CXII.—*The Isomerism of the Butylideneacetones.*

By EUSTACE NEVILL ECCOTT and REGINALD PATRICK LINSTEAD.

THE movement of the double bond in unsaturated ketones containing an unbranched carbon chain has been but little investigated, although a considerable number of allied substances with a β-substituent, of the type of mesityl oxide, have been studied. The only direct investigation of the normal ketones is that of Blaise (*Bull. Soc. chim.*, 1905, **33**, 40), who showed that allyl alkyl ketones were readily converted into their Δ^{α}-propenyl isomerides by both acid and alkaline catalysts, a process involving an apparently irreversible movement of the double bond from the βγ- to the αβ-position. In attempting to correlate these earlier observations with the recent work on three-carbon tautomerism, we were led to examine the related pentenyl methyl ketones. At the outset, however, certain unexpected features were encountered in the preparation of the αβ-ketone, *n*-butylideneacetone, from *n*-butaldehyde and acetone, and this reaction was systematically reinvestigated.

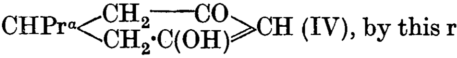
The condensation of aldehydes with ketones, and more particularly acetone, originally examined by Schmidt and by Claisen and extended to aliphatic aldehydes by Barbier and Bouveault (*Compt. rend.*, 1895, **120**, 1270), was first applied to *n*-butaldehyde by Weizmann and Garrard (J., 1920, **117**, 324), who isolated an unsaturated ketone to which the formula (I) was given.

$CH_2Me{\cdot}CH_2{\cdot}CH{:}CH{\cdot}COMe$ (I.)

$CH_2Me{\cdot}CH_2{\cdot}CH(OH){\cdot}CH_2{\cdot}COMe$ (II.)

Under milder conditions, Grignard and Dubien (*Ann. Chim.*, 1924, **2**, 287) were able to isolate the ketol (II), a type of compound already recognised as an intermediate in such reactions (Claisen, *Ber.*, 1892, **25**, 3164; Francke and Kohn, *Monatsh.*, 1899, **20**, 876). Dehydration of (II) with iodine yielded a ketone (semicarbazone, m. p. 118°) identical with that of Weizmann and Garrard.

As a result of a large number of experiments on this condensation, using aqueous alkali as catalyst, we find that under most conditions mixtures of unsaturated ketones and ketol are produced. It has, however, been possible to develop one method by which an unsaturated ketone is obtained direct in a state of considerable purity, and one, similar to that of Grignard and Dubien, for preparing the pure ketol (II). Dehydration of this has been investigated with iodine, acetic anhydride, and anhydrous oxalic acid, all of which produce an unsaturated ketone giving a semicarbazone melting at 124° after repeated crystallisation, the purest material being that obtained with oxalic acid as dehydrating agent. The butylideneacetone of previous workers is believed to be essentially this substance. If the original condensation is carried out rapidly and no attempt is made to check the development of heat, the product is composed of unsaturated ketone almost free from ketol. This ketone is, however, not identical with that obtained by dehydration of the ketol. It is higher-boiling, denser, and more refractive and readily gives a semicarbazone, m. p. 152°. Both ketones give the analytical figures required for $C_7H_{12}O$ and the semicarbazones also give the correct analytical values and depress each other's melting point. It is clear that these are two distinct substances, which may represent either structural isomerides differing in the position of the double bond or geometrical isomerides with the same position of the double bond.

Both ketones showed exaltations in the molecular refractivity (1·11 and 1·15 units) and had low iodine addition values (8 and 2%) (Linstead and May, J., 1927, 2565). Again, both resisted the action of ozone but yielded acetic and *n*-butyric acids on complete oxidation with alkaline permanganate. All doubt as to their constitution was finally removed by the synthesis of the compound with the only possible alternative formula, the βγ-isomeride (III), from the acid chloride of Δ^{β}-*n*-hexenoic acid (Eccott and Linstead, J., 1929, 2153) and zinc methyl iodide. The ketone so prepared, $CH_2Me\cdot CH{:}CH\cdot CH_2\cdot COMe$ (III), was a different substance. It had a high iodine addition value (70%), readily yielded propaldehyde on ozonisation, and gave a *semicarbazone*, m. p. 109—110°. No solid compound was formed when it was treated with ethyl sodiomalonate, whereas the other two ketones yielded the same 5-n-*propyldihydroresorcinol*,  $CHPr^{\alpha}{<}\begin{matrix}CH_2\text{——}CO\\ CH_2\cdot C(OH)\end{matrix}{>}CH$ (IV), by this reaction and subsequent hydrolysis. The first two ketones must therefore be regarded as *cis-* and *trans*-modifications of *n*-butylideneacetone about the αβ-double bond.

Geometrical isomerism of this type in ketones has only recently been observed and has received no systematic study. Locquin and Heilmann (*Compt. rend.*, 1928, **186**, 705) have isolated two forms of two α-alkyl unsaturated ketones, and the presence of a similar isomerism in the homomesitones is suggested by certain properties of these substances (Abbott, Kon, and Satchell, J., 1928, 2514). In addition, a number of styryl ketones containing the skeleton $CHPh{:}CH\cdot COR$ have been found to exist in coloured and colourless modifications (Haber, *Ber.*, 1891, **24**, 618; McGookin and Heilbron, J., 1924, **125**, 2099, and subsequent papers; Dilthey and Radmacher, *Ber.*, 1925, **58**, 361, *et cet.*). The isomerism shown by these compounds differs materially from that of the butylideneacetones. The isomeric styryl ketones have the same melting points and give identical derivatives (Wilson, Heilbron, and Sutherland, J., 1914, **105**, 2892). They are also noteworthy for the ease with which the less stable pass into the more stable forms.

In determining the configuration of the *n*-butylideneacetones, advantage was taken of their close relationship with Δ^{α}-*n*-hexenoic acid. Von Auwers and Wissebach have shown (*Ber.*, 1923, **56**, 715) that solid crotonic acid is almost unquestionably the *trans*-isomeride and von Auwers (*Annalen*, 1923, **431**, 46) found that it is this form of the acid which is produced from acetaldehyde by the Döbner reaction. It is reasonable to suppose that Δ^{α}-*n*-hexenoic acid (m. p. 33°), which is the almost exclusive product from *n*-butaldehyde in the Döbner reaction, also has the *trans*-configuration. When its acid chloride was condensed with zinc methyl iodide, the lower-boiling butylideneacetone was obtained, yielding the semicarbazone of m. p. 124° in a state of purity. The connexion indicated by this reaction was confirmed by the oxidation of this modification of the ketone with sodium hypochlorite, pure solid Δ^{α}-*n*-hexenoic acid being obtained. As a first assumption, therefore, this butylideneacetone is the *trans*-isomeride and the *cis*-configuration must be assigned to the ketone with semicarbazone of m. p. 152°, prepared by direct condensation. We endeavoured to confirm this view by studying the relative ease of cyclisation of the two ketones, *e.g.*, with concentrated sulphuric acid, to dihydrotoluenes, but deep-seated changes invariably occurred. When the *cis*-ketone was oxidised with sodium hypochlorite, a liquid acid was obtained giving long needles of m. p. 3°. This acid yielded the dibromide and anilide of solid (*trans-*)*n*-hexenoic acid and is regarded as a mixture of this acid with its as yet unknown *cis*-isomeride. It will be further investigated.

The isomeric *n*-butylideneacetones strongly resist configurational changes : for instance, the ketones regenerated from the semicarbazones by dilute acid re-form these derivatives in a state of purity. Bromine in an inert solvent, which has so marked an effect on configurational changes in acids, is rapidly absorbed with no apparent change in the unattacked ketone. Boiling dilute sulphuric acid has no pronounced effect, although it somewhat diminishes the purity of the ketones as measured by the readiness with which they yield pure semicarbazones. Hydrobromic acid, however, combines additively with both isomerides, giving a bromo-ketone which, when decomposed with aqueous potassium bicarbonate, yields the *trans*-ketone. In this way it is possible to convert the *cis*-form into its isomeride.

It was hoped to study the tautomeric change between the βγ- and the two αβ-ketones under the conditions previously used for such determinations. Unfortunately, all these ketones were readily converted into high-boiling products by the action of alkaline catalysts such as piperidine, sodium ethoxide and even sodium *iso*propoxide (Kon and Linstead, J., 1929, 1269). The βγ-ketone was, however, converted into the *trans*-αβ-ketone with boiling 20% sulphuric acid (compare Blaise, *loc. cit.*; Kon and Linstead, J., 1925, **127**, 815). Treatment in this way for 9 hours yielded a mixture of ketones with an iodine addition value of 32% (equivalent to about 75% of αβ-ketone), giving the *trans*-αβ-semicarbazone, and further treatment did not appreciably affect this. It is remarkable that it was not found possible to produce the βγ-ketone—as shown by an increase in iodine addition—from either form of the αβ-ketone under these conditions. In any case, it is clear that the αβ-position of the double bond is the more stable as in the corresponding acids (Fittig, *Annalen*, 1894, **283**, 47; Goldberg and Linstead, J., 1928, 2343). The βγ-ketone could also be converted into the αβ- by addition and elimination of hydrogen bromide. Here the product had an iodine addition value of 32% and yielded the semicarbazone of the *trans*-αβ-ketone. In view of the proved "abnormal" addition of hydrogen bromide to many βγ-unsaturated compounds, for example, to Δ^1-*cyclo*hexenylacetic acid (Wallach, *Annalen*, 1907, **353**, 289), the bromine entering the β- and the hydrogen the γ-position, it is unnecessary to assume with Blaise (*loc. cit.*) that the first stage in such a process is an isomeric change to the αβ-form, followed by a "normal" addition.

Attention was next directed to the isomeric ketones derived from *iso*butaldehyde. The condensation of this with acetone has been studied by Barbier and Bouveault (*loc. cit.*), who appear to have isolated only a crude product, and by Francke and Kohn (*loc. cit.*), who isolated both a ketol (V), the dehydration of which was not studied, and an unsaturated ketone (VI), b. p. 157°/750 mm.

(V.) $CHMe_2 \cdot CH(OH) \cdot CH_2 \cdot COMe$ $CHMe_2 \cdot CH{:}CH \cdot COMe$ (VI.)

Kishner (*J. Russ. Phys. Chem. Soc.*, 1913, **45**, 987) records the formation of an *iso*butylideneacetone (semicarbazone, m. p. 162—163°).

Using the method of Francke and Kohn, we isolated an unsaturated ketone which readily yielded a pure semicarbazone of m. p. 126°. The ketol (V) was prepared by a method similar to that used in the *n*-series and was dehydrated by iodine to yield an unsaturated ketone very similar to the first but giving a semicarbazone, m. p. 160°, which depressed the m. p. of the derivative already prepared. Francke and Kohn oxidised their ketone to Δ^α-*iso*hexenoic acid, and we have confirmed this relationship by synthesising this form of the ketone (semicarbazone, m. p. 126°) from Δ^α-*iso*hexenoyl chloride and zinc methyl iodide. As before, therefore, the ketone with the lower-melting semicarbazone is taken to be the *trans*-form. To show conclusively that neither form had the βγ-structure (VII), this ketone was independently prepared from pyroterebyl chloride (VIII) and zinc methyl iodide.

(VII.) $CMe_2{:}CH \cdot CH_2 \cdot COMe$ $CMe_2{:}CH \cdot CH_2 \cdot COCl$ (VIII.)

It is of interest that, although the action of thionyl chloride on pyroterebic acid fails to yield a pure product owing to the addition of hydrogen chloride to the double bond (Linstead, J., 1929, 2498), the action of phosphorus trichloride in benzene gives the unsaturated acid chloride (VIII) in a state of purity. The new ketone (VII) has a high affinity for iodine, whereas the *iso*butylideneacetones have practically none, and moreover yields a distinct semicarbazone.

It has been shown that the presence of two γ-methyl groups in a three-carbon system is accompanied by great stability of the βγ-double bond; for example, in pyroterebic acid (Goldberg and Linstead, *loc. cit.*) and its ethyl ester (Linstead, *loc. cit.*). It was therefore of great interest to find that the ketones in the *iso*-series differed abruptly from those of the normal series in that the βγ- were the more stable forms. The *trans*-αβ-ketone was converted to the extent of some 80% into its βγ-isomeride on being boiled with dilute sulphuric acid, and the same change could be effected by the addition and elimination of hydrogen bromide. In some respects these ketones resemble those investigated by Kon (J., 1926, 1792) with a *cyclo*hexane ring in place of the γ-*gem*-dimethyl group.

Another difference between the two series is that on dehydration the *n*-ketol yields the *trans*-, and the *iso*-ketol the *cis*-, form of the unsaturated ketone. Direct condensation under vigorous conditions proceeds differently in the two cases, for the *n*-aldehyde gives a *cis*-ketone, and the *iso*-aldehyde the *trans*-, but this difference appears to depend largely upon the experimental conditions. For instance, Weizmann and Garrard (*loc. cit.*) obtained a fairly pure *trans*-*n*-butylideneacetone by direct condensation, whereas Kishner's ketone (*loc. cit.*) seems to have been the *cis*-form of *iso*butylideneacetone. In many condensations in the early stages of the present work mixtures of αβ-ketones were obtained and it is probably largely a matter of chance that the methods eventually developed to give individual products yielded a *trans*-form in one series and a *cis*-form in the other. In any case, it must be assumed that, whatever the configuration of the final product, the reaction first proceeds through the ketol, which subsequently loses water under the conditions used in the " direct condensation." This being so, it is a matter of interest that the pure *isolated* ketol is not dehydrated when treated with alkali under these conditions.

The investigation of these and related compounds will be continued.

[*Added to proof.*]—The publication of an abstract (*A.*, 1930, 325) has directed our attention to a paper of Locquin and Heilmann (*Bull. Soc. chim.*, 1929, **45**, 1126). These authors obtained an *iso*butylideneacetone of indefinite b. p. which failed to yield a pure semicarbazone. This they regard as indicating the existence of stereoisomeric forms of the ketone and semicarbazone, a view which is amply confirmed by the isolation in the present work of the two individual ketones and their derivatives. There seems little doubt that the βγ-ketone of Locquin and Heilmann is identical with ours, but we consider Kishner's ketone, produced by direct condensation (*loc. cit.*), to be the *cis*-αβ-form and not the βγ- as suggested by Locquin and Heilmann. The semicarbazones provide no useful evidence, but the physical properties of Kishner's ketone agree with those of our αβ-forms rather than with those found for the βγ- by Locquin and Heilmann and in the present work. Further, Kishner prepared 3-methyl-5-*iso*propylpyrazoline in 90% yield from his ketone by a reaction which Locquin and Heilmann themselves use as being selective for αβ-ketones (*loc. cit.*, p. 1118).

EXPERIMENTAL.

Normal Series.

Condensation of n-*Butaldehyde with Acetone*.—(a) *Production of the ketol.* Grignard and Dubien's method gave good yields of total condensation product, but this always contained a considerable proportion of dehydrated material. The following process caused less dehydration than any other used. To a mechanically stirred mixture of caustic soda (20 g.) in water (40 c.c.) and acetone (116 g.) kept between 5° and 10°, *n*-butaldehyde (72 g.), diluted with acetone (58 g.), was added during 3 hours. After an hour's stirring, the aqueous layer was separated and extracted with ether, and the extract added to the oil. The combined product was neutralised with dilute acetic acid, washed with sodium bicarbonate solution and a little water, and dried over anhydrous potassium carbonate. The acetone and ether were removed by suction and the residue was distilled under reduced pressure. A little water and then a fraction (b. p. 68—92°/12 mm.; 30 g.) containing some unsaturated material distilled over, followed by the ketol (40 g.), b. p. 95°/12 mm.

Reducing the *amount* of caustic soda lowers the yield and reducing its *concentration* by the addition of water has the same effect and results in the formation of high-boiling material derived from the aldehyde.

Heptan-δ-ol-β-one (II) (Grignard and Dubien, *loc. cit.*) is a pale yellow liquid with a faint odour, $d_{4^\circ}^{19\cdot5^\circ}$ 0·9296, $n_D^{19\cdot5^\circ}$ 1·4357 (Found: C, 64·8; H, 10·7. Calc.: C, 64·6; H, 10·8%). Treatment of the ketol with 25% aqueous caustic soda (8 vols.) at the b. p. or with shaking in the cold for 3 hours gave only unchanged ketol and high-boiling material.

(b) *Production of* cis-n-*butylideneacetone* (I). To a mixture of acetone (145 c.c.) and 15% aqueous caustic soda (320 c.c.), *n*-butaldehyde (178 c.c.) was added in a slow stream. The vigorous reaction was at first allowed to proceed under reflux and finished by mechanical shaking for 2—3 days. The aqueous layer was extracted with ether and the extract was added to the organic portion, which was then washed with water and dried with calcium chloride. After removal of the low-boiling material, the residue was fractionated under reduced pressure. The crude ketone had b. p. 70°/12 mm., but contained water which could not be removed by ordinary drying agents. An equal volume of dry benzene was added which was then distilled off at ordinary pressure through a column (compare Grignard and Dubien, *loc. cit.*). The dry ketone obtained by fractionation of the residue (50 g.) had b. p. 67—70°/12 mm., $d_{4^\circ}^{23^\circ}$ 0·8507, $n_D^{23^\circ}$ 1·4470, $[R_L]_D$ 35·22. The iodine addition value was 4%. This and all other iodine addition values referred to in this paper were obtained by using 10-minute reactions in chloroform solution (Linstead and May, *loc. cit.*). If the amount of alkali and water used in the condensation was similar to that used in the preparation of the ketol, and the reaction was allowed to proceed vigorously, mixtures of ketol and ketone were obtained.

The *cis*-ketone so prepared was nearly free from its isomeride, as shown by the purity of the semicarbazone, which could only be obtained in quantity when the following precautions were observed. The ketone (20 g.) was added to a cold solution of semicarbazide hydrochloride (20 g.) in the minimum quantity of saturated aqueous sodium acetate. Miscibility was established with alcohol, and a seeding crystal introduced together with enough water to prevent its solution. Precipitation of the *semicarbazone* was allowed to occur at room temperature, the product being cooled in a freezing mixture before filtration. The material so obtained was microcrystalline, melting at 143°, and at 152° after one crystallisation. The m. p. could not be further raised (Found : C, 57·1 ; H, 9·1. $C_8H_{15}ON_3$ requires C, 56·8 ; H, 8·9%). The semicarbazone (22 g., m. p. 152°) was intimately mixed with 25 g. of crystallised oxalic acid and the very volatile ketone was distilled in a current of steam, isolated by means of ether, and dried in the manner already described. Yield, 80%.

cis-*Butylideneacetone* so obtained is a colourless pleasant-smelling liquid, b. p. 70°/15 mm., $d_{4^\circ}^{22^\circ}$ 0·8555, $n_D^{22^\circ}$ 1·4505, $[R_L]_D$ 35·22 (calc., 34·07) (Found : C, 74·7 ; H, 10·7. $C_7H_{12}O_2$ requires C, 74·9 ; H, 10·8%). The pure ketone has an iodine addition value of 2·3% and immediately yields the semicarbazone, m. p. 152°, in a state of purity.

Dehydration of the Ketol.—(i) *With iodine.* By the method of Grignard and Dubien, 40 g. of the ketol yielded 24 g. of ketone, b. p. 58—62°/16 mm., $d_{4^\circ}^{18^\circ}$ 0·8493, $n_D^{18^\circ}$ 1·4408, $[R_L]_D$ 34·8, iodine addition value 23·4%.

(ii) *With acetic anhydride* (Claisen, *Annalen*, 1899, **306**, 326). The ketol (42 g.) was refluxed with acetic anhydride (50 g.) for 3 hours. Direct distillation of the product under reduced pressure yielded no evidence of acetylation, the material boiling between 50° and 71°/5 mm. After the addition of an excess of sodium carbonate the product was distilled in steam and the ketone was isolated in the usual way and redistilled. The product (28 g.) had b. p. 60°/10 mm., $d_{4^\circ}^{15^\circ}$ 0·8507, $n_D^{15^\circ}$ 1·4449, $[R_L]_D$ 35·06, iodine addition 11·2%.

(iii) *With oxalic acid* (Pauly and von Berg, *Ber.*, 1901, **34**, 2092). 32 G. of the ketol were heated on the water-bath for 2 hours with 46 g. of anhydrous oxalic acid. Hydrated oxalic acid crystallised from the reddish-brown syrupy residue, which was distilled in a current of steam. The ketone, isolated in the usual way (19 g.), had b. p. 62—64°/12 mm., $d_{4^\circ}^{20^\circ}$ 0·8450, $n_D^{20^\circ}$ 1·4432, $[R_L]_D$ 35·18, iodine addition 8·2%.

The products obtained by all these methods yielded a *semicarbazone* which crystallised from dilute alcohol in white silvery plates, m. p. 128° (Found : C, 56·9; H, 9·2. $C_8H_{15}ON_3$ requires C, 56·8; H, 8·9%). The product from the iodine dehydration yields this with comparative difficulty, and the oxalic acid method is the most satisfactory for preparing a homogeneous ketone. The ketone from each method contains water which cannot be removed by ordinary drying agents (compare Grignard and Dubien, *loc. cit.*) (Found : C, 72·9; H, 10·4%). Dried by distillation with benzene in the manner already described, *trans-n*-butylideneacetone was obtained as a colourless liquid with a pleasant odour differing somewhat from that of the *cis*-isomeride. It had b. p. 62°/15 mm., $d_{4^\circ}^{20^\circ}$ 0·8445, $n_D^{20^\circ}$ 1·4430, $[R_L]_D$ 35·18, iodine addition 9·0%. Ultimate analysis is difficult and tends to give low results for this type of ketone, as has been noticed by other workers (Claisen, Francke and Kohn, Weizmann and Garrard, *locc. cit.*) (Found : C, 74·3; H, 10·5. Calc. : C, 74·9; H, 10·8%). Unlike the *cis*-ketone, the *trans*-ketone was regenerated from its semicarbazone with considerable loss. In one experiment 16 g. of semicarbazone gave 2 g. of ketone having b. p. 62°/10 mm., $d_{4^\circ}^{21^\circ}$ 0·8483, $n_D^{21^\circ}$ 1·4423, iodine addition 8·1%; and in another, 12 g. yielded 2 g., b. p. 64°/10 mm., $d_{4^\circ}^{21^\circ}$ 0·8454, $n_D^{21^\circ}$ 1·4424. The ketone prepared by the oxalic acid method and purified by distillation with benzene and under reduced pressure was used as *trans*-ketone in the experiments described later.

trans-*Ketone from* Δ^{α}-n-*Hexenoyl Chloride.*—36 G. of the acid chloride (Goldberg and Linstead, *loc. cit.*) were added to zinc methyl iodide, prepared in the usual way from 41·6 c.c. of methyl iodide and 43 g. of zinc–copper couple in 21·6 c.c. of ethyl acetate and 50 c.c. of benzene (Blaise and Maire, *Ann. Chim. Phys.*, 1908, **15**, 556). A typical product, isolated in the usual way (*loc. cit.*), had b. p. 69—71°/20 mm., iodine addition 8% (16 g.). This synthesis was carried out many times in the present work, but the physical constants of the products agreed neither among themselves nor with those already found for the two isomeric ketones, as may be seen from the following table :

	B. p.	$d_{4°}^{20°}$.	$n_D^{20°}$.
trans-Ketone	62°/15 mm.	0·8445	1·4430
cis-Ketone	70/15	0·8571	1·4513
Ketone from acid chloride	69—71/20	0·8672	1·4404
,, ,, ,, ...	69/15	0·8603	1·4420
,, ,, ,, ...	63/10	0·8786	1·4387
,, ,, ,, ...	66/10	0·8723	1·4407
,, ,, ,, ...	62—63/12	0·8658	1·4414

The high density and low refractivity of the material prepared from the acid chloride point to the presence of traces of ester (such as is often produced in these reactions) which cannot be completely removed by fractionation. This impurity somewhat inhibits the formation of the semicarbazone, which is best prepared by mixing the components in a freezing mixture and keeping the mixture ice-cold until crystallisation is at an end. The derivative then separates almost pure, m. p. 124° alone or when mixed with the *trans*-semicarbazone. A mixture with equal parts of the *cis*-semicarbazone melts at 110°.

Preparation of Δ^{δ}*-Hepten-*β*-one* (III).—Δ^{β}-Hexenoyl chloride was prepared from Δ^{β}-*n*-hexenoic acid which had been purified by one partial esterification (followed by fractionation) (Eccott and Linstead, *loc. cit.*). The purity of this acid chloride was checked by conversion of a small portion into the *p*-toluidide, m. p. 90° (crude), 95—96° after one crystallisation (mixed m. p. 96°). The acid chloride (25 g.), treated exactly as its αβ-isomeride, yielded the ketone (12 g.) as a sweet-smelling liquid, b. p. 61—62°/20 mm., $d_{4°}^{21°}$ 0·8618, $n_D^{21°}$ 1·4290, iodine addition, 71%. The *semicarbazone* crystallised in small white plates, m. p. 109—110° (Found : C, 57·0; H, 8·7. $C_8H_{15}ON_3$ requires C, 56·8; H, 8·9%). Satisfactory analytical figures could not be obtained for the ketone itself.

Oxidation of the Ketones.—*trans*-Butylideneacetone (5 g.) was mixed with saturated sodium carbonate solution (10 g.-mols. per g.-mol. of ketone), and 3% aqueous potassium permanganate added until no more was reduced. The product, worked up in the usual way, yielded 5 g. of total oxidation product : this had a strong odour of acetic acid, which was separated by distillation and converted into acetanilide (m. p. and mixed m. p. 115°). The higher-boiling material was converted into chloride, and butyryl chloride separated by fractionation and identified by conversion into *n*-butyramide (m. p. and mixed m. p. 115°). The *cis*-ketone was treated in the same way and yielded the same products.

Both *cis*- and *trans*-ketones were recovered unchanged after treatment with ozonised oxygen for 20 hours. The βγ-ketone (III), however, readily yielded an ozonide. This was decomposed with water, and the product, after being made alkaline, distilled. The first fraction contained propaldehyde, which was identified as the *p*-nitrophenylhydrazone, m. p. and mixed m. p. 120°.

The *trans*-ketone (11 g.) was added slowly to excess of an ice-cold, freshly prepared solution of sodium hypochlorite. The mixture was removed from the ice and shaken thoroughly for an hour; the temperature then rose sharply. The cold product was extracted with ether to remove unchanged ketone, treated with an excess of sodium sulphite, acidified, and extracted with ether. The residue from the ether yielded an acid (3 g.), b. p. 116—120°/15 mm., which solidified at room temperature and melted after crystallisation at 33°, alone or when mixed with authentic Δ^{α}-*n*-hexenoic acid. The anilide had m. p. and mixed m. p. 109—110°.

The *cis*-ketone (11 g.) was oxidised exactly as above and yielded 3 g. of an acid, b. p. 120—126°/14 mm., m. p. 3°, $d_{4^{\circ}}^{18^{\circ}}$ 1·00, $n_{D}^{18^{\circ}}$ 1·4520, iodine addition 0·9% (Linstead and May, *loc. cit.*). A mixture of this acid with a quarter of its weight of the acid of m. p. 33° melted at 6° and the m. p. was further raised by the addition of more 33°-acid. The acid slowly yielded the dibromide of the 33°-acid (m. p. and mixed m. p. 68—70°) and readily gave the anilide through the acid chloride (m. p. and mixed m. p. 109°).

5-n-*Propyldihydroresorcinol* (IV).—(a) *From the* trans-*ketone.* 4·5 G. of the ketone were added to ethyl sodiomalonate made from 0·92 g. of sodium, 18 c.c. of alcohol, and 6·2 g. of the ester, and the mixture was heated on the water-bath under reflux for 3 hours. The solid sodio-compound of the intermediate ester (6 g.) was collected, washed with a little alcohol, and hydrolysed with crystallised sodium carbonate (10 g.) in water (12 c.c.). The product was worked up in the usual way, and the 5-n-*propyldihydroresorcinol* purified by treatment with sodium bicarbonate. From this it was obtained by acidification and extraction as a viscous oil, which gradually solidified (1 g.). On recrystallisation this melted at 107° (Found: C, 69·8; H, 8·9. $C_9H_{14}O_2$ requires C, 70·1; H, 9·1%). If the solid sodio-compound was not hydrolysed as such but was acidified and the dihydroresorcinol ester itself was extracted before hydrolysis, the solidification of the final product was much delayed. Hydrolysis with baryta yielded gummy products.

(b) Under similar conditions the *cis*-ketone (5 g.) yielded the same product (1 g.), m. p. and mixed m. p. 107°.

Interconversion of the Isomeric Ketones.—Reference data. Mixtures of the βγ- and the *trans*-αβ-ketone reacted with iodine as follows:

% αβ-ketone	100	90	80	75	66·6	50	33·0	20	0
% Iodine addition	8·1	17·5	28·0	30·4	37·6	48·2	58·0	64·6	71·0

(a) *Sodium ethoxide.* The *trans*-αβ-ketone (7·4 g.) was treated with 1 equiv. of anhydrous *N*-sodium ethoxide (Kon and Linstead, *loc. cit.*, 1929). The entire product boiled above 170°/20 mm. The βγ-ketone was also converted into high-boiling material.

(b) *Sodium* iso*propoxide* gave the same result.

(c) *Barium hydroxide* (compare Hugh, Kon, and Linstead, J., 1927, 2585). The *trans*-αβ-ketone (2 g.) was mixed with 10 c.c. of 0·17*N*-barium hydroxide, and miscibility established by addition of alcohol. After 4 hours' boiling, the ketone was isolated unchanged ($d_{4^\circ}^{19^\circ}$ 0·8757, $n_{\mathrm{D}}^{19^\circ}$ 1·4376, iodine addition 2·5%; semicarbazone, m. p. 124°).

(d) *Piperidine.* A mixture of *trans*-αβ-ketone (4 g.) and piperidine (6·1 g.) was heated under reflux for 2 days on the water-bath and was finally boiled for 2 hours. Only high-boiling material was recovered. The *cis*-αβ- and the βγ-ketone were similarly affected.

(e) *Dilute sulphuric acid.* The *trans*-αβ-ketone (3 g.) was refluxed with 9 g. of 20% (by weight) sulphuric acid for 8 hours. The ketonic product (1 g.) had b. p. 70°/15 mm., iodine addition 10%, and gave a semicarbazone, m. p. 100° (crude), which yielded the pure *trans*-derivative on recrystallisation (m. p. and mixed m. p. 124°). Similarly treated, the *cis*-αβ-ketone (3 g.) gave 1 g. of product, b. p. 70°/15 mm., with unchanged iodine addition. After one crystallisation the semicarbazone gave the almost pure *cis*-derivative (m. p. 148°).

The βγ-ketone (3 g.), mixed with 6 g. of 20% sulphuric acid, was heated under reflux for 1 hour. The recovered ketone (1·8 g.) had b. p. 63—68°/18 mm., $d_{4^\circ}^{19^\circ}$ 0·8654, $n_{\mathrm{D}}^{19^\circ}$ 1·4332, iodine addition 51%. The semicarbazone was a mixture, m. p. 78°, which could not be separated into its constituents. A similar experiment was carried out for 9 hours. The recovered ketone (1·0 g.) had $d_{4^\circ}^{21^\circ}$ 0·8680, $n_{\mathrm{D}}^{21^\circ}$ 1·4390, iodine addition 32·4%. The semicarbazone melted (crude) at 95—96° and after recrystallisation gave the white plates of the *trans*-αβ-semicarbazone, m. p. 122°, mixed m. p. 123—124°. In a further experiment, the βγ-ketone (5 g.) was treated as before for 9 hours; the product was then isolated and given a further 9 hours' treatment. The final product (2 g.) had $d_{4^\circ}^{25^\circ}$ 0·8539, iodine addition 29·4% (equivalent to 77% of *trans*-αβ-ketone) and yielded the *trans*-αβ-semicarbazone.

(f) *Hydrobromic acid* (compare Blaise, *loc. cit.*). The *trans*-αβ-ketone (5 g.) was added slowly to 12 g. of ice-cold hydrobromic acid, saturated at 0°. The black liquid was kept at 0° for ½ hour and then poured into water and extracted with ether. The extract was washed with sodium bicarbonate solution and dried over anhydrous sodium sulphate. After removal of the solvent the residue was distilled; the bromo-ketone (4 g.) then came over at 70°/3 mm. as a colourless liquid, which quickly darkened in light and had a faint characteristic odour distinct from that of the unsaturated ketone. It was boiled with potassium bicarbonate (5 g.) in water (30 c.c.) for 2 hours. The ketone obtained had b. p. 70°/15 mm., $d_{4^\circ}^{21^\circ}$ 0·8460, and iodine addition 17·3% (an increase of 8·0%). The semicarbazone melted at 100° (crude) and yielded the pure *trans*-derivative after recrystallisation (m. p. and mixed m. p.).

Similarly treated, the *cis*-ketone reacted less completely and the crude bromo-ketone was accordingly mixed with a further 12 g. of hydrobromic acid. The bromo-ketone isolated from the product had b. p. 80°/5 mm. and gave with bicarbonate a ketone the semicarbazone of which melted (crude) at 100° and after recrystallisation at 124°. Its identity with the *trans*-derivative was confirmed by a mixed melting-point determination.

The βγ-ketone (3·5 g.), treated in the same way with hydrobromic acid (8·4 g.), yielded a bromo-ketone, b. p. 80°/5 mm. The ketone obtained from this by treatment with bicarbonate had b. p. 72°/15 mm., $d_{4^\circ}^{20^\circ}$ 0·8835, $n_D^{20^\circ}$ 1·4337, iodine addition 32%. The crude semicarbazone melted at 103° and furnished the pure *trans*-αβ-derivative on recrystallisation.

iso-*Series.*

Condensation of iso*Butaldehyde with Acetone.*—(a) *Production of ketol.* The *iso*butaldehyde was partly prepared by Fossek's method (*Monatsh.*, 1881, **2**, 614) and partly purchased from Messrs. Poulenc Frères. The aldehyde (50 g.) was added during 5 hours with mechanical stirring to a mixture of acetone (100 g.), aqueous caustic soda (50 c.c. of 12%), and ether (20 g.) maintained at 10°. The product was isolated as in the *n*-series and yielded 32 g. of the pure ketol and a considerable quantity of dehydrated material. ε-Methylhexan-δ-ol-β-one (V) (Francke and Kohn, *loc. cit.*) was thus obtained as a colourless liquid, b. p. 92°/23 mm., $d_{4^\circ}^{22^\circ}$ 0·9432, $n_D^{22^\circ}$ 1·4357 (Found: C, 64·7; H, 10·5. Calc.: C, 64·6; H, 10·8%).

(b) *Production of* trans-iso*butylideneacetone* (VI) (compare Francke and Kohn, *loc. cit.*). *iso*Butaldehyde (50 g.) was added in a slow stream to a mixture of acetone (52 c.c.) and aqueous caustic soda (120 c.c. of 10%). The mixture was subsequently shaken for 2 days and worked up in the usual way. The ketone obtained (20 g.) had b. p. 63—65°/20 mm., $d_{4^\circ}^{22^\circ}$ 0·8407, $n_D^{22^\circ}$ 1·4395, $[R_L]_D$ 35·06 (calc., 34·07), iodine addition 4·5%. The *semicarbazone* melted in the crude state at 120° and formed white silvery plates, m. p. 126°, from dilute alcohol (Found: C, 56·7; H, 9·1. $C_8H_{15}ON_3$ requires C, 56·8; H, 8·9%).

Dehydration of the Ketol.—Anhydrous oxalic acid caused considerable charring and only a few drops of material, b. p. 62°/12 mm., could be obtained. This yielded a mixture of semicarbazones.

Dehydration with iodine in the usual manner gave a 70% yield of *cis*-*iso*butylideneacetone, b. p. 64°/18 mm., $d_{4°}^{20°}$ 0·8558, $n_{D}^{20°}$ 1·4374, $[R_L]_D$ 34·32 (calc., 34·07), iodine addition 8%. The *semicarbazone* crystallised in small plates, m. p. 160° (Found : C, 57·0; H, 9·2. $C_8H_{15}ON_3$ requires C, 56·8; H, 8·9%). A mixture of equal parts of this and the *trans*-semicarbazone (m. p. 126°) melted at 110°.

Δ^{α}-*iso*Hexenoyl chloride (Goldberg and Linstead, *loc. cit.*), treated with zinc methyl iodide in the usual way, yielded *trans*-*iso*butylideneacetone in 45% yield. This had b. p. 64°/23 mm., $d_{4°}^{28°}$ 0·8549, $n_{D}^{28°}$ 1·4357, $[R_L]_D$ 34·22 (calc., 34·07), iodine addition 1%, and was identified with that prepared by direct condensation by the formation of the semicarbazone, m. p. and mixed m. p. 126°.

βγ-*Ketone.*—Pyroterebic acid prepared by equilibration of Δ^{α}-*iso*hexenoic acid (Goldberg and Linstead, *loc. cit.*) had b. p. 103°/14 mm., $d_{4°}^{24°}$ 0·9694, $n_{D}^{24°}$ 1·4442. It was dissolved (18 g.) in an equal volume of dry benzene, and phosphorus trichloride (10% excess) was cautiously added. The mixture was heated on the water-bath for $\frac{3}{4}$ hour and then yielded 15 g. of pyroterebyl chloride (VIII), b. p. 54°/15 mm. The *anilide* prepared from this formed flattened needles, m. p. 98°, from benzene and light petroleum (Found : C, 76·1; H, 7·9. $C_{12}H_{15}ON$ requires C, 76·2; H, 8·0%). Repeated crystallisation failed to raise the melting point : the derivative, m. p. 106°, of Goldberg and Linstead (*loc. cit.*) probably contained some γ-chloroanilide.

Pyroterebyl chloride so prepared gave with zinc methyl iodide a 35% yield of ε-methyl-Δ^{δ}-hexen-β-one (VII), b. p. 72—74°/30 mm., obviously contaminated with non-ketonic by-products. It had $d_{4°}^{21·5°}$ 0·9012, $n_{D}^{21·5°}$ 1·4317, iodine addition 66%, and yielded a very pure *semicarbazone*, which crystallised from dilute alcohol in white silvery flakes, m. p. 158° (crude) and 159—160° (after recrystallisation) (Found : C, 57·0; H, 9·2. $C_8H_{15}ON_3$ requires C, 56·8; H, 8·9%). A mixture with the *cis*-αβ-semicarbazone melted at 154°.

Conversion of the trans-αβ- *into the* βγ-*form.* (a) *With sulphuric acid.* The procedure used in the *n*-series was followed. Reaction for 16 hours almost completely destroyed the ketone, only 10% being recovered. This yielded the βγ-semicarbazone, m. p. and mixed m. p. 159—160°. Reaction for 3 hours left 40% of ketone, b. p. 64°/20 mm., iodine addition 51·3% (an increase of 46·8%), which gave the βγ-semicarbazone.

(b) *With hydrobromic acid.* This was carried out as in the *n*-series, two treatments with the reagent being used. The bromo-ketone decomposed slightly on distillation, but a sample of b. p. 90°/5 mm. was decomposed with bicarbonate in the usual way and yielded the βγ-ketone, identified in the form of its semicarbazone. In another experiment, only one treatment with the reagent was given and the bromo-ketone was treated with bicarbonate without distillation: 40% of ketone was recovered, b. p. 64°/20 mm., iodine addition 52·4%, which readily yielded the βγ-semicarbazone, m. p. and mixed m. p. 159—160°.

All the unsaturated ketones described in the present communication deteriorate rapidly on keeping with the formation of high-boiling products (compare Weizmann and Garrard, *loc. cit.*). On one occasion an old sample of *cis*-*iso*butylideneacetone exploded on attempted distillation, which suggests that some type of oxidation occurs.

Our thanks are due to the Government Grant Committee of the Royal Society and to the Chemical Society for grants which have largely defrayed the cost of this work.

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY,
LONDON, S.W. 7.
[*Received, February* 11*th*, 1930.]