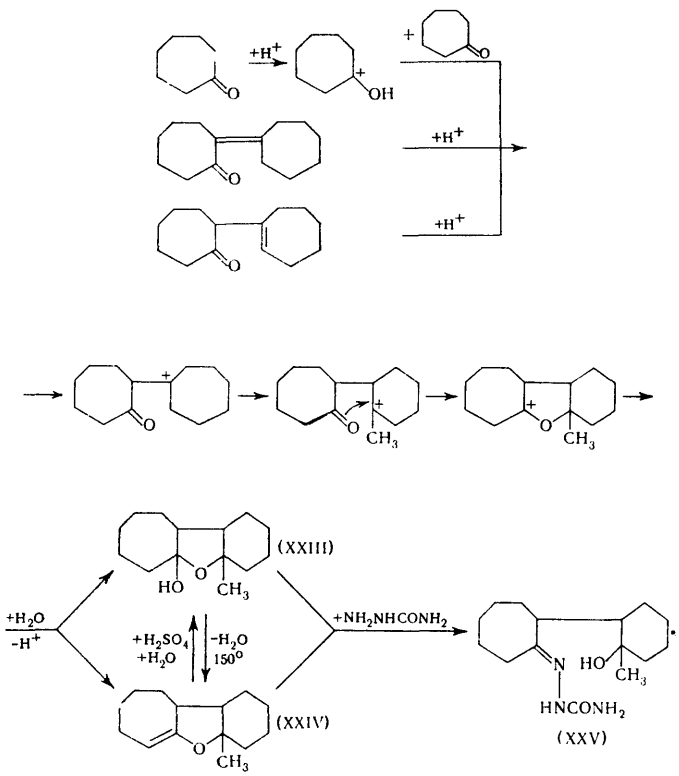
2-, 3-, and 4-Methylcyclohexanones undergo similar reactions. Two compounds (XIX) and (XX) were isolated[66] from the products of the reaction of 2-methylcyclohexanone with concentrated sulphuric acid[66], while in the case of 3-methylcyclohexanone[66,91] and 4-methylcyclohexanone[66], only the substituted tetrahydrofurans (XXI) and (XXII) respectively were obtained:



(XIX) (XX) (XXI) (XXII)

When cycloheptanone or the dimeric product of its autocondensation in the presence of sulphuric acid is allowed to stand[93], rearrangement with intramolecular cyclisation also takes place. A distinctive feature of this reaction is the formation together with the liquid unsaturated tetrahydrofuran derivative (XXIII) of a solid substituted tetrahydrofuran derivative (XXIV) without a double bond but containing an associated hydroxy-group.

The scheme below shows that compounds (XXIII) and (XXIV) can be interconverted and yield the same semicarbazone (XXV) on reaction with semicarbazide:



It is noteworthy that the contraction of one of these rings on autocondensation of cycloheptanone may lead to the formation not of a six-membered ring, as shown in the mechanism [compounds (XXIII) and (XXIV)], but a five-membered ring[93]. To determine more accurately the structure of compounds (XXIII) and (XXIV), additional studies are necessary.

Thus the common reaction of the cycloalkanones considered in this section is autocondensation with formation of dimeric unsaturated carbonyl compounds, which are mixtures of ketones with endocyclic and exocyclic carbon–carbon double bonds.

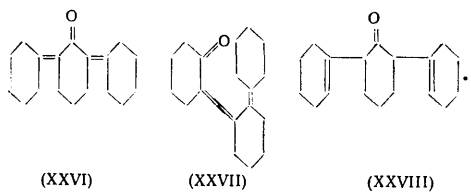
Cycloalkanones behave differently in reactions with concentrated sulphuric acid: cyclohexanone, 2-, 3-, and 4-methylcyclohexanones, and cycloheptanone are converted into tetrahydrofuran derivatives, while cyclopentanone and 2-ethylcyclohexanone do not enter into this reaction[66]. The inertness of cyclopentanone is probably due to the fact that the conversion of five-membered rings into four-membered rings is unfavourable owing to energy factors. A product of type A also was not obtained from 2-ethylcyclohexanone, probably because of the hindrance of the carbonyl oxygen by the ethyl group[66] in the 2-position.

III. TRIMERIC AND POLYMERIC AUTOCONDENSATION PRODUCTS

1. Ketones

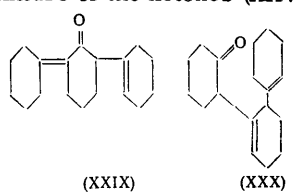
As early as 1896 Wallach[13] isolated from the products of the reaction of cyclohexanone with sodium ethoxide a steam-involatile liquid substance, which set on standing into a yellow crystalline mass. Wallach suggested that the substance is an unsaturated ketone with the formula $C_{18}H_{26}O$ formed by the condensation of three cyclohexanone molecules with evolution of two water molecules. On heating cyclohexanone in methanol solution with concentrated sulphuric acid, Mannich[21] obtained a liquid product D with the composition $C_{18}H_{26}O$, from which no solid compound of any kind could be obtained even after prolonged standing. The product D was also synthesised by the autocondensation of cyclohexanone under the influence of zinc chloride[29], alumina[31], titanium tetraisopropoxide[38], ion-exchange resins[40], 60% sulphuric acid[91], etc.

The liquid product D has been regarded[21,31,38] as an unsaturated ketone—2,6-dicyclo hexylidenecyclohexanone (XXVI):



(XXVI) (XXVII) (XXVIII)

The structures of the $\alpha\beta$- $\gamma\delta$-unsaturated ketone[29] (XXVII) and 2,6-dicyclohexenylcyclohexanone (XXVIII)[16] have also been attributed to the trimeric autocondensation product of cyclohexanone. It has been stated[18,36] that the product D is a mixture of the ketones (XXVI) and (XXIX):



(XXIX) (XXX)

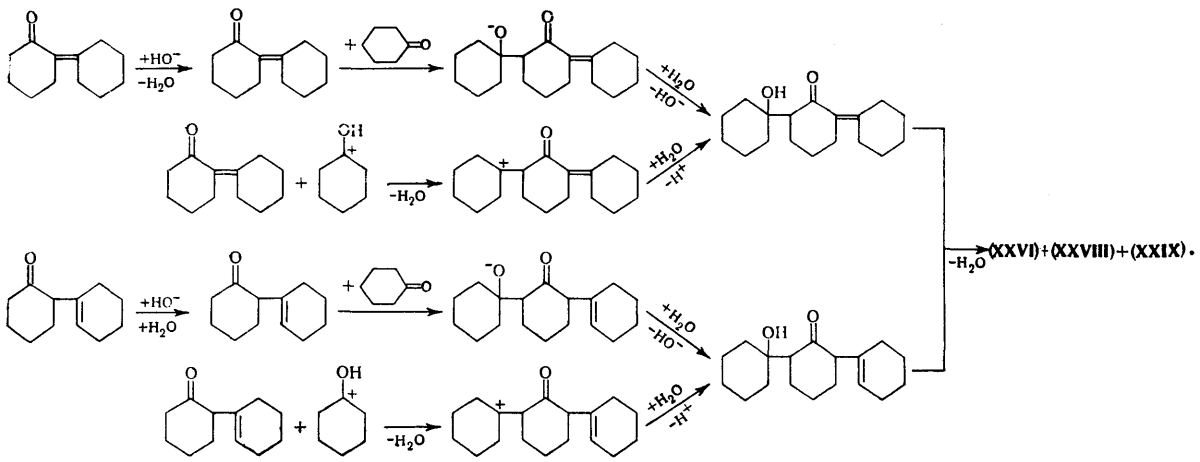
Among the structures quoted, that of compound (XXVII) is quite unacceptable, since this ketone cannot exist owing to steric hindrance[94]. The other hypothesis also proved to be incorrect. The most correct appears to be the view of Munk and coworkers[56,95], who showed that the liquid product D is a mixture of the ketones (XXVIII) and (XXIX). The infrared spectrum of this product does not show a band at 1662 cm^{-1}, which would have been characteristic of the ketone (XXVI), but bands at 1716 cm^{-1} (isolated C=O group) and 1685 cm^{-1} (C=C–C=O group) have been found.

Further studies on the composition of the liquid product D, obtained by refluxing cyclohexanone in toluene solution with sodium hydroxide, with continuous removal of the water formed, showed[19] that it is a mixture of three ketones: *cis*-(XXVIII) (m.p. 79°C), *trans*-(XXVIII) (colourless liquid), and (XXIX) with a very small amount of the ketone (XXVI).

The *cis*-isomer of the ketone (XXVIII) was obtained as a pure solid compound also by other investigators[17,18]. It is noteworthy that Mleziva[17], who was the first to isolate this ketone, erroneously attributed to it the structure of compound (XXX). 2,6-Dicyclohexylidenecyclohexanone (XXVI) (m.p. 144.5–146.5 °C) was synthesised[95] by eliminating

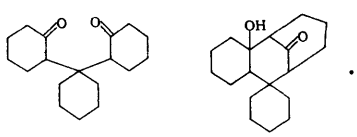
hydrogen chloride from the products of the addition of hydrogen chloride to a liquid mixture of ketones D or to 2,6-dicyclohexenylcyclohexanone (XXVIII).

The liquid trimeric product D is also formed[17,29] on heating a mixture of cyclohexanone with the mixed dimeric ketones (I) and (II) or the product A alone[18] in the presence of condensing agents. Therefore, one may assume[17,29] that in the synthesis of a mixture of trimeric ketones D directly from cyclohexanone the intermediates are the dimeric ketones (I) and (II). On the other hand, the formation of the product D from the liquid mixture of ketones (I) and (II) alone[18] must be preceded by their hydrolysis[96]. The formation of a liquid mixture of trimeric ketones in the autocondensation of cyclohexanone or its condensation with the liquid product A may be represented by the following mechanisms:



The interaction of 4-methylcyclohexanone with tri-isobutylaluminium gives a mixture[36] of trimeric autocondensation products, the structure of which was not investigated.

Prolonged standing of cyclohexanone with sodium methoxide in methanol or heating the ketone with sodium hydroxide in methanol lead to the formation of a solid product (m.p. 182°C), to which the structure of compound (XXXI) was attributed[20]. However, more detailed studies showed[97] that the 1,5-diketone formed initially readily cyclises and exists as a tetracyclic hydroxyketone with the structure (XXXII):

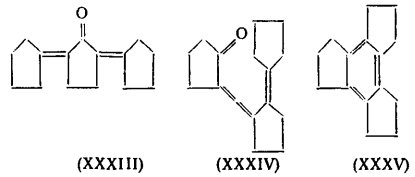


(XXXI) (XXXII)

The reaction of cyclohexanone or the liquid mixture of ketones (I) and (II) with concentrated sulphuric acid in the presence of water, methanol, or butanol leads to a product of the autocondensation of six cyclohexanone molecules with the composition $C_{36}H_{52}O_2$, which is a diketone with three double bonds, two of which are conjugated with the carbonyl group and one is isolated[98].

Cyclopentanone. When cyclopentanone is heated with potassium hydroxide[16,71,75-77], sodium methoxide, or a complex of butyl-lithium with trimethylboron[72], potassium t-butoxide[73], potassium n-butoxide[74], and tri-isobutylaluminium[36], when it reacts with sodium ethoxide[13,70] and solid sodium hydroxide[78], or when its vapour is passed over alumina[75,77], an unsaturated trimeric autocondensation product E with the composition $C_{15}H_{20}O$ is obtained as a yellow solid[56,78] with m.p. 83–84°C.

The structure of 2,5-dicyclopentylidenecyclopentanone (XXXIII) has been attributed to product E.[13,16,70-74,78] It has been suggested[76,77] that the product E (m.p. 83–84°C) is a ketone with the structure (XXXIV). However, Mayer[70] and Plešek[71] disproved this hypothesis on the basis of numerous observations and in particular the following findings: (a) the saturated ketone 2,5-dicyclopentylcyclopentanone obtained in the reduction of the ketone (XXXIII) does not react with benzaldehyde[70], while the product of the reduction of the unsaturated ketone (XXXIV), which has an active methylene group, does react with this reagent; (b) heating of the ketone (XXXIII) in acids or alkalis does not lead to the formation of the hydrocarbon 1,2,3,4,5,6-tricyclotrimethylenebenzene (XXXV), which should have formed from the ketone with the structure (XXXIV):



(XXXIII) (XXXIV) (XXXV)

The infrared spectrum of 2,5-dicyclopentylidenecyclopentanone (XXXIII) has a band at 1692 cm^{-1} and the ultraviolet spectrum has an absorption maximum at 300 nm (ϵ_{max} = 20900)[56].

The ketone (XXXIII) is also formed[71] when the unsaturated ketone (XI) is heated with potassium hydroxide in toluene, as a result of a reversible aldol condensation (hydrolysis of 2-cyclopentylidenecyclopentanone).

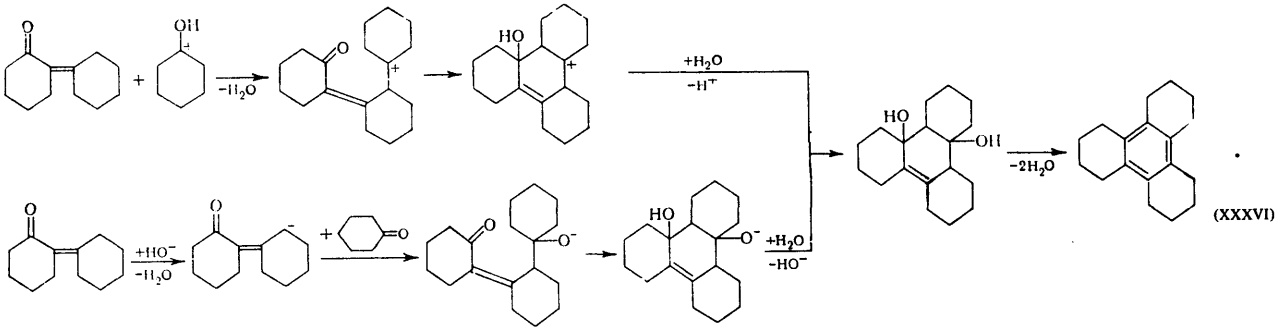
2. Hydrocarbons

Cyclohexanone. When cyclohexanone is allowed to stand with concentrated sulphuric acid in methanol[98] and with 60% sulphuric acid[91], on heating cyclohexanone with concentrated sulphuric acid[17], *p*-toluenesulphonic acid[18], zinc chloride[39], polymeric dichlorogermane[39], polyphosphoric acid[99], activated aluminosilicate[100], alumina (under pressure)[31], thorium oxide, and a mixture of calcium, aluminium, and cerium (or thorium) oxides[101], or simply on heating under pressure without any condensing

agent[27], a hydrocarbon—1,2,3,4,5,6,7,8,9,10,11,12-dodecahydrotriphenylene (XXXVI)—is obtained in a yield not exceeding[101] 13%. This hydrocarbon (m.p. 232°C) is formed as a side product in the reaction of cyclohexanone with acetic anhydride in nitromethane in the presence of perchloric acid[23].

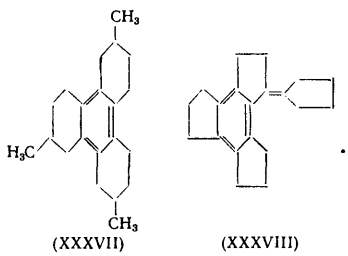
It has been shown[96] that dodecahydrotriphenylene (XXXVI) can be obtained in a low yield by heating under pressure a mixture of the dimeric ketones (I) and (II) with aqueous potassium hydroxide. The formation of the hydrocarbon (XXXVI) is probably preceded by the hydrolysis of the ketones (I) and (II). Compound (XXXVI) is also formed on heating a mixture of the ketones (I) and (II) with cyclohexanone in the presence of zinc chloride[29] or when a mixture of the ketones (I) and (II) is allowed to stand with sulphuric acid in methanol[96].

As in the synthesis of the mixture of the trimeric ketones (product D), in the synthesis of dodecahydrotriphenylene (XXXVI) the intermediates are probably the ketones (I) and (II):



(XXXVI)

On heating with sulphuric acid in methanol or with a mixture of thorium and aluminium oxides, 4-methylcyclohexanone is converted into 2,6,10-trimethyl-1,2,3,4,5,6-7,8,9,10,11,12-dodecahydrotriphenylene (XXXVII):[101]



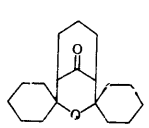
(XXXVII) (XXXVIII)

When hydrogen chloride is passed into cyclopentanone[70,71,80] and when the latter is heated with potassium hydroxide[76] or with concentrated sulphuric acid[81], triscyclotrimethylenebenzene (XXXV) is obtained (m.p. 97.5–98.0°C). It is also formed when a mixture of cyclopentanone and 2-cyclopentylidenecyclopentanone (XI) is saturated with hydrogen chloride[70,71].

When the ketone (XI) is heated with *p*-toluenesulphonic acid, a hydrocarbon with the composition $C_{20}H_{24}$ is formed, to which the structure (XXXVIII) is attributed[71].

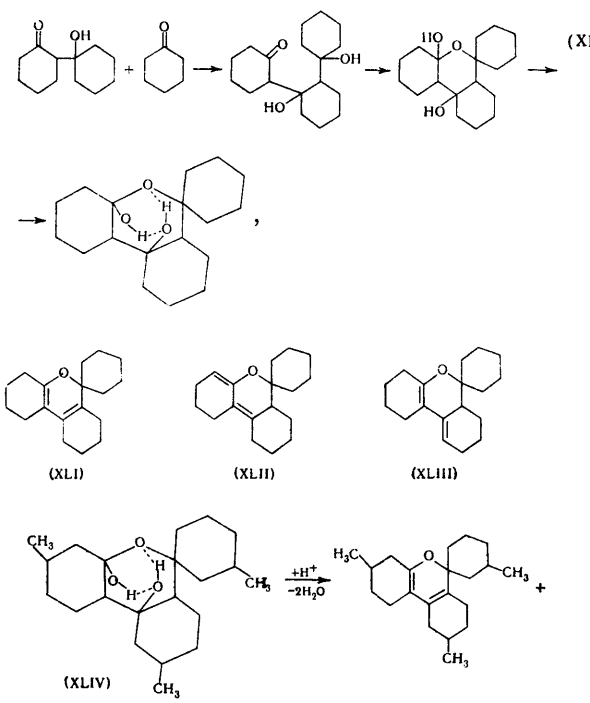
3. Oxygen-containing Heterocyclic Compounds

After the reaction of cyclohexanone with sodamide[14], a compound with the composition $C_{18}H_{28}O_2$ (m.p. 186°C) was isolated and was assigned the structure of the saturated heterocyclic ketone (XXXIX):



(XXXIX)

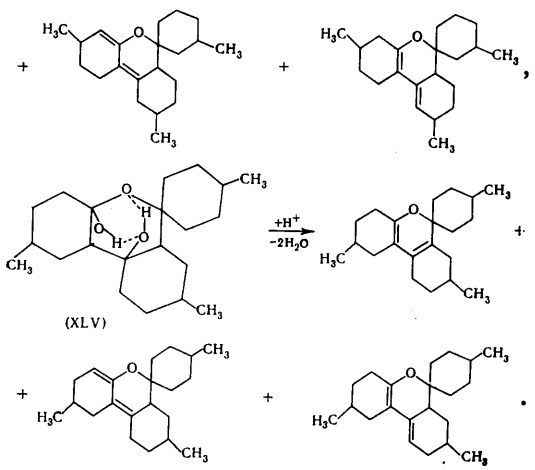
It was shown[94] that, when cyclohexanone is kept for a long time in contact with powdered sodium hydroxide, a solid compound with the composition $C_{18}H_{30}O_3$ (m.p. 175°C), having the structure of an internal cyclic hydrogen-bonded hemiacetal (XL)[102], is formed. The maximum yield (75%) of compound (XL) was achieved[102] at 10°C when the duration of the reaction was 24 h. Under the influence of catalytic amounts of sulphuric acid[102], this cyclohexanone trimer (see the mechanism below) splits off two molecules of water and is converted into a mixture[19] of the pyran (XLI) and the dihydropyrans (XLII) and (XLIII) which are its isomers:



(XL)

(XLI) (XLII) (XLIII)

(XLIV)



Compound (XL) and also the mixture of (XLI), (XLII), and (XLIII), are converted on heating into dodecahydrotriphenylene (XXXVI) in high yields.

It is noteworthy that initially the structure of an $\alpha\beta$–$\delta\epsilon$-unsaturated ketone, and not the pyran (XLI) or the dihydropyrans (XLII) and (XLIII), was attributed to the product formed on elimination of two water molecules from compound (XL).

It has been shown[78] that the interaction of 3- and 4-methylcyclohexanones with solid sodium hydroxide leads to the formation of the analogous trimeric products (XLIV) and (XLV). 2-Methylcyclohexanone does not trimerise owing to steric hindrance. In the presence of sulphuric acid the trimeric compounds (XLIV) and (XLV) are dehydrated to compounds which on heating yield the same hydrocarbon—2,6,10-trimethyl-1,2,3,4,5,6,7,8,9,10-11,12-dodecahydrotriphenylene (XXXVII). By analogy with the products formed in the reaction of cyclohexanone with sodium hydroxide[102], the trimeric compounds (XLIV) and (XLV) should also be internal cyclic hemiacetals and the products of their dehydration by sulphuric acid should consist of a mixture of the corresponding pyrans and dihydropyrans.

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