

XCII.—*The Formation and Stability of spiro-Compounds. Part IV. Ketones Derived from Open-chain and Cyclic Glutaric Acids.*

By GEORGE ARMAND ROBERT KON.

THE tetrahedral theory of the structure of the carbon atom which forms the basis of the Baeyer strain hypothesis leads, as is well known, to the prediction that five-membered carbon rings are those which should be most easy of formation, whereas rings composed of a greater or a smaller number of carbon atoms are correspondingly more difficult to produce, the figures calculated by Baeyer (*Ber.*, 1885, 18, 2278; 1890, 23, 1275) for the angles through which the normal tetrahedral angle ($109^{\circ} 28'$) has to be deflected in order to form the ring—a figure which Baeyer regards as indicating the relative stabilities of the rings when once formed—being

<i>cyclo</i> Propane	$24^{\circ} 44'$	<i>cyclo</i> Hexane	$-5^{\circ} 16'$
<i>cyclo</i> Butane	$9^{\circ} 44'$	<i>cyclo</i> Heptane	$-9^{\circ} 33'$
<i>cyclo</i> Pentane	$0^{\circ} 44'$	<i>cyclo</i> Octane	$-12^{\circ} 51'$

Although experimental evidence is on the whole in support of this hypothesis, there are certain outstanding discrepancies in view of which it appears necessary to remould the theory in a somewhat fundamental manner. For this purpose careful comparative investigations of the conditions governing the formation of the different carbon rings are essential, and it is the purpose of the present paper to deal with the factors affecting the closing and disruption of four-membered carbon rings, in particular of rings which may be described as extra-annular, that is to say, those which are external to some other ring.

Now, of the many methods which have been used for the preparation of alicyclic derivatives two are of primary importance. They are :

(1) The distillation of the calcium salts of dibasic acids (Wislicenus, *Annalen*, 1893, 275, 309).

(2) The elimination of alcohol from esters of dibasic acids (Dieckmann, *Ber.*, 1894, 27, 102).

These two methods are of particular interest for purposes of comparison because they are both concerned with the transformation of dibasic acids into ring ketones. Together they constitute some of the strongest evidence supporting the Baeyer strain hypothesis, for, hitherto, the only members of the series of dibasic acids which

have been found to undergo these reactions at all smoothly are those of the adipic and pimelic series, that is, those which produce five- and six-membered ring ketones respectively. Moreover, it is of importance to note that those acids which can be converted into ketones are incapable of yielding anhydrides under the usual experimental conditions, and that those acids which can be converted into anhydrides have not been found to produce ring ketones by means of either of the reactions mentioned above. Thus, whilst succinic and glutaric acids readily yield anhydrides but not corresponding cyclic ketones, adipic, pimelic, and suberic acids give no stable anhydrides, but, on the other hand, are readily converted into ketones.*

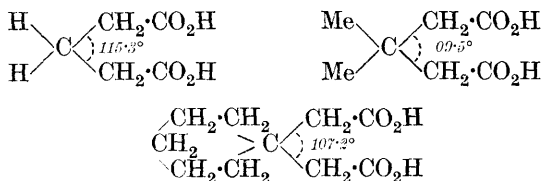
In each case the limiting condition appears to lie between those which hold in glutaric and in adipic acids. There can, however, be no question but that there is a very great difference of stability between the cyclic products derived from these two acids, and that in order to ascertain the limiting condition with any degree of accuracy the investigation of compounds having intermediate stabilities is required.

In a recent paper (this vol., p. 305) Ingold has directed attention to the remarkable effect of the *gem*-dialkyl group in promoting the formation of three-, four-, and five-membered carbon rings, as well as of certain five- and six-membered heterocyclic rings. This is ascribed to the fact that in a normal polymethylene chain the angle between each pair of carbon-to-carbon valencies is not $109\cdot5^\circ$, as the Baeyer hypothesis requires, but a greater angle, namely, $115\cdot3^\circ$, which is governed by the principle that the spatial arrangement of valencies not concerned in ring formation is determined by the relative atomic volumes of the atoms to which they are attached. This hypothesis receives further support from the relative ease of formation and the stabilities of the various types of carbon ring, in particular from the difficulty with which the closure of the *cyclobutane* ring is attended (*loc. cit.*) and from the almost equal stabilities of five- and six-membered carbon rings. When, however, a *gem*-dialkyl group is introduced into a normal polymethylene chain, the angle between the carbon valencies is deformed from $115\cdot3^\circ$ to $109\cdot5^\circ$; consequently, the formation of the carbon rings the internal

* It is true that in a preliminary note (*J. Russ. Phys. Chem. Soc.*, 1897, 29, 280) Zelinsky states that two of his pupils, Yakovlev and Bieltzoff, had succeeded in preparing small quantities of dimethyl- and diethyl-*cyclobutanones* by distilling the barium salts of the corresponding dialkylglutaric acids. These ketones, however, were only characterised by somewhat indefinite boiling points, and no proofs were given of their cyclic structure. It is shown in this paper (p. 815) that there is reason to doubt the correctness of the constitutions assigned to them.

angles of which are less than 115.3° , namely, the *cyclopropane*, *cyclobutane*, and *cyclopentane* rings, takes place with greater readiness from the *gem*-substituted than from the unsubstituted open-chain.

When the constituents of the *gem*-grouping themselves form part of a ring, a further convergence may occur. Thus it has been shown by Beesley, Ingold, and Thorpe (T., 1915, **107**, 1080; see also Ingold and Thorpe, T., 1919, **115**, 320) that if the angle between the valencies joining the acetic acid residues to the central carbon atom of $\beta\beta$ -dimethylglutaric acid is 109.5° , the corresponding angle in *cyclohexanedi*acetic acid is appreciably less, namely, 107.2° . Consequently the formation of rings by the interaction of the acetic residues, or substituents attached thereto, takes place with greater facility in the latter case than in the former :



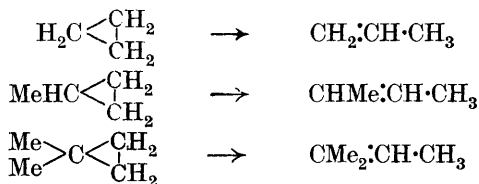
These *gem*-substituted glutaric acids, therefore, occupy various positions intermediate between glutaric and adipic acids in the scale of stability of the ketones to which they should give rise; in particular, they, in all probability, occupy positions in the restricted region common to ketone- and anhydride-forming dibasic acids. If "figure of instability" * be used to represent the various degrees of instability of the different potential ring compounds, then there must be some "critical figure" corresponding to the limit beyond which the closure of the ring by a given method becomes impossible. Since the figures for the ketones derived from the various open-chain and cyclic *gem*-substituted glutaric acids clearly lie in the region of the critical figure, it should be possible by an examination of these cases to make a close estimate of this important constant. It was therefore decided in the first

* The author is asked by Prof. J. F. Thorpe to give the following definition of the term "figure of instability." In the first place, it must be clearly understood that it is not suggested that the alteration in the tetrahedral angle produces any distortion of the molecule such as would lead to a form of stereoisomerism which has not yet been observed and which it is unnecessary for the present purposes to consider capable of occurrence. The stress set up by the altered tetrahedral angle is borne by the whole molecule, partly by the curved valencies and partly by the carbon atoms themselves. It does not lead to the production of asymmetry, but gives rise to a condition of strain of which the "figure of instability" is a direct measure.

place to investigate, besides glutaric, β -methylglutaric, and $\beta\beta$ -dimethylglutaric acids, the three cyclic derivatives which have already been prepared, namely, *cyclopentanediacetic*, *cyclohexanediacetic*, and *cycloheptanediacetic* acids, with reference to their capacity for passing into ring ketones by means of the reactions mentioned on p. 810. The present part of this series deals primarily with the complete investigation of the products formed when the calcium salts of these acids are distilled.

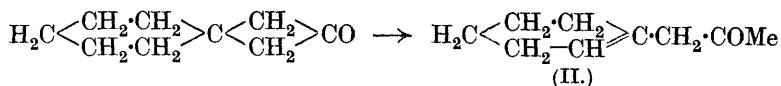
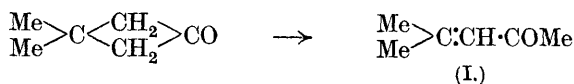
Now it is shown in this paper that, although the cyclic ketones derived from the different glutaric acids in no case survive the conditions of a calcium-salt distillation, it is possible, fortunately, to recognise their formation with certainty owing to the fairly simple character of the decompositions which ensue. It is therefore of the highest importance to observe that, whilst with glutaric acid and β -methylglutaric acid there was obtained no evidence of the production of four-carbon, cyclic ketones, in every case in which a *gem*-substituted glutaric acid was used, namely, $\beta\beta$ -dimethylglutaric acid, $\beta\beta$ -diethylglutaric acid, and *cyclopentane*-, *cyclohexane*-, and *cycloheptane*-diacetic acids, the formation of the ring ketone was the primary reaction.

Comparatively few investigations on the thermal decomposition of compounds containing alicyclic rings of the more highly strained types appear to have been carried out hitherto, but those which have been made have shown unquestionably that the primary reaction is always a transformation into the corresponding unsaturated isomeride. Thus Tanatar showed that *cyclopropane* passes at red heat into propylene (*Ber.*, 1896, **29**, 1297; 1899, **32**, 702), whilst Ipatieff and Hahn (*Ber.*, 1903, **36**, 2014, 2016) proved that in the presence of a contact material such as alumina the reaction takes place below 400° , and that methyl*cyclopropane* and 1:1-dimethyl*cyclopropane* undergo an analogous transformation when subjected to similar conditions.

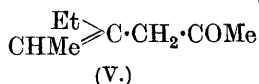
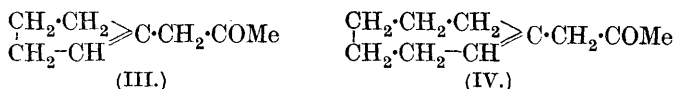


Consequently it is not altogether surprising that the cyclic ketones produced during the calcium-salt distillation, in all those cases in which they are undoubtedly the primary products, isomerise under the experimental conditions employed, yielding unsaturated ketones in agreement with Tanatar and Ipatieff's observations.

Thus the cyclic ketone from dimethylglutaric acid yields mesityl oxide (I),



whilst that from *cyclohexanediacetic* acid is transformed into Wallach's *cyclohexenylacetone* (II).^{*} Similarly, *cyclopentandi-*acetic acid yields *cyclopentenylacetone* (III), *cycloheptandi-*acetic acid *cycloheptenylacetone* (IV), and $\beta\beta$ -diethylglutaric acid the ketone (V).



No trace, however, of the corresponding unsaturated ketones could be isolated from the distillates of the calcium salts of glutaric and β -methylglutaric acids. In each of these cases the yield of distillate was very small and its character quite different from that of the distillates from the $\beta\beta$ -disubstituted glutarates already mentioned. In fact, it was an exceedingly difficult matter to identify any of the products with certainty, and almost impossible to account for any considerable proportion of the mixture as pure separated substances. However, the experiments carried out (see pp. 828—830) with the calcium salts of these two acids make it evident that the decompositions which take place on distillation are of a deep-seated character, and, unlike the other cases dealt with, cannot be traced to the formation of cyclic ketones.

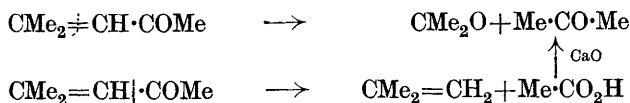
With regard to the unsaturated ketones obtained from the $\beta\beta$ -disubstituted glutaric acids, it should be added that an exhaustive investigation of the distillates revealed in each case the presence

^{*} This ketone and a few of its homologues have been prepared by Wallach (*Annalen*, 1912, **394**, 376), who assigned to them the above constitution mainly on account of their optical properties. A similar constitution is temporarily assigned to the new ketones (III), (IV), and (V), as their properties are undoubtedly similar.

The intracyclic character of the double bond in all these compounds is, however, called in question by some experiments now in progress in this laboratory, and it is possible that the alternative formulæ of the type

$\begin{array}{c} \cdot \text{CH}_2 \\ \cdot \text{CH}_2 \end{array} > \text{C} : \text{CH} \cdot \text{COMe}$ may have to be substituted for those given above.

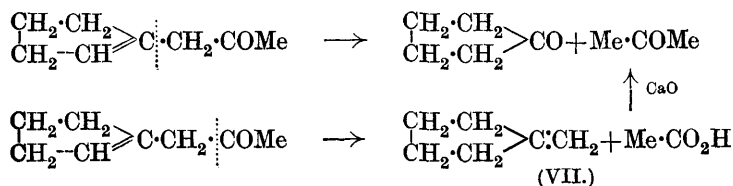
of three decomposition products evidently derived from the unsaturated substances by the hydrolytic action of the water which was invariably present under the conditions of the distillation. Thus from dimethylglutaric acid there were obtained acetone and β -methylpropylene :



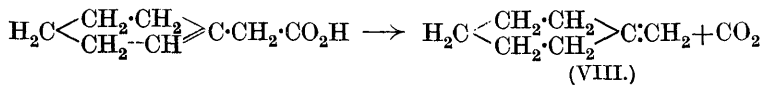
whilst isophorone (VI), which was also isolated in this case, was probably formed by the condensation, under the influence of the calcium oxide, of one molecule of mesityl oxide with one of acetone :



Similar products were found in the other cases, but the character of the least volatile constituents could not be elucidated with certainty. Acetone and a hydrocarbon of the general formula $\text{CR}_2 \cdot \text{CH}_2$ were isolated in each case, and also, in the cases of *cyclopentanediacetic* and $\beta\beta$ -diethylglutaric acids, *cyclopentanone*, and diethyl ketone respectively. The nature of these products clearly accords with the general scheme,



although their formation is more easily accounted for if the alternative formula $\text{C}_4\text{H}_8 > \text{C} \cdot \text{CH} \cdot \text{COMe}$ (see footnote, p. 814) is assumed for *cyclopentenylacetone*. It must, however, be borne in mind that in a very similar case Wallach obtained methylenecyclohexane from *cyclohexeneacetic acid* (*Annalen*, 1907, **353**, 287).



The formation of saturated ketones (diethyl and dipropyl ketones) was also observed by Yakovleff and Bieltzoff (*loc. cit.*) in the cases studied by them. These substances would be expected to result from the fission in accordance with the above scheme of compounds of the general type $\text{CH}_2 \cdot \text{CR} \cdot \text{CO} \cdot \text{CH}_2\text{R}$ (where $\text{R} = \text{Me}$ or Et) and it

appears highly probable from the results of the present investigation that the Russian observers were actually dealing with compounds of this type.

[The following note has been written by Mr. C. K. Ingold.]

Probably the best analytical expression with which to identify the figure of instability for any type of ring is that for the maximal curvature of its valencies (Ingold and Thorpe, *loc. cit.*) in the limiting condition in which they are the seat of the whole of the intramolecular strain. This curvature may be defined as $\frac{\delta\alpha}{\delta s}$, where α is the inclination of the straight path to any tangent to the corresponding curved path, and ds is an element of the latter. If 2θ be the inclination between two adjacent terminal tangents at a point of junction of two curved paths, then for any given type of ring θ will differ from $\alpha - \int ds \frac{\delta\alpha}{\delta s}$ only by a quantity which, so far as the partial differentiation is concerned, is a constant. Hence, for an n -membered ring, the figure of instability reduces to

$$\left[\frac{\delta\alpha}{\delta s} \right]_{s=0} = -2 \cos \left(\theta + \frac{\pi}{n} \right),$$

since the variability of the differential is negligible (*loc. cit.*). For four-membered rings the expression becomes

$$\sqrt{2} (\sin \theta - \cos \theta).$$

The application of these formulæ to the cases under discussion clearly involves the tacit assumption that it is unnecessary to make any special allowance for the influence of the ketonic group on the strains borne by the cyclic valencies. That this view is not altogether justified has already been indicated in general terms (Ingold, *loc. cit.*), but, unfortunately, it is not possible at the present time to make any precise estimate of the effect on stability of the cyclic ketonic group. It happens, however, that this is not a matter of prime importance in the present connexion, for, as the ketone groups are similar both in number and situation in all the cases here dealt with, the scale of relative values of the figures of instability as calculated by the method given will still remain valid, although the reduction of these figures to any absolute standard may require the introduction of a correction into all of them.

It is necessary, therefore, merely to substitute appropriate values for θ in the above expressions in order to obtain figures of instability for the various cyclic ketones. A method of calculating θ for those ketones containing no second ring attached to the first has already

been described in the paper referred to above (Ingold, *loc. cit.*), whilst the general expression

$$\cos \theta = \frac{1}{4} \{ \sqrt{\cos^2 \beta + 8} - \cos \beta \}$$

for the same angle for ketones which correspond with the various cyclic *gem*-diacetic acids, and which are therefore *spiro*-compounds, has been given in Part III of this series (Becker and Thorpe, T., 1920, 117, 1579).

The arithmetical figures to which these formulæ lead for the instabilities of the ketones corresponding with the normal-chain dibasic acids are as follows :

Succinic acid	0.927	Pimelic acid	0.084*
Glutaric „	0.436	Suberic „	0.203*
Adipic „	0.126*	Azelaic † „	0.343

It will be noticed that only those acids indicated by the asterisk have actually been shown to yield the appropriate ketones when their calcium salts are distilled. The figure 0.436, therefore, clearly represents a ketone too unstable to survive the conditions of a calcium-salt distillation, even if originally formed; on the other hand, a ketone of instability 0.126 is sufficiently stable to be prepared in this way. The critical figure, therefore, lies somewhere in the rather wide interval between 0.436 and 0.126. Whether this can be narrowed down to the interval between the figures 0.343 and 0.203 for azelaic and suberic acids is doubtful, as in these cases the figures given by the formulæ are actually negative and the significance, if any, of the sign (omitted in the table) is uncertain.

The manner in which the interval between 0.436 and 0.126 is subdivided by the figures representing the substituted glutaric acids is exhibited in the following table :

[Glutaric acid	0.436]	<i>cyclo</i> Hexanediactic acid	0.301
<i>cyclo</i> Pentanediacetic acid	0.344	<i>cyclo</i> Heptanediacetic acid	0.266
Dimethylglutaric acid ...	0.339	[Adipic acid	0.126]

Of equal importance with the figure of critical stability is the corresponding figure for the formation of the ring. It has elsewhere been indicated that these are by no means necessarily identical (Ingold, *loc. cit.*), a fact which, although made evident by a considerable amount of experimental testimony,[†] appears hitherto to have been largely ignored. Following the method previously used, it can be shown that the “formation-numbers,” that is, the figures

† Compare Harries and Tank, *Ber.*, 1907, 40, 4555.

‡ Thus there are numerous instances showing that although *cyclobutane* rings are much more difficult to close than *cyclopropane* rings, when once produced the former are actually more stable than the latter (Perkin and Simonsen, T., 1907, 91, 817; Campbell and Thorpe, T., 1910, 97, 2418).

representing the difficulty with which the closure of the ring is attended, are given with sufficient accuracy by the expression

$$\sin^2 \theta - 0.29,$$

where θ has the same meaning as before. From this we obtain the following values :

Glutaric acid	0.43	<i>cyclo</i> Hexanediacetic acid...	0.36
$\beta\beta$ -Dimethylglutaric acid }	0.38	<i>cyclo</i> Heptanediacetic acid...	0.35
<i>cyclo</i> Pentanediacetic acid }			

In the present paper it is shown that, although the cyclic ketones are undoubtedly the products first formed when the calcium salts of the $\beta\beta$ -disubstituted glutaric acids are distilled, none of them survives the experimental conditions but is converted into an isomeric ketone or other product of ring fission. Consequently the figure for the critical stability governing this reaction must lie within the narrower range 0.266 to 0.126. On the other hand, there is no evidence of the formation of tetramethylene ketones from either glutaric or β -methylglutaric acid and it can be inferred that the critical formation number for such ketones is limited to the interval between 0.43 and 0.38.

EXPERIMENTAL.

Preparation of Substituted Glutaric Acids.

Glutaric acid was prepared by the oxidation of *cyclopentanone* by means of dilute nitric acid (D 1.2) (Wislicenus and Hentzschel, *Annalen*, 1893, **275**, 309), β -methylglutaric acid by Day and Thorpe's method (T., 1920, **117**, 1465), and all the other acids by Guareschi's method (compare Kon and Thorpe, T., 1919, **115**, 686).

For the preparation of large quantities of material by the last method it has been found advantageous to work with $1\frac{1}{2}$ gram-molecules of ketone at a time and to carry out the condensation in the cold: the reaction mixture contained in a wide-mouthed, stoppered bottle is left in a freezing mixture for some hours and then at the ordinary temperature, instead of being kept at 40° .

Except in the cases of diethyl ketone and suberone (Day, Kon, and Stevenson, T., 1920, **117**, 644), the contents of the bottle become solid, the reaction being completed after twenty-four to forty-eight hours.

The solid is purified by grinding with ether, dissolved in hot water (about $1\frac{1}{2}$ litres), and the solution acidified, precipitating the imide. The yields are good, reaching 75 per cent. of the theoretical in some cases.

For the hydrolysis Thole and Thorpe's method (T., 1911, **99**, 422) was used and gave excellent results.

*Preparation and Distillation of Calcium Salts.**

Of the several methods tried, that described below was found to give the best results and was adopted as the standard for all the acids examined.

One gram-molecule of the acid is dissolved in dilute ammonia, the excess of ammonia boiled off and the solution poured on a paste made by slaking 100 grams of calcium oxide (this is a considerable excess). The mixture is thoroughly stirred, evaporated to dryness on a steam-bath, and the salt powdered and well dried at 100°. The powder is divided into twelve portions, and these are subjected to distillation in a stream of nitrogen in the apparatus described by Day, Kon, and Stevenson (*loc. cit.*).

The distillate is separated from a small amount of water which always collects, dried over calcium chloride, and fractionated.

1. *Acids containing a Quaternary Carbon Atom in the β -Position.*

$\beta\beta$ -Dimethylglutaric Acid.

The yield of distillate from a gram-molecule of this acid was usually 70 to 80 grams. The distillate was quite transparent and of a dark amber colour.

Result of fractionation :

(1) below 100°	19·4 grams	(3) 140—190°	4·8 grams
(2) 100—140°	3·8 ,,	(4) 190—250°	42·0 ,,

On progressive fractionation, the following compounds were isolated :

(1) *Acetone*.—This was identified by the boiling point and the formation of the semicarbazone melting at 187° (Found : N=36·74. Calc., N=36·48 per cent.).

The yield of acetone was about 17 grams, or 30 per cent.

(2) *Mesityl Oxide*.—This was contained in the second fraction and 2 grams (5 per cent.) of rather indefinite b. p. were isolated; the compound was identified by its semicarbazone (m. p. 162° [decomp.]) (Harries and Kaiser, *Ber.*, 1899, **32**, 1339), which was directly compared with a specimen prepared in the usual way (Found : N=27·28. Calc., N=27·08 per cent.).

(3) *isoPhorone* (VI).—The third and the fourth fractions contained this ketone, which was not accompanied by any other compound. It was isolated by means of its semicarbazone, which, when purified by repeated crystallisation from alcohol, was

* Barium salts were found to give the same results as calcium salts, without noticeable difference in yield; lead salts were unsatisfactory.

obtained in fine plates melting at 190—191° (Crossley and Gilling, T., 1909, **95**, 19). The semicarbazone was identified by direct comparison with a specimen prepared from the ketone obtained by Knoevenagel's method (*Annalen*, 1897, **297**, 113) (Found: C=61·42; H=8·83; N=21·98. Calc., C=61·51; H=8·77; N=21·53 per cent.).

The ketone regenerated from the semicarbazone by treatment with oxalic acid and steam distillation had the following properties :

b. p. 212°/763·5 mm. *; $d_{20}^{22\cdot0}$ 0·91985; n_D^{20} 1·47613;

whence $[R_L]_D$ 42·35, which is in good agreement with the figures found by Knoevenagel, as recalculated by Auwers and Eisenlohr (*J. pr. Chem.*, 1910, [ii], **82**, 129).

On treatment with hydroxylamine under the conditions described by Brecht and Rübel (*Annalen*, 1898, **299**, 170), an oxime was obtained, which on repeated crystallisation from ether and light petroleum could be separated into two forms, melting respectively at 79° and 102° (Wolff, *Annalen*, 1901, **322**, 380). In accordance with the observation of Kerp and Müller (*Annalen*, 1898, **299**, 220; 1896, **290**, 140) these oximes gave high results when analysed for nitrogen (Found: N=10·60, 10·62. Calc., N=9·14 per cent.).

The yield of isophorone is about 45 grams, or 33 per cent.

(4) The formation of an unsaturated hydrocarbon was demonstrated by passing the gaseous products of the reaction through a U-tube cooled by means of liquid air. The liquid condensed in this way contained much acetone and a hydrocarbon which volatilised when the temperature of the mixture was allowed to rise. The hydrocarbon was passed into bromine and on removing the excess of the latter a heavy liquid was obtained, which was distilled. The portion boiling at 148—150° consisted of isobutylene dibromide, as it gave on heating with water in a sealed tube the odour of isobutylaldehyde (Eltekoff, *Ber.*, 1878, **11**, 990) (Found: Br=73·29. Calc., Br=74·04 per cent.).

ββ-Diethylglutaric Acid.

Only one experiment was carried out with this acid, in which 1·2 gram-molecules (226 grams) were used. The yield of wet distillate was 109 grams. Result of fractionation :

(1) below 100°.....	22·3 grams	(5) 190—220°	10·6 grams
(2) 100—140°	11·3 "	(6) 220—230°	17·7 "
(3) 140—165°	10·2 "	Residue	8 "
(4) 165—190°	22·6 "		

* Pure naphthalene boils at 215° under similar conditions.

From the fraction of lowest b. p. two compounds were isolated by refractionation and treatment with water.

(1) *Acetone*.—This was separated from the other constituent of the mixture owing to its solubility in water and identified by means of the semicarbazone melting at 187°. The yield of acetone appeared to be about 12 grams, or 16 per cent.

(2) β -*Ethyl- Δ^{α} -butylene*, C_6H_{12} .—The oil remaining after the acetone had been removed was carefully dried and fractionated with the aid of a short column. After two distillations it boiled at 67–68° as a colourless, mobile liquid with a slight odour of garlic (Found: C=85.14; H=14.18. C_6H_{12} requires C=85.60; H=14.40 per cent.). Physical properties: $d_{20}^{20.5}$ 0.69403, $n_D^{20.5}$ 1.40276, whence $[R_L]_D$ 29.55. Calc. for C_6H_{12} , 29.44.

When the hydrocarbon was treated with bromine in chloroform solution two atoms of the halogen were taken up. The resulting *dibromide* boiled at 108–110°/50 mm. and possessed a pleasant, camphoraceous odour. On heating with water in a sealed tube for several hours, this yielded an *aldehyde*, recognised by the silver-mirror test, thus confirming the constitution of the hydrocarbon.

(3) *Diethyl Ketone*.—This compound was isolated from the portions of the distillate boiling between 100° and 140° in the form of its characteristic semicarbazone, which forms glistening, flattened needles melting at 139°. It was identified by direct comparison (Found: N=29.70. Calc., N=29.35 per cent.). The amount formed appears to be about 5 grams, or 5 per cent.

(4) On refractionating the third, fourth, and fifth fractions a very considerable portion of the distillate boiled between 160° and 190°. The weight of this fraction was 38 grams, corresponding with a yield of 25 per cent. It consisted of a *ketone*, $\text{C}_8\text{H}_{14}\text{O}$, to which the constitution V was assigned. The fraction, b. p. 160–190°, was treated with semicarbazide acetate and the *semicarbazone* collected and purified by rubbing with light petroleum. It was very soluble in most organic solvents and difficult to purify; it crystallised best from a mixture of ethyl acetate and light petroleum (b. p. 60–70°), from which it separated in silky, flattened needles melting at 145–146° (Found: N=23.13. $\text{C}_8\text{H}_{17}\text{ON}_3$ requires N=22.93 per cent.).

The existence of a more fusible modification of this semicarbazone could not be definitely established. The ketone reacted also with semicarbazide hydrochloride, although very slowly; the compound obtained was identical with the one described above.

The ketone regenerated from the semicarbazone by means of oxalic acid was a colourless liquid with a characteristic odour reminiscent both of *isophorone* and *mesityl oxide* and boiling at

164—166°/759 mm. (Found: C=75·86; H=11·19. $C_8H_{14}O$ requires C=76·13; H=11·18 per cent.). Physical properties: $d_{20}^{18.9}$ 0·85444; $n_D^{18.9}$ 1·44241; whence $[R_L]_D$ 38·83. Calc. for $C_8H_{14}O$ 38·72.

The *oxime* of the ketone was prepared by warming it with hydroxylamine hydrochloride and sodium carbonate in alcoholic solution for one hour. On removing the alcohol by evaporation, the oxime separated as a colourless oil, which was taken up in ether and purified by distillation. It boiled at 118—119°/19 mm. and did not solidify when cooled in a freezing mixture (Found: N=9·76. $C_8H_{15}ON$ requires N=9·92 per cent.).

The catalytic reduction of the ketone $C_8H_{14}O$ to the compound $CH_3CH_2CH_2CO_2Me$ by means of colloidal palladium and hydrogen was found to proceed very sluggishly and incompletely, and although the treatment was repeated three times the product still reduced permanganate. After being purified by shaking with a solution of the latter reagent, the new *ketone*, $C_8H_{16}O$, was isolated in the form of its *semicarbazone*, which melted at 141—142°. It crystallised from a mixture of ethyl acetate and light petroleum (b. p. 60—70°) in silvery plates or from methyl alcohol in long, flattened needles (Found: C=58·37; H=10·27. $C_8H_{16}ON_3$ requires C=58·34; H=10·34 per cent.). It appeared to be less soluble than the semicarbazone of the unsaturated compound.

(5) The fraction of highest b. p. obtained in this experiment was distilled under ordinary pressure, and several fractions were collected. The most important was that boiling between 240° and 260°.

The composition of this fraction approximates to that required by the formula $C_{11}H_{18}O$ (Found: C=79·51; H=10·49. Calc., C=79·47; H=10·90 per cent.), but a definite substance has not, as yet, been isolated from it, as a crystalline oxime or semicarbazone could not be obtained.

cycloPentanediacetic Acid.

The yield of the distillate, which was dark green in colour, was usually about 90 grams.

Result of fractionation :

(1) below 100°	12·5 grams	(4) 210—250°	12·0 grams
(2) 100—160°	5·9 „	(5) 250—320°	24·0 „
(3) 160—210°	21·2 „		

On progressive fractionation, 16 grams of liquid boiling below 100° were obtained and about 27 grams boiling between 160° and 210°.

The lowest fraction was separated into two constituents by shaking with water, exactly as described in the foregoing case (see p. 821).

(1) *Acetone* was identified as before by its boiling point and the formation of the semicarbazone. Yield about 12 grams, or 20 per cent.

(2) *Methylenecyclopentane* (VII).—The portion insoluble in water, which amounted to about 4 grams, boiled, after careful drying, between 70° and 82° and consisted of the above hydrocarbon. On refractionation, this was obtained as a mobile, colourless liquid with a penetrating odour resembling that of garlic and having the following properties: d_{20}^{20} 0.7905; n_D^{20} 1.44070; whence $[R_L]_D$ 27.41, in good agreement with the figures given by Wallach (*Annalen*, 1906, **347**, 325) (Found: C=87.39; H=11.81. Calc., C=87.70; H=12.30 per cent.). The substance was further identified by the formation of the nitrosochloride melting at 82°.

(3) From the fraction, b. p. 100—160°, a little *cyclopentanone* was isolated and recognised by the formation of its semicarbazone melting and decomposing at 205—206° (Wallach, *Annalen*, 1906, **347**, 326) (Found: N=29.95. Calc., N=29.76 per cent.).

(4) The large middle fraction, on redistillation, yielded nearly 20 grams of an oil boiling between 178° and 188° and consisting of *cyclopentenylacetone* (III); this substance can also be recovered in considerable quantity from the fractions, b. p. 160—178° and 188—210° respectively, by means of semicarbazide.

The ketone was obtained in the pure state through its semicarbazone, although this proved to be an extremely tedious operation.

The *semicarbazone* is readily produced, and consists of a mixture of two forms. It is first purified by drying on porous plates and rubbing with light petroleum to remove oily impurities. Rubbing with ether, as recommended by Wallach for the separation of the two semicarbazones of *cyclohexenylacetone* (*loc. cit.*), is unsatisfactory, as both forms dissolve to some extent; repeated crystallisation from methyl alcohol was found to be the best method. The less fusible form, when fairly pure, is but sparingly soluble in alcohol, although mixtures dissolve easily in a small quantity of the solvent; also, the less fusible form, which tends to separate first, is present in small quantity, thus adding to the difficulty of purifying the compound.

The less soluble form separates from methyl or ethyl alcohol in fan-shaped aggregates of needles melting and decomposing at 189° (Found: C=59.85; H=8.54; N=23.56. $C_9H_{15}ON_3$ requires C=59.64; H=8.34; N=23.19 per cent.).

The more soluble form separates from ethyl alcohol or benzene

in rosettes of small crystals melting at 138° (Found : N=23.44 per cent.).

An experiment was made to ascertain whether the two semicarbazones were derived from the same ketone. It was found that the ketone obtained from the pure compound melting at 189° still gave a mixture of the two forms on treatment with semicarbazide.

The ketone can be easily regenerated by boiling the semicarbazone with aqueous oxalic acid and isolated by distillation in steam.

It is a colourless liquid boiling at $181-184^{\circ}/760$ mm. The odour is strong and not very pleasant, somewhat resembling that of amyl acetate. The physical properties are : $d^{24.3}_{20}$ 0.9294; $d^{19.4}_{20}$ 0.9332; $n^{24.3}_{D}$ 1.46500, $n^{19.4}_{D}$ 1.46728; whence $[R_L]_D$ 36.91. Calc. for $C_8H_{12}O$ 36.61 * (Found : C=77.09; H=9.91. $C_8H_{12}O$ requires C=77.37; H=9.85 per cent.).

*cyclo*Pentenylacetone is fairly readily reduced to *cyclopentylacetone*, $C_5H_9 \cdot CH_2 \cdot COMe$. The ketone (10 grams) was mixed with 5 c.c. of a 10 per cent. solution of palladium chloride, 5 c.c. of 10 per cent. gum arabic solution, 10 c.c. of water, and enough alcohol to give a clear solution. The mixture was shaken in an atmosphere of pure hydrogen maintained under a pressure of about 1800 mm. for six hours.

At the end of that time no further absorption seemed to occur. The ketone was isolated and converted into the *semicarbazone*, which was purified by crystallisation from ethyl acetate, from which it separated in glistening plates melting at $171-171.5^{\circ}$ after several crystallisations; from methyl alcohol it separated in long, flattened needles (Found : N=23.06. $C_9H_{17}ON_3$ requires N=22.93 per cent.). The ketone regenerated from this semicarbazone was a perfectly colourless liquid boiling at $179^{\circ}/768$ mm. and possessing an agreeable, intense odour resembling that of amyl acetate. Its physical properties were : $d^{20.0}_{20}$ 0.9022; $n^{21.0}_{D}$ 1.44452; whence $[R_L]_D$ 37.15. Calc. for $C_8H_{14}O$, 37.01 (Found : C=75.92; H=11.33. $C_8H_{14}O$ requires C=76.13; H=11.18 per cent.).

The reduced ketone is stable to permanganate in the cold.

(5) The fraction of highest b. p. was usually obtained as a deep blue, oily liquid. Its colour disappeared on reduction with palladium and hydrogen, although the composition of the oil appeared to remain unchanged. On distillation under reduced pressure, it did not boil very constantly, the greater part passing over at about $140-142^{\circ}/11$ mm. The composition of this fraction agrees with the formula $C_{16}H_{22}O$, so that it is probably derived from the condensa-

* The molecular refractivity of this ketone is unaccountably high, although scarcely as high as would be expected in the conjugated system $>C:CH \cdot CMe:O$ (compare footnote on p. 814).

tion of two molecules of *cyclopentenylacetone* with the elimination of a molecule of water (Found: C=82.98; H=9.65. $C_{16}H_{22}O$ requires C=83.40; H=9.64 per cent.). Up to the present a crystalline compound with semicarbazide or hydroxylamine has not been obtained.

cycloHexanediacetic Acid.

The yield of distillate from this acid was usually about 96 grams. Result of fractionation :

(1) below 100°	10.8 grams	(4) 180—230°	33.1 grams
(2) 100—120°	5.6 „	(5) 230—290°	8.7 „
(3) 120—180°	17.1 „	(6) 290—350°	12.7 „

(1) On progressive fractionation, about 8 grams of a liquid, boiling below 60°, were obtained from the fraction of lowest b. p.

The liquid possessed the characteristic properties of acetone; this was confirmed by the formation of the semicarbazone melting at 187° (Found: N=36.73. Calc., N=36.48 per cent.). The yield of acetone was usually 12—15 per cent.

(2) The next definite fraction boiled between 100° and 110°, after repeated rectification at 105—106°, and was a colourless, oily liquid with a characteristic smell. It consisted of pure methylene-*cyclohexane* (VIII) (Found: C=87.45; H=12.41. Calc., C=87.50; H=12.50 per cent.).

Its physical properties were found to be as follows: d_{20}^{20} 0.80596; n_D^{20} 1.45153; whence $[R_L]_D$ 32.14 (calc., 31.81), in good agreement with the figure quoted by Wallach (*Annalen*, 1906, **347**, 329).

The identity of the substance was established by preparing the nitrosopiperidide by the method recommended by Favorsky and Borgmann (*Ber.*, 1907, **40**, 4867). This derivative was readily obtained, although in poor yield, and melted on crystallisation from 50 per cent. alcohol at 126.5—127° (Found: N=13.33. Calc., N=13.33 per cent.).

The hydrocarbon was oxidised by an ice-cold, alkaline, 1 per cent. solution of potassium permanganate (compare Wallach, *loc. cit.*). The glycol, $C_7H_{14}O_2$, obtained melted at 77.5° and crystallised very well from a mixture of ether and light petroleum in long, thin needles or from ether with a little methyl alcohol in large, transparent plates (Found: C=64.25; H=10.84. Calc., C=64.57; H=10.84 per cent.).

The yield of hydrocarbon appears to vary according to the conditions of the experiment and increases at the expense of the ketonic fraction if the experiment is conducted without passing nitrogen through the apparatus; it is usually about 11 per cent.

(3) *cyclo*Hexenylacetone (II) formed the greater part of the distillate and was contained in the portion boiling between 180° and 230°. The amount of this fraction was 42 grams, representing a yield of more than 30 per cent., but it did not boil very constantly, and the ketone could only be obtained from it by a tedious method of purification. Both the sodium hydrogen sulphite and the semicarbazide methods can be used, but the latter is preferable.

The semicarbazone is readily obtained, but it is very caseous in nature and consists of two forms, as in the case of the lower homologue (see p. 823). The two forms can be separated by rubbing the mixture with ether in accordance with the observation of Wallach. The residue, on repeated crystallisation from methyl alcohol and finally from benzene, is obtained in long, flattened needles, which lose their silky lustre on exposure and melt at 145° (Found : N=21·58. Calc., N=21·53 per cent.).

The compound also crystallises well from ethyl alcohol or ethyl acetate, but it is rather freely soluble in these solvents and especially so in chloroform. Dilute alcohol is not to be recommended, as the compound often separates from it in an amorphous form.

The ether extract, obtained as above, contains the more fusible form, which can be isolated by removing the ether, rubbing the residue with light petroleum, and crystallising repeatedly first from methyl alcohol and finally from benzene. It is thus obtained in flattened needles melting at 136—137° and closely resembling the foregoing compound in appearance (Found : C=61·67; H=8·92; N=21·65. Calc., C=61·51; H=8·77; N=21·53 per cent.).

Both forms were directly compared and found to be identical with the corresponding compounds obtained by Wallach's method.

When regenerated from the semicarbazone by means of oxalic acid, the ketone is obtained as a perfectly colourless oil with a pleasant odour reminiscent of amyl acetate and acetoacetic ester. It boils at 202°/754 mm. (pure naphthalene boils at 215° under similar conditions) and has the following physical properties : $d_{20}^{24.1}$ 0·9304; $n_D^{24.1}$ 1·46867; whence $[R_L]_D$ 41·34, in good agreement with Wallach's figure (41·32) (Found : C=78·04; H=10·23. Calc., C=78·20; H=10·21 per cent.).

The oxime of *cyclo*hexenylacetone is a liquid, as found by Wallach (Found : N=9·29. Calc., N=9·15 per cent.).

(4) The fraction of highest b. p., of which about 15 grams were obtained, was an amber-coloured oil with a faint smell. It boiled for the most part at about 175°/11 mm., but the analytical figures obtained (Found : C=82·48, 82·70; H=9·58, 9·63 per cent.) did not lead to any definite formula and, as a solid derivative was not

formed with semicarbazide, the investigation of the substance was not continued.

cycloHeptanediacetic Acid.

Only a quarter of a gram-molecule (55 grams) of this acid was available. The yield of distillate was 24 grams.

Result of fractionation :

(1) below 120°	1.1 grams	(5) 240—300°	3.7 grams
(2) 120—150°	2.5 „	(6) Residue distilled	
(3) 150—190°	3.2 „	under reduced	
(4) 190—240°	5.9 „	pressure	5.0 „

(1) On redistillation, only a small amount was found to boil at about 60° and this fraction was identified as acetone by its semicarbazone.

(2) The second fraction increased to about 4 grams on progressive fractionation, the major part boiling at 135—140°. This consisted of a hydrocarbon, but was still impure (Found : C=86.18; H=11.63. C_8H_{14} requires C=87.20; H=12.80 per cent.). An attempt was therefore made to identify it by oxidation, but it was unfortunately lost owing to an accident. In smell and other properties the compound resembled methylenecyclohexane, and consisted, without doubt, of Wallach's methylenecycloheptane (*Annalen*, 1900, **314**, 158; 1906, **345**, 146).

(3) Fractions (3), (4), and (5) were treated with an excess of semicarbazide acetate in aqueous alcoholic solution. The semicarbazone was precipitated by adding water after four days and purified by drying on porous plates, grinding first with light petroleum, and then with a mixture of light petroleum and ether.

The semicarbazone crystallises well from methyl alcohol in spherical clusters of needles, melting at 166.5—167° (Found : N=20.25. $C_{11}H_{19}ON_3$ requires N=20.09 per cent.).

The compound also occurs in a more fusible form, but the quantity of this appears to be small. It melts with sudden decomposition at 96°.

The ketone, cycloheptenylacetone (IV), regenerated from the semicarbazone in the usual way, was obtained as a colourless liquid closely resembling cyclohexenylacetone in its properties. It boiled at 223—225°/776 mm. (pure naphthalene boiled at 216.5° under the same conditions) and had $d_{20}^{23.3}$ 0.9396, $n_D^{23.3}$ 1.47917, whence $[R_L]_D$ 45.92. Calc. for $C_{10}H_{16}O$ 45.82 (Found : C=78.50; H=10.72. $C_{10}H_{16}O$ requires C=78.90; H=10.58 per cent.).

(4) The least volatile fraction was distilled under reduced pressure and a fraction boiling at 196—198°/11 mm. was collected. This appeared to be entirely analogous to the least volatile fraction

obtained from *cyclohexanediacetic acid*, but so far its constitution has not been definitely settled (Found : C=82·83 ; H=10·32 per cent.).

2. *Acids Having a Free Hydrogen Atom attached to the β -Carbon Atom.*

Glutaric Acid.

The acid yielded under standard conditions 26 grams of distillate. This had a sweet, incense-like smell and gave on fractionation the following result :

(1) below 80°	2·7 grams	(5) 220—260°	4·1 grams
(2) 80—100°	1·9 „	(6) 260—320°	4·1 „
(3) 100—160°	1·6 „	Residue	7·0 „
(4) 160—220°	2·6 „		

On refractionating with a column the fractions (2) and (3) became still less, whereas a little more than 3 grams of a liquid boiling below 60° was obtained. This was identified as acetone by its odour and by the formation of its semicarbazone melting at 187°.

From the fraction (3), a very minute quantity of a semicarbazone was obtained on treating it with semicarbazide acetate and allowing to stand for three weeks. The semicarbazone could not be definitely identified, but gave, on treatment with a mineral acid, the characteristic odour of *cyclohexanone*.

From the fractions (4) and (5) a small quantity of phenol was isolated on treatment with sodium hydroxide solution. The neutral oil which remained had no definite boiling point and did not react with semicarbazide and it appeared hopeless to attempt its identification.

β -Methylglutaric Acid.

The yield of distillate from a gram-molecule of this acid was about 42 grams (wet). The liquid was very dark and the smell incense-like and slightly phenolic.

Result of fractionation :

(1) below 100°	8·6 grams	(4) 200—250°	10·8 grams
(2) 100—140°	3·4 „	(5) 250—300°	5·2 „
(3) 140—200°	8·6 „	Residue	about 6 „

(1) On refractionating with a column, acetone (8 grams) was obtained and identified by its semicarbazone. This corresponds with a yield of 15 per cent. approximately.

(2) The next definite fraction obtained boiled between 100° and 130°, but amounted to not more than 2 grams. Repeated distillation gave an oil with a sweet, camphoraceous odour, boiling mainly between 110° and 112°.

The analysis of the oil did not lead to a definite formula (Found : $C=72.69$, 73.36 ; $H=11.11$, 11.14 per cent.). When purified by repeated distillation it combined with semicarbazide to give a very soluble compound, which on repeated crystallisation from light petroleum (b. p. $60-70^\circ$) was obtained in iridescent plates melting at $105-106^\circ$ (Found : $N=29.01$. Calc., $N=29.35$ per cent.).

This was proved to be the semicarbazone of methyl propyl ketone, as an admixture of this substance did not depress its melting point; when mixed with the *isopropyl* compound, the melting point was depressed nearly 20° .

(3) The fraction (3) yielded a certain amount of a semicarbazone when treated with semicarbazide acetate. It was found, however, that this consisted of a very soluble mixture, which on recrystallising three times from methyl alcohol formed clusters of flattened needles and melted at 174° . The ketone was regenerated from this before it was discovered that the semicarbazone was still contaminated with another compound. The ketone boiled somewhat indefinitely, the greater part at $170-175^\circ$, and on analysis gave numbers agreeing with the formula $C_7H_{12}O$ (Found : $C=74.98$, 75.24 ; $H=10.75$, 10.91 . Calc., $C=74.94$; $H=10.80$ per cent.). Its physical properties approximated to those of inactive 3-methylcyclohexanone ($d_{20}^{20.8}$ 0.9124 ; $n_D^{20.8}$ 1.44853 ; whence $[R_L]_D$ 32.92 . Calc., 32.34).

The ketone was therefore reconverted into the semicarbazone and this subjected to careful crystallisation from dilute methyl alcohol. The semicarbazone was finally obtained in glistening plates melting at $180-181^\circ$; it did not depress the melting point of the semicarbazone of 3-methylcyclohexanone, prepared from the synthetic ketone, which was also found to melt at the same temperature (Found : $N=24.91$. Calc., $N=24.83$ per cent.).

(4) Another semicarbazone was present in the mixture first obtained. It occurred in smaller quantity than the foregoing compound and accumulated in the mother liquors from the latter: it could only be separated with great difficulty. It melted at $156-158^\circ$ after repeated crystallisation from dilute alcohol, but its crystalline form was somewhat indefinite (Found : $N=23.44$. $C_9H_{15}ON_3$ requires $N=23.19$ per cent.).

The corresponding ketone would therefore have the formula $C_8H_{12}O$, but it has not yet been obtained in sufficient quantity for identification.

(5) The fractions (4) and (5) were shaken with a 10 per cent. solution of sodium hydroxide, the aqueous extract separated from the oil, traces of oil removed by means of ether, and the liquid acidified. A copious precipitation of a phenolic substance occurred; this was taken up in ether and isolated in the usual manner. It

boiled between 200° and 210° , and gave on analysis figures in fair agreement with the formula C_7H_8O . Ferric chloride gave a violet colour with a solution of the substance, and it was identified as *m*-cresol by the formation of the tribromo-compound melting at $80-82^{\circ}$ (Found : Br=69.88. Calc., Br=69.55 per cent.) and the trinitro-compound melting at $105-106^{\circ}$.

(6) The neutral oil which remained after the *m*-cresol had been dissolved was subjected to distillation; it boiled between 200° and 230° without giving any very definite fractions. It reacted very sluggishly and imperfectly with semicarbazide acetate; the semicarbazone melting at $156-158^{\circ}$ was isolated in small quantity from the product. The investigation of this oil has been temporarily abandoned.

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