LXXXIV.—*The Chemistry of the Three-carbon System. Part XX.* cyclo*Pentylideneacetone and* cyclo-*Pentylidenemethyl Ethyl Ketone.*

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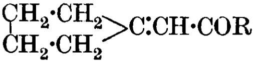
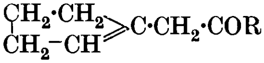
In Part XVII (Dickins, Hugh, and Kon, J., 1928, 1630) it was shown that *cyclo*hexylideneacetone and its βγ-isomeride, and also the corresponding ethyl ketones, could be prepared in a state of purity and a quantitative study was made of their conversion into equilibrium mixtures.

(I.)



$$\begin{matrix}CH_2\cdot CH_2\\ CH_2\cdot CH_2\end{matrix}\!>C{:}CH\cdot COR$$



$$\begin{matrix}CH_2\cdot CH_2\\ CH_2-CH\end{matrix}\!\geqslant C\cdot CH_2\cdot COR$$

(II.)

$(R = Me$ or $Et)$.

The present paper deals with the corresponding *cyclo*pentane derivatives (I and II), which are of considerable interest from the point of view of tautomerism. In the first place, in a number of instances (compare Kon and Nutland, J., 1926, 3101; Kon and Speight, *ibid.*, p. 2727) the point of equilibrium in *cyclo*pentane derivatives is different from that in the corresponding *cyclo*hexane compounds. Means of determining the exact point of equilibrium now being available, the compounds mentioned above appeared to be well suited for the investigation of this problem. Again, Goldberg and Linstead (J., 1928, 2343) have shown that the conversion of *cyclo*pentylidene- and *cyclo*pentenyl-acetic acids into the equilibrium mixture of the two proceeds very rapidly, compared with that of the *cyclo*hexane analogues; this mobility is somewhat unexpected, as the principal factor should be the nature of the activating group and this is the same in both cases. Substituents undoubtedly do influence mobility—a good example has lately been observed (Abbott, Kon, and Satchell, J., 1928, 2514)—but even if the *cyclo*hexane acids are regarded as substitution products of the *cyclo*pentane compounds, the substituent methylene group is attached to the δ-carbon atom, or rather shared between the two δ-carbons; it is not in the direct vicinity of the three-carbon system itself and therefore would not be expected to produce an appreciable effect.

A substance thought to be *cyclo*pentenylacetone was obtained by one of us from calcium *cyclo*pentanediacetate (Kon, J., 1921, **119**, 810) and later synthesised by Kon and Linstead (J., 1925, **127**, 815); the ketone in both cases gave a mixture of two semicarbazones, and it is now clear that it consisted of a mixture of *cyclo*pentylidene- and *cyclo*pentenyl-acetone (I and II; R = Me). The physical properties recorded by Kon and by Kon and Linstead, which also support such a view, refer to the ketone regenerated from a *mixture* of semicarbazones, although an experiment was made (Kon, *loc. cit.*) showing that the ketone regenerated from the pure high-melting semicarbazone again gave a mixture of semicarbazones.

In the light of past experience it was thought preferable to start with the two ethyl ketones (I and II; R = Et). These were prepared, but as they could not be obtained free from esters, etc., they had to be isolated in the form of their semicarbazones, that of the αβ-compound (I) being the higher-melting and less soluble; a semicarbazido-semicarbazone also was isolated in small amount. The pure ketones regenerated from these semicarbazones had the physical properties to be expected of their structure.

The methyl ketones (I and II; R = Me) were somewhat more easily obtained pure, notably the αβ-compound. The semicarbazone obtained from this consisted almost entirely of the sparingly soluble, high-melting substance already obtained by Kon and by Kon and Linstead and cyclo*pentylideneacetone* (I) was regenerated from it seemingly unchanged. The ketone so obtained was, however, much more reactive towards alcoholic iodine chloride than the ketone purified by repeated distillation and was therefore partly "equilibrated," and this accounts for Kon's observation (*loc. cit.*) that a mixture of semicarbazones is obtained from the regenerated ketone. The preparation of the βγ-ketone (II) presented many difficulties and mixtures were obtained in spite of all precautions. The crude ketone is best purified by conversion into the semicarbazone and subsequent treatment of the regenerated ketone with aluminium amalgam: the product has a sharp boiling point and a high reactivity towards iodine chloride and gives the low-melting semicarbazone, already described by Kon, as the sole product. Hydrolysis of the semicarbazone leads to a ketone which has physical properties closely approaching those of the βγ-ketone, but its iodine addition is low.

The equilibrium established between the two pairs of ketones was determined quantitatively by the method of Linstead and May (J., 1927, 2565) exactly as in the case of the *cyclo*hexane compounds. Either of the isomeric ethyl ketones gives a mixture containing about 89·5% of the αβ-ketone; but as the ketones used for the reference curves were regenerated from the semicarbazones, this value is probably not accurate (compare above), especially as the equilibrium is on the side of the αβ-compound; it is probably nearer 85% αβ.

The mobility of the system is extremely high and equilibrium is practically completely established at the end of 20 minutes in the presence of an equivalent of *N*-sodium ethoxide at 25°; and it is not surprising that the βγ-ketone undergoes the Michael reaction with great readiness.

The methyl ketones behave similarly: the equilibrium mixture in this case contains 84% of the αβ-compound, and this figure is regarded as trustworthy. The iodine additions of the equilibrium mixtures of ethyl and methyl ketones are very similar, and the difference in point of equilibrium is probably due to the partial equilibration of the αβ-ethyl ketone. The regenerated αβ-methyl ketone has a higher iodine addition than the equilibrium mixture and therefore must contain more than 16% of βγ-ketone. It is remarkable that isomerisation should proceed past the equilibrium point in this case, but the presence of an acid reagent in place of alkali doubtless materially alters the nature of the reaction and the point of equilibrium. A similar excess of βγ-ketone over the equilibrium amount is also obtained in the preparation of the ketone from calcium *cyclo*pentanediacetate: in a recent preparation, the ketone regenerated from the crude semicarbazone contained approximately 36% of the βγ-ketone; and that originally prepared (Kon, *loc. cit.*) must have contained a good deal more, since the βγ-semicarbazone was obtained in some quantity in spite of its great solubility. The two methyl ketones are also obtained on heating an intimate mixture of calcium acetate and calcium *cyclo*pentenylacetate. The production of the "less stable" form in a pyrogenic reaction is perhaps attributable to its greater vapour pressure, leading to a different equilibrium in the vapour phase: a comparable case has lately been described by Jupp, Kon, and Lockton (J., 1928, 1638).

The mobility of the methyl ketones is so great that exact quantitative measurements could not be carried out under the conditions now adopted as standard; the equilibrium is practically complete at the end of 20 minutes in the presence of *N*-sodium ethoxide at 25°.

The experiments suffice to show that both the ethyl and the methyl ketones are very much more mobile than the corresponding *cyclo*hexane derivatives (experiments on the mobility of *cyclo*hexylideneacetone are now in progress and will shortly be described) and thus fall into line with Goldberg and Linstead's observations. The point of equilibrium of the *cyclo*pentane ketones is on the side of the αβ-form : this agrees with the results already obtained with other *cyclo*pentane derivatives (*loc. cit.*), although we cannot at present offer an adequate explanation of the fact.

An attempt was made to ascertain the point of equilibrium in *cyclo*pentylidene*cyclo*pentanone. The ketone was prepared both by the action of hydrochloric acid and of sodium ethoxide on *cyclo*pentanone and a specimen was regenerated from the pure semicarbazone, m. p. 223°. All the samples examined showed very much the same iodine addition; this was low (6—7%) and did not change appreciably on treatment with sodium ethoxide. The point of equilibrium, therefore, must lie very near the αβ-ketone, but it cannot be ascertained exactly until the unknown βγ-isomeride is prepared. Experiments with the related *cyclo*hexenyl*cyclo*hexanone were even less conclusive, inasmuch as Linstead and May's iodometric method failed in this case : the ketone absorbed more than three times the theoretical quantity of the reagent in a few minutes.

EXPERIMENTAL.

cyclo*Pentylidenemethyl Ethyl Ketone* (I; R = Et).—The ketone was prepared from *cyclo*pentylideneacetyl chloride in the same way as the *cyclo*hexane analogue (Dickins, Hugh, and Kon, *loc. cit.*); a 30% yield of a crude ketonic fraction, b. p. 94—96°/15 mm., was obtained. This was treated with semicarbazide acetate and the crude semicarbazone was freed from adhering esters, etc., by washing with petroleum and recrystallised from methyl alcohol. A small portion was insoluble, m. p. 215° (decomp.), and was probably the *semicarbazido-semicarbazone* (Found : N, 30·5. $C_{11}H_{22}O_2N_6$ requires N, 31·1%). The soluble portion crystallised in long needles, m. p. 174° (Found : C, 61·3; H, 8·9. $C_{10}H_{17}ON_3$ requires C, 61·5; H, 8·8%).

The ketone regenerated from the semicarbazone by means of oxalic acid had b. p. 96°/20 mm., $d_{4°}^{22·9°}$ 0·93179, $n_{D}^{22·9°}$ 1·47801, $[R_L]_D$ 41·96 (calc., 41·21), and gave a semicarbazone melting at 171° without recrystallisation.

Δ^1-cyclo*Pentenylmethyl Ethyl Ketone* (II; R = Et).—Δ^1-*cyclo*-Pentenylacetic acid, from which the ketone was ultimately synthesised, was mostly prepared from its ester by Wallach's method (*Annalen*, 1906, **347**, 324; Kon and Linstead, J., 1925, **127**, 616). Another method, which yields a very pure product, consists in the dry distillation of *cyclo*pentylidenemalonic acid (Kon and Speight, *loc. cit.*) under reduced pressure. As the αβ-structure of the acid is unquestionable, having been again confirmed by us by oxidation with permanganate, this decomposition involves a shifting of the double bond into the ring.

The first attempt to prepare the ketone by the Blaise–Maire reaction led to the isolation of the αβ-semicarbazone, m. p. 174°. The mother-liquor, however, contained a small quantity of a more fusible substance; after repeated crystallisation, this formed needles, m. p. 135°.

Δ^1-*cyclo*Pentenylacetyl chloride (20 g.) was dropped into a well-cooled solution of zinc diethyl (10 g.) in dry ether, dry carbon dioxide being bubbled through the reaction vessel. On decomposing the product with ice, a ketonic substance (about 3 g.), b. p. 85—90°/19 mm., was obtained, but this gave the αβ-semicarbazone, m. p. 174°, as the sole product.

A slight excess of magnesium ethyl iodide in dry ether was added to a well-cooled ethereal solution of the acid chloride (20 g.); after decomposition with ice, about 3 g. of a ketonic substance were obtained, but this again yielded the αβ-semicarbazone. When the amide was substituted for the acid chloride, no ketonic product at all was obtained.

The best results were finally achieved by carrying out the Blaise–Maire reaction very slowly and using a very carefully fractionated acid chloride, b. p. 82°/19 mm. (the higher fraction generally contains the isomeric αβ-chloride). Even then the preparation failed sometimes for no apparent reason; the yield of ketone never exceeded 30% and a quantity of ester was always formed.

The *semicarbazone* melted at about 113°, but formed needles, m. p. 135°, after repeated crystallisation (Found : C, 61·4; H, 8·9. $C_{10}H_{17}ON_3$ requires C, 61·5; H, 8·8%). The ketone regenerated from it had b. p. 90°/21 mm., $d_{4^\circ}^{22\cdot5^\circ}$ 0·92429, $n_D^{22\cdot5^\circ}$ 1·46509, $[R_L]_D$ 41·31 (calc., 41·21); it gave on recombination with semicarbazide a product, m. p. 134° after one crystallisation from methyl alcohol.

Condensation with Ethyl Sodiomalonate.—The ketone was condensed with ethyl sodiomalonate in alcoholic solution (compare Dickins, Hugh, and Kon, *loc. cit.*), and the resulting ester hydrolysed with barium hydroxide; the cyclo*pentane*-spiro-4-*methyl*-cyclo*hexane*-3 : 5-*dione* obtained on acidification crystallised from dilute methyl alcohol in needles, m. p. 174—175° (Found : C, 73·2; H, 8·9. $C_{11}H_{16}O_2$ requires C, 73·3; H, 8·9%).

Equilibrium between the Ethyl Ketones.—The quantitative analysis of mixtures of the two ketones was carried out iodometrically by the method of Linstead and May. A reference curve was constructed from the following values obtained with *M*/300-chloroform solutions in 10 minutes :

Mixture (% $\alpha\beta$) ...	0	10	25	50	75	90	100
Addition (%)	88·4	82·5	74·5	60·5	45·8	37·6	33·0

The addition of the $\alpha\beta$-ketone was unusually high, probably owing to partial equilibration during the hydrolysis of the semicarbazone (compare p. 573).

Point of equilibrium. The pure $\alpha\beta$-ketone was kept with a slight excess of alcoholic sodium ethoxide for 24 hours, then isolated and analysed iodometrically; it had an iodine addition of 37·9% (corresponding to 90% of $\alpha\beta$-ketone). The $\beta\gamma$-ketone was similarly treated; it had b. p. 101—103°/25 mm. and gave an addition value of 38·5% (corresponding to 89% of $\alpha\beta$-ketone); the equilibrium mixture thus contains approximately 89·5% of the $\alpha\beta$-ketone. As already explained, this figure is probably too high because any error due to the impurity of the $\alpha\beta$-ketone would have a considerable effect.

Mobility. The following experiments were carried out with the $\beta\gamma$-ketone : the ketone was kept with *N*-alcoholic sodium ethoxide (1 equiv.) at 25° and portions were isolated and analysed.

Time	20 mins.	40 mins.	24 hours
Addition (%)	39·6	39·0	37·9
$\alpha\beta$-Ketone (%)	87·0	88·0	89·9

Equilibrium is thus practically reached at the end of 20 minutes; shorter periods were not used owing to the scarcity of the material and the inevitably high experimental errors.

cyclo*Pentylideneacetone* (I; R = Me).—The ketone was prepared from *cyclo*pentylideneacetyl chloride in the same way as its higher homologue. The ketonic product on redistillation gave a small amount, b. p. 72—74°/12 mm., a large fraction, b. p. 74—75°/12 mm., and another small one, b. p. up to 88°/12 mm. The lowest fraction gave a semicarbazone, m. p. 172—173° : on recrystallisation from methyl alcohol, needles, m. p. 185—186°, were obtained, identical with the high-melting form obtained by Kon and by Kon and Linstead (*locc. cit.*). The large fraction gave a somewhat higher-melting semicarbazone; the yield was rather poor. The ketone can be regenerated from the semicarbazone if a small quantity is employed. For instance, 3 g. of the pure compound, m. p. 189°, gave a ketone, b. p. 70°/12 mm., $d_{4^\circ}^{16\cdot9^\circ}$ 0·94205, $n_{\mathrm{D}}^{16\cdot9^\circ}$ 1·47937, $[R_L]_{\mathrm{D}}$ 37·16 (calc., 36·60) : the semicarbazone prepared from this ketone had m. p. 174°, rising to 180—181° after one crystallisation. The regenerated ketone had an iodine absorption of 44·7% (in 5 minutes). Another sample prepared in the same way had an even higher molecular refraction (37·43), but the iodine addition was 45·8% (compare below).

The ketone was finally prepared by repeated fractionation of the crude ketonic product. It boiled at 74—76°/14 mm., its iodine addition was 27·8%, and its purity was proved by the fact that the equilibrated ketone obtained from it had approximately the same iodine addition as that obtained both from the regenerated ketone and from the βγ-isomeride.

cyclo*Pentenylacetone* (II; R = Me).—The preparation of this ketone was carried out exactly as described on p. 576. The yield of ketonic fraction, the b. p. of which was lower than in the preceding case, was poor. It gave a caseous semicarbazone from which the compound, m. p. 189°, could generally be obtained. The product of several preparations was combined and carefully redistilled, a fraction, b. p. 72—74°/15 mm., being obtained, $d_{4°}^{17·0°}$ 0·95400, $n_{D}^{17·0°}$ 1·46569, iodine addition 73·3% (5 minutes). On treatment with aluminium amalgam (compare Hugh, Kon, and Linstead, J., 1927, 2585) this value rose to about 84%. A part of the crude ketone was therefore converted into the semicarbazone, which was very soluble in all solvents and to some extent even in water; it was purified by repeated grinding with light petroleum (b. p. 40—60°), and the ketone regenerated from it. This was dissolved in much ether and treated with aluminium amalgam in excess. After the reaction had continued for about 4 hours the ketone was isolated; it boiled at 69—70°/16 mm., had $d_{4°}^{20·4°}$ 0·93568, $n_{D}^{20·4°}$ 1·46211, $[R_L]_D$ 36·58 (calc. 36·60), iodine addition 87·7%, and was evidently pure *cyclo*pentenylacetone. The semicarbazone prepared from it was the low-melting form obtained by Kon and by Kon and Linstead (*locc. cit.*); it melted at 129° without purification.

An attempt was made to prepare the ketone from the acid chloride by the Grignard reaction; the yield of ketonic product was very small and only the αβ-semicarbazone was obtained from it.

Ketone from Calcium cyclo*Pentanediacetate.*—Calcium *cyclo*pentanediacetate was distilled exactly as described by Kon (*loc. cit.*). The appropriate ketonic fraction was converted into the semicarbazone, which was ground with petroleum and hydrolysed with oxalic acid. The regenerated ketone had b. p. 66—70°/15 mm., $d_{4°}^{19·6°}$ 0·93070, $n_{D}^{19·6°}$ 1·46420, iodine addition 51·8% (corresponding to 64% of αβ-ketone; see below).

A similar product was obtained by distilling an intimate mixture of calcium acetate and calcium *cyclo*pentenylacetate under the same conditions. The ketone purified through the semicarbazone had b. p. 80—84°/24 mm., $d_{4^\circ}^{19\cdot 2^\circ}$ 0·93405, $n_D^{19\cdot 6^\circ}$ 1·46847, iodine addition 47·8%.

Equilibrium between the Methyl Ketones.—The analysis of mixtures of the two ketones was carried out as in the previous case, but, owing to the high additive power of the ketones, 5 minutes was chosen as the standard time. A reference curve was constructed from the following values :

Mixture (% αβ) ...	0	10	25	50	75	90	100
Addition (%)	86·1	82·7	75·1	60·3	45·2	34·9	27·8

The αβ-ketone used for the reference curve was the specimen described above, purified by fractionation; the βγ-ketone was purified by regeneration and treatment with aluminium amalgam.

Point of equilibrium. The αβ-ketone (iodine addition, 44·7%; see p. 578) regenerated from the semicarbazone of m. p. 189° was kept with a slight excess of sodium ethoxide for 24 hours; the mixture became very dark. The ketone isolated had an iodine addition of 39·1% (corresponding to 84% of αβ-ketone) and gave an immediate precipitate of the semicarbazone, m. p. 189°, on treatment with semicarbazide. The fully equilibrated material thus contained more αβ-ketone than the regenerated αβ-ketone. Another specimen prepared in the same way (iodine addition, 45·8%) was treated for 3 hours only, *N*-sodium ethoxide being used; the ketone isolated had $d_{4^\circ}^{20\cdot 0^\circ}$ 0·93947, $n_D^{20\cdot 0^\circ}$ 1·47751, and iodine addition 38·8% (corresponding to 84·5% of αβ-ketone). A separate experiment showed that the αβ-ketone purified by distillation only, gave the same equilibrium mixture as the regenerated material.

Only one experiment was performed with the βγ-ketone, *N*-sodium ethoxide being used; at the end of 3 hours the iodine addition fell to 35·9% (corresponding to 88·5% of αβ-ketone) and the mixture had $d_{4^\circ}^{20\cdot 0^\circ}$ 0·94190 and $n_D^{20\cdot 0^\circ}$ 1·48005.

Mobility. The pure βγ-ketone was mixed with *N*-sodium ethoxide (1 equiv.) and kept in a thermostat at 25°; one half of the liquid was removed at the end of 10 minutes and poured into water containing the calculated amount of acetic acid, and the remainder was similarly treated at the end of 20 minutes. The ketones were isolated and analysed; the first portion had an iodine addition of 41·9% (corresponding to 80% of αβ-ketone), the second 41·2% (80·5% of αβ-ketone). The two portions were then combined and kept with a slight excess of sodium ethoxide for 1½ hours; when isolated, the ketone had an iodine addition of 39·2% (corresponding to 84% of αβ-ketone), thus confirming the point of equilibrium previously found. It will be seen that equilibrium is practically established at the end of 10 minutes.

The authors' thanks are due to the Royal Society and to the Chemical Society for grants which have partly defrayed the cost of this investigation.

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[*Received, December 17th,* 1928.]