624. *Anionotropic Systems. Part III.* The Synthesis and Rearrangement of 3-Hydroxy-3 : 5-dimethylhex-4-en-2-one.*

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The first example of anionotropy in a three-carbon system terminated by a carbonyl group is described. As would be expected the anionotropic mobility of such a system is very low and the reaction succeeds only in a suitably designed structural environment.

Addition of *iso*butenyl-lithium to 3 : 3-dimethoxybutan-2-one furnished the ketal (XIII) which on mild acid hydrolysis gave 3-hydroxy-3 : 5-dimethylhex-4-en-2-one (VIII). This βγ-ethylenic α-hydroxy-ketone undergoes anionotropic rearrangement under carefully controlled acid conditions, to the isomeric αβ-ethylenic γ-hydroxy-ketone (XIV), the structure of which is established by degradation. Prolonged acid treatment of (VIII) results in cyclisation to the dihydrofuran (XV), isolated as the ether (XVI), and dehydration to the dienone (XVII).

DURING the last ten years, many examples of anionotropic systems of the type

$$\text{(I)}\quad \mathrm{C{:}C{\cdot}CX{\cdot}OH} \longrightarrow \mathrm{C(OH){\cdot}C{:}C{\cdot}X}\quad \text{(II)}$$

where X is one of a variety of unsaturated groups, including ethylenic, acetylenic, aromatic, and heteroaromatic functions, have been described (for a summary, see Braude, *Quart. Reviews*, 1950, **4**, 404). In all these rearrangements, the equilibrium is displaced almost completely to the right owing to the additional stabilisation associated with the conjugated

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* Part II, *J.*, **1953**, 2202.

systems $\mathrm{C{:}CX}$. A carbonyl function should also have this effect, since its conjugating properties are well established, but the nearest example of such a reaction which appears in the literature involves $\mathrm{X = CO_2H}$ and occurs in the conversion of 2-hydroxypent-3-enoic acid (III) into lævulic acid (IV) (Fittig and Schaak, *Annalen*, 1898, **299**, 42), where the anionotropic rearrangement is followed by a double prototropic change :

$$\begin{tikzcd}
\text{(III)}\ \mathrm{Me{\cdot}CH{:}CH{\cdot}CH(OH){\cdot}CO_2H} \arrow[r] & \mathrm{HO{\cdot}CHMe{\cdot}CH{:}CH{\cdot}CO_2H} \arrow[d] \\
\text{(IV)}\ \mathrm{Me{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H} & {[\mathrm{HO{\cdot}CMe{:}CH{\cdot}CH_2{\cdot}CO_2H}]} \arrow[l]
\end{tikzcd}$$

A possible route to a system of type (I) with $\mathrm{X = COMe}$ was investigated by Heilbron, Jones, Smith, and Weedon (*J.*, 1946, 54; cf. Braude and Timmons, *J.*, 1953, 3144) who attempted the hydration of the acetylenic alcohol (V) to the keto-alcohol (VI), but obtained instead the diketone (VII) formed by prototropic rearrangement under the acidic reaction conditions. These authors commented on the fact that the strongly electron-attracting properties of the carbonyl group would retard anionotropic rearrangement while favouring the alternative prototropic change, and their work indicated that anionotropic rearrangements of the type (I) $\longrightarrow$ (II), where X is a ketone function, would be difficult, if not impossible, to realise.

$$\begin{tikzcd}
\text{(V)}\ \ \mathrm{CHMe{:}CH{\cdot}CH(OH){\cdot}C{\vdots}CH} \arrow[r] & \mathrm{CHMe{:}CH{\cdot}CH(OH){\cdot}COMe}\ \ \text{(VI)} \arrow[d] \\
\text{(VII)}\ \ \mathrm{CH_2Me{\cdot}CH_2{\cdot}CO{\cdot}COMe} & {[\mathrm{CH_2Me{\cdot}CH{:}C(OH){\cdot}COMe}]} \arrow[l]
\end{tikzcd}$$

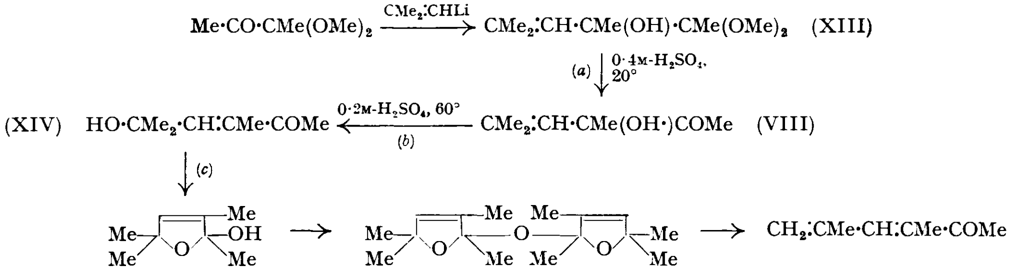
Since the possible isomerisation of $\beta\gamma$-ethylenic α-hydroxy-ketones to $\alpha\beta$-ethylenic γ-hydroxy-ketones is of considerable practical as well as theoretical interest, we set out to produce a system with structural features more favourable to the occurrence of such a reaction. The simplest such is (VIII), in which complete alkylation in the α- and the γ-position will preclude prototropy, and at the same time increase anionotropic mobility (cf. Braude and Jones, *J.*, 1946, 122, 128). The synthesis of (VIII), and its acid-catalysed anionotropic rearrangement to (XIV), are described below. Kinetic studies, recorded in the following paper, show that the rate of isomerisation of (VIII) is slower by a factor of *ca.* 10^5 than that of the corresponding phenyl analogue (Ph replacing COMe), in agreement with expectation.

The majority of standard methods for the synthesis of α-keto-alcohols are inapplicable to a system such as (VIII), but the monoaddition of *iso*butenyl-lithium (Braude and Timmons, *J.*, 1950, 2000, 2007; Braude and Coles, *J.*, 1952, 1425) to diacetyl appeared to afford a possible route. Only the diaddition product (IX) could be isolated, however, even when an excess of diacetyl was employed. Although the monoaddition of Grignard reagents to diacetyl is possible (cf. Wilson and Hyslop, *J.*, 1924, 1556; Kleinfeller and Eckert, *Ber.*, 1929, **62**, 1598; 1939, **72**, 249; Lapkin and Golovkova, *J. Gen. Chem., U.S.S.R.*, 1949, **19**, 701), the failure to effect monoaddition of the lithium-alkenyl is not altogether surprising, since lithium derivatives are known to be less selective than Grignard reagents in their action on polyfunctional compounds (cf. Carter, *Iowa State Coll. J. Sci.*, 1940, **15**, 63). An attempt to effect the monoaddition of *iso*butenylmagnesium bromide (Krestinsky, *Ber.*, 1922, **55**, 2773) to diacetyl was also unsuccessful; this Grignard reagent could only be formed in reasonable yield in the presence of methylmagnesium bromide, and the main products were 3-hydroxy-3-methylbutan-2-one $\mathrm{HO{\cdot}CMe_2{\cdot}COMe}$ and the glycol (XII), although a small amount of (VIII) was also obtained. The structures of the ditertiary glycols (IX) and (XII) were established by fission with aqueous sodium periodate, which gave mesityl oxide in the first case, and acetone and mesityl oxide in the second. It is of interest that the reaction of the glycols (IX) and (XII) with sodium periodate is very slow and requires several days at room temperature; similar effects have been noted with other tertiary glycols (cf. Wintersteiner and Moore, *J. Amer. Chem. Soc.*, 1950, **72**, 1923). With Brady's reagent the glycol (IX) slowly gave the 2 : 4-dinitrophenylhydrazone of a ketone evidently formed by pinacol–pinacone rearrangement. Since the ultra-violet light absorption of the derivative ($\lambda_{max.}$ 3680 Å) shows that the functional group is not conjugated (cf. Braude and Jones, *J.*, 1945, 498), the ketone is formulated as (X) rather than (XI).

$$\begin{tikzcd}
\begin{array}{c}\mathrm{CMe_2{:}CH{\cdot}CMe(OH){\cdot}COMe}\\ \text{(VIII)}\end{array} \arrow[d, "\mathrm{CMe_2{:}CHLi}"] & \mathrm{MeCO{\cdot}COMe} \arrow[l, "\mathrm{CMe_2{:}CHLi}"'] \arrow[r, "\mathrm{CMe_2{:}CH{\cdot}MgBr}", "\mathrm{MeMgBr}"'] & \begin{array}{c}\mathrm{CMe_2{:}CH{\cdot}CMe(OH){\cdot}CMe_2{\cdot}OH}\\ \text{(XII)}\end{array} \\
\begin{array}{c}\mathrm{CMe_2{:}CH{\cdot}CMe(OH){\cdot}CMe(OH){\cdot}CH{:}CMe_2}\\ \text{(IX)}\end{array} \arrow[r] & \begin{array}{c}\mathrm{(CMe_2{:}CH)_2CMe{\cdot}COMe}\\ \text{(X)}\end{array} & \begin{array}{c}\mathrm{CMe_2{:}CH{\cdot}CMe_2{\cdot}CO{\cdot}CH{:}CMe_2}\\ \text{(XI)}\end{array}
\end{tikzcd}$$

Attention was then directed to the addition of *iso*butenyl-lithium to a diacetyl derivative in which one of the carbonyl groups is temporarily protected. Reaction with diacetyl dimethyl monoketal (3 : 3-dimethoxybutan-2-one; Calder and Fleer, U.S.P. 2,401,336) afforded a moderate yield of the ketal (XIII). Mild acid hydrolysis (0·4M-sulphuric acid at room temperature) of the latter gave the desired keto-alcohol, 3-hydroxy-3 : 5-dimethylhex-4-en-2-one (VIII). It was characterised by a 3 : 5-dinitrobenzoate and a 2 : 4-dinitrophenylhydrazone, the latter being prepared in pyridine instead of under the usual acid conditions.* The keto-alcohol and its 2 : 4-dinitrophenylhydrazone exhibited the ultra-violet light absorption characteristic of an isolated keto-group and its derivative.

The anionotropic rearrangement of the βγ-ethylenic α-hydroxy-ketone (VIII) to the isomeric αβ-ethylenic γ-hydroxy-ketone (XIV) was accomplished by treatment with 0·2M-sulphuric acid at 65° for 2 hr., optimum conditions having been found by trial experiments in which the reaction was followed spectrometrically (cf. following paper). 5-Hydroxy-3 : 5-dimethylhex-3-en-2-one (XIV) showed the expected ultra-violet light absorption ($\lambda_{max.}$ 2290 and 3160 Å) and was characterised by a 2 : 4-dinitrophenylhydrazone, prepared in dilute aqueous solution. Reaction of (XIV) with 2 : 4-dinitrophenylhydrazine sulphate in methanolic or ethanolic solution gave the derivatives of the corresponding methyl or ethyl ethers (XIV; OMe or OEt for OH), which could also be obtained directly from the unrearranged hydroxy-ketone (VIII) by treatment with the acidic reagent. The 2 : 4-dinitrophenylhydrazone of the ethyl ether of (XIV) is polymorphic; crystallisation from benzene–hexane gives an orange form which is slowly transformed into a red form of identical m. p.; recrystallisation of the red form again gives the metastable orange modification. The structure of the ketone (XIV) was confirmed by ozonolysis, which furnished diacetyl and α-hydroxy*iso*butyraldehyde, isolated as the 2 : 4-dinitrophenylhydrazones.



When the acid treatment of (VIII) is prolonged beyond the optimum period, the yield of (XIV) decreases and after 26 hr. at 65° two different products are obtained. The main product is a much higher-boiling substance $C_{16}H_{26}O_3$ which contains no reactive hydrogen (Zerewitinoff), affords no 2 : 4-dinitrophenylhydrazone in the cold, and exhibits no high-intensity ultra-violet absorption. It is evidently the ether (XVI), produced by the cyclisation of the γ-hydroxy-ketone (XIV) to the dihydrofuran (XV), followed by self-etherification. The comparatively ready cyclisation of (XIV) is not unexpected; saturated

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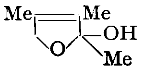
* No previous example of the preparation of a 2 : 4-dinitrophenylhydrazone under basic conditions, which may also be advantageous in other cases, appears to have been recorded.

γ-hydroxy-ketones are well-known to exist in equilibrium with the furanose form (cf. Helferich, *Ber.*, 1919, **52**, 1804; 1922, **55**, 702; 1924, **57**, 1911; Owen, *Ann. Reports*, 1945, **42**, 157) and an example more closely related to the present case has recently been recorded by Adams and Govindachari (*J. Amer. Chem. Soc.*, 1950, **72**, 158) who postulated the conversion of (XVIII) into (XIX) to explain the absence of functional reactivity. Other

(XVIII) $OH{\cdot}CH_2{\cdot}CMe{:}CMe{\cdot}COMe \longrightarrow$  (XIX)

examples of this type, involving the formation of phenyl-substituted 2 : 5-dihydrofurans have been described (Zalkind and Teterin, *J. pr. Chem.*, 1932, **133**, 195; Venus-Danilova *et al.*, *J. Gen. Chem., U.S.S.R.*, 1943, **13**, 93; 1947, **17**, 1549, 1849; 1949, **19**, 1755).

The second product obtained from the prolonged treatment of (VIII) with dilute sulphuric acid was a diethylenic ketone which was characterised by a 2 : 4-dinitrophenylhydrazone. The light absorption properties of the ketone ($\lambda_{max.}$ 2650 Å) indicate that it is the conjugated dienone (XVII), evidently formed by dehydration of (XIV) under the acid conditions. The dienone (XVII) was also obtained when the ether (XVI) was treated with 85% phosphoric acid, a method used by Woods and Temin (*J. Amer. Chem. Soc.*, 1950, **72**, 139) for the somewhat analogous conversion of bisdihydropyranyl ether into penta-2 : 4-dienal both ether fission and dehydration taking place.

The synthesis of (VIII) by the method outlined and its conversion into (XIV) clearly owe their success to the circumstance that the reactions (*a*) and (*c*), though also acid-catalysed, both have rates sufficiently different from that of the isomerisation (*b*) under appropriate conditions. The quantitative aspects and mechanisms of these changes are further discussed in the following paper.

EXPERIMENTAL

M. p.s marked K were determined on a Kofler micro-melting point block and are corrected. Light-absorption data were determined photographically on a Hilger-Spekker instrument. Active hydrogen values were determined by the modified Zerewitinoff method described by Braude and Stern (*J.*, 1946, 404). Oxygen analyses were carried out by Mr. F. H. Oliver by the method of Unterzaucher (*Ber.*, 1940, **73**, 391).

2 : 4 : 5 : 7-*Tetramethylocta*-2 : 6-*diene*-4 : 5-*diol* (IX).—Diacetyl (25 g.) in anhydrous ether (100 ml.) was slowly added with stirring and cooling in a cold-water bath to *iso*butenyl-lithium (Braude and Timmons, *J.*, 1950, 2000) (from Li, 10·5 g., and *iso*butenyl bromide, 102 g.) in anhydrous ether (1·5 l.) during ½ hr. The mixture was stirred for a further ½ hr. and an aqueous solution (400 ml.) of ammonium chloride (55 g.) was added. Isolation by means of ether and distillation gave two main fractions : one (10 g., 26%), b. p. *ca.* 30°/8 mm., on redistillation had b. p. 132—133°, m. p. 11°, n_D^{19} 1·4780, being 2 : 5-dimethylhexa-2 : 4-diene (cf. Braude and Timmons, *loc. cit.*); the other was the crude *glycol* (15 g., 25%), b. p. 80—82°/0·2 mm., 115°/9 mm., n_D^{17} 1·4907, which after several crystallisations from cold pentane, formed colourless needles, m. p. 57—61° (K) [Found : C, 70·6; H, 11·0%; *M* (Rast), 160; Active H, 1·76. $C_{12}H_{22}O_2,\frac{1}{2}H_2O$ requires C, 69·5; H, 11·1; O, 19·3%; *M*, 207]. The analytical data correspond to a *hemihydrate*, but were not appreciably changed after sublimation at 10^{-2} mm., which raised the m. p. to 65—71° (Found : C, 69·5; H, 11·1; O, 19·6%). The m. p. range also suggests the presence of a mixture of stereoisomers. Glacet (*Bull. Soc. chim.*, 1950, 16) gives b. p. 122—126°/11 mm., two forms, m. p.s 52·5° and 56°, but no analytical data. No significant amount of (VIII) was isolated either in this experiment or in experiments in which an excess of diacetyl was added to the *iso*butenyl-lithium solution or *vice versa* (so as to favour monocondensation).

Periodate Oxidation of 2 : 4 : 5 : 7-*Tetramethylocta*-2 : 6-*diene*-4 : 5-*diol* (IX).—An aqueous solution (100 ml.) of the glycol (IX) (180 mg.) and sodium metaperiodate (300 mg.) was kept at room temperature for 1 week. The resulting solution was steam-distilled and the distillate was added to excess of 2 : 4-dinitrophenylhydrazine in aqueous ethanolic sulphuric acid. The precipitate was purified by chromatography on alumina from benzene–ethyl acetate and yielded 65 mg., which after recrystallisation from ethyl acetate had m. p. 202—203°, undepressed on admixture with the 2 : 4-dinitrophenylhydrazone of mesityl oxide. In one experiment the oxidation was allowed to proceed for only 1 hr. On working up as above, the 2 : 4-dinitrophenylhydrazone of 4-acetyl-2 : 4 : 6-trimethylhepta-2 : 5-diene (m. p. 130—132° undepressed by the specimen obtained by direct acid treatment of the glycol) and not the derivative of mesityl oxide was isolated.

Acid Treatment of 2 : 4 : 5 : 7-*Tetramethylocta*-2 : 6-*diene*-4 : 5-*diol* (IX).—A solution (10 ml.) of the glycol (IX) (100 mg.) and 2 : 4-dinitrophenylhydrazine (100 mg.) in aqueous-ethanolic sulphuric acid was kept at room temperature for 2 hr. The 2 : 4-*dinitrophenylhydrazone* (45 mg.), after purification by chromatography on alumina from benzene–ethyl acetate, crystallised from aqueous methanol in orange crystals, m. p. 130—132°, and is formulated as the derivative of 4-acetyl-2 : 4 : 6-trimethylhepta-2 : 5-diene (X) (Found : C, 60·4; H, 6·8; N, 15·3. $C_{18}H_{24}O_4N_4$ requires C, 60·0; H, 6·7; N, 15·6%). Light absorption in $CHCl_3$: Max. at 3680 Å; $\varepsilon = 28{,}000$.

Reaction of iso*Butenylmagnesium Bromide with Diacetyl.*—Methyl bromide (7 g.) was added with stirring to magnesium (48 g.) in anhydrous ether (1 l.) under nitrogen. When the reaction had commenced a mixture of *iso*butenyl bromide (135 g.) and methyl bromide (95 g.) in anhydrous ether (200 ml.) was added at such a rate as to give gentle refluxing under cooling in a cold-water bath. After the reaction was complete, the mixture was stirred for a further ½ hr. The flask was fitted with a specially designed hollow stirrer, lightly packed at the lower end with glass wool as previously described (Braude and Timmons, *loc. cit.*), so that the ethereal solution of the Grignard reagents could be forced through the stirrer by nitrogen into a separating funnel. The filtered Grignard solution was then added with stirring to diacetyl (170 g.) in anhydrous ether (300 ml.). The mixture was stirred overnight and decomposed by the addition of a saturated aqueous solution of ammonium chloride (400 g.) whilst cooled in a freezing mixture. Isolation by means of ether afforded a mixture which on fractionation yielded 3-hydroxy-3-methylbutan-2-one, impure 3-hydroxy-3 : 5-dimethylhex-4-en-2-one (VIII) and 2 : 3 : 5-*trimethylhex*-4-*ene*-2 : 3-*diol* (XII). The butanone was obtained as a colourless oil (9 g.), b. p. 49—51°/17 mm., $n_{\rm D}^{24}$ 1·4158 (Favorskii and Venscheidt, *J. Russ. Phys. Chem. Soc.*, 1912, **44**, 1361; *J. pr. Chem.*, 1913, **88**, 662, give b. p. 50°/18 mm., *n* 1·415) (Found : C, 58·3; H, 9·7%; active hydrogen, 0·92 atom. Calc. for $C_5H_{10}O_2$: C, 58·7; H, 9·9%). Light absorption in EtOH : Max. at 2810 and 2910 Å; inflection at 2560 Å; $\varepsilon = 26$, 26, and 64 respectively. The semicarbazone had m. p. 162—165° (Favorskii and Venscheidt, *loc. cit.*, give m. p. 164—165°). Light absorption in ethanol : Max. 2235 Å; $\varepsilon = 14{,}300$. The yellow 2 : 4-*dinitrophenylhydrazone*, crystallised from aqueous methanol, had m. p. 71—72° (Found : N, 20·2. $C_{11}H_{14}O_5N_4$ requires N, 19·9%). Light absorption in $CHCl_3$: Main max. at 3550 Å; $\varepsilon = 22{,}900$. The crude 3-hydroxy 3 : 5-dimethylhex-4-en-2-one (10 g.) had b. p. 58—66°/17 mm., $n_{\rm D}^{24}$ 1·4448—1·4467, and was identified by the formation of the 2 : 4-dinitrophenylhydrazone of the methyl ether of (XIV) on reaction with an aqueous-methanolic sulphuric acid solution of 2 : 4-dinitrophenylhydrazine (cf. below). The glycol (XII) distilled over as a viscous oil (12 g.), b. p. 102—105°/20 mm., 113—115°/25 mm., which slowly crystallised in a refrigerator. Recrystallisation from pentane afforded colourless needles, m. p. 33—37° [Found : C, 68·0, 67·5; H, 11·1, 11·3%; *M* (Rast), 136; active hydrogen : 2·08 atoms. $C_9H_{18}O_2$ requires C, 68·3; H, 11·5%; *M*, 158].

Periodate Oxidation of 2 : 3 : 5-*Trimethylhex*-4-*ene*-2 : 3-*diol.*—A solution of the glycol (XI) (200 mg.) and sodium metaperiodate (500 mg.) in water (15 ml.) was kept at room temperature for 6 days. After steam-distillation, the ketones were converted into their 2 : 4-dinitrophenylhydrazones, separated by chromatography from benzene on alumina and identified by the m. p.s of the derivatives [acetone, m. p. 121—124° (7 mg.), and mesityl oxide, m. p. 200—202° (40 mg.)], both undepressed on admixture with authentic samples. If the reaction mixture was kept for only 17 hr. before steam-distillation, no appreciable oxidation occurred.

3 : 3-*Dimethoxybutan*-2-*one.*—Freshly distilled diacetyl (300 g.) was refluxed for ½ hr. with absolute methanol (1500 ml.) containing ammonium chloride (6 g.) and set aside overnight (cf. Calder and Fleer, U.S.P., 2,401,336). The mixture was made alkaline with dilute sodium carbonate solution and fractionated through a 14″ Fenske column. After distillation of the methanol and ketal–water mixture, water (100 ml.) was added to the residue and fractionation afforded a further amount of ketal–water mixture. The fraction of b. p. 88—98° separated into two layers. The top layer of ketal (70 g.) was separated and the bottom layer, together with all the other fractions, was extracted with light petroleum (b. p. 40—60°) continuously for a week. The light petroleum layer was separated and evaporated through a column. The combined crude ketal fractions were dried (Na_2SO_4) and fractionated, to give the ketal (200 g., 57%) as a colourless liquid, b. p. 145—146°, $n_{\rm D}^{18}$ 1·4084 (Calder and Fleer, *loc. cit.*, give b. p. 145° and do not state the yield). Light absorption in ethanol : Max. at 2960 Å; $\varepsilon = 26·4$.

3 : 3-*Diethoxybutan*-2-*one.*—A solution of diacetyl (200 ml.) and concentrated sulphuric acid

(2 ml.) in absolute ethanol (1 l.) was kept overnight and afterwards poured into aqueous sodium hydroxide (50 g. in 2 l.). The resulting solution was carefully fractionated. Since none of the fractions separated into two layers (cf. Calder and Fleer, *loc. cit.*), the total distillate was extracted with ether. The ethereal solution was dried (Na_2SO_4) and the ether removed by slow distillation through a 14″ Fenske column. Fractionation of the residue afforded 3 : 3-diethoxybutan-2-one (11 g., 5%), which on redistillation had m. p. 164°, n_D^{18} 1·4109. Light absorption : In EtOH, max. at 2910 Å (ε = 42) ; in hexane, max. at 2900 Å (ε 40). Calder and Fleer (*loc. cit.*) obtained 200 ml., of b. p. 163—165°. Harris (*J.*, 1950, 2247) records n_D^{25} 1·4033 and light absorption (solvent not stated) : Max. at 2940 Å; ε = 34.

2 : 2-*Dimethoxy*-3 : 5-*dimethylhex*-4-*en*-3-*ol* (XIII).—3 : 3-Dimethoxybutan-2-one (165 g.) in anhydrous ether (200 ml.) was added to *iso*butenyl-lithium (from Li, 21·1 g., and *iso*butenyl bromide, 220 g.; Braude and Timmons, *loc. cit.*) in anhydrous ether (3 l.). After being stirred overnight, the mixture was cooled to 0° and a saturated aqueous solution of ammonium chloride (83 g.) was added. Isolation with ether and fractionation gave a product (61 g., 26%), b. p. 112°/35 mm., which on refractionation afforded 2 : 2-*dimethoxy*-3 : 5-*dimethylhex*-4-*en*-3-*ol* as a colourless oil, b. p. 100°/16 mm., n_D^{24} 1·4538 (Found : C, 64·5; H, 10·7; Active H, 0·93 atom. $C_{10}H_{20}O_3$ requires C, 63·8; H, 10·7%).

In one experiment in which the *iso*butenyl-lithium solution was filtered (cf. Braude and Timmons, *loc. cit.*) and added to the ethereal solution of the ketal no appreciable yield of (XIII) could be isolated.

3-*Hydroxy* 3 : 5-*dimethylhex*-4-*en*-2-*one* (VIII).—2 : 2-Dimethoxy-3 : 5-dimethylhex-4-en-3-ol (73 g.) was shaken overnight with 2% (v/v) aqueous sulphuric acid (500 ml.). Isolation by means of ether and fractionation gave 3-*hydroxy*-3 : 5-*dimethylhex*-4-*en*-2-*one* as a colourless liquid (46 g., 83%), b. p. 80·5—80·7°/16 mm., n_D^{25} 1·4508 (Found : C, 67·3; H, 10·1. $C_8H_{14}O_2$ requires C, 67·6; H, 9·9%). Light absorption in hexane : Max. 2800 Å; ε = 227. Light absorption in 40% aqueous ethanol : Max. at 2810 Å; ε = 227. The *semicarbazone*, crystallised from water, had m. p. 154—157° (Found : N, 21·3. $C_9H_{17}O_2N_3$ requires N, 21·1%). Light absorption in EtOH : Max. at 2260 Å; ε = 17,200. These data correspond to the derivative of a saturated ketone; thus acetone semicarbazone shows $\lambda_{max.}$ 2240 Å (ε 12,000), *cyclo*hexanone semicarbazone $\lambda_{max.}$ 2280 Å (ε 13,000), and 3-hydroxy-3-methylbutan-2-one semicarbazone $\lambda_{max.}$ 2235 Å (ε 14,300). The 2 : 4-*dinitrophenylhydrazone* was prepared by refluxing a solution of the hydroxy-ketone (1 g.) and 2 : 4-dinitrophenylhydrazine (1·5 g.) in anhydrous pyridine (5 ml.) for about 3 min. and then allowing the reaction mixture to cool to room temperature. Benzene (20 ml.) was added and the resulting solution was chromatographed on alumina. Elution with benzene–ethyl acetate gave the derivative as an oil, which after crystallisation from benzene–hexane as orange needles had m. p. 107—109° (K) (1·1 g.) (Found : C, 52·5; H, 5·7; N, 17·3. $C_{14}H_{18}O_5N_4$ requires C, 52·2; H, 5·6; N, 17·4%). Light absorption in $CHCl_3$: Main max. 3580 Å; ε = 22,700. The 3 : 5-*dinitrobenzoate* crystallised from hexane as colourless prisms, m. p. 96—99° (K) (Found : C, 53·7; H, 5·3; N, 8·4. $C_{15}H_{16}O_7N_2$ requires C, 53·6; H, 4·8; N, 8·3%). Light absorption in EtOH : Max. at 2270 Å; inflection at 2330 Å; ε = 23,500 and 20,900 respectively.

5-*Hydroxy*-3 : 5-*dimethylhex*-3-*en*-2-*one* (XIV).—A mixture of 3-hydroxy-3 : 5-dimethylhex-4-en-2-one (20 g.) and 1% (v/v) aqueous sulphuric acid (400 ml.) was maintained at 65° for 2¼ hr. and then cooled to room temperature and was extracted with ether. The extract was washed with dilute aqueous sodium carbonate and dried (Na_2SO_4–K_2CO_3). After distillation of the ether, the residue on fractionation afforded unchanged 3-hydroxy-3 : 5-dimethylhex-4-en-2-one (7 g.) and 5-*hydroxy*-3 : 5-*dimethylhex*-3-*en*-2-*one* (8·5 g., 42%) as a colourless oil, which on refractionation had b. p. 69—70·5°/0·3 mm., n_D^{19} 1·4759 (Found : C, 67·4; H, 10·1. $C_8H_{14}O_2$ requires C, 67·6; H, 9·9%). Light absorption in EtOH : Max. at 2290 Å (ε 11,000) ; inflection at 3090 Å (ε 45). Light absorption in dioxan : Max. at 2290 Å (ε 11,400) ; inflection at 3160 Å (ε = 45). Treatment with 2 : 4-dinitrophenylhydrazine in aqueous-ethanolic sulphuric acid gave a mixture which was separated by chromatography from benzene on alumina and afforded the 2 : 4-*dinitrophenylhydrazones* of (XIV) and of the ethyl ether of (XIV). The former derivative crystallised from benzene–hexane in red plates, m. p. 155—156° (K) (Found : C, 52·1; H, 5·6; N, 17·4. $C_{14}H_{18}O_5N_4$ requires C, 52·1; H, 5·6; N, 17·4%). Light absorption in $CHCl_3$: Max. at 2560, 2800, 3780 Å; inflection at 2920 Å; ε = 16,500, 12,300, 28,000, and 9000 respectively. The latter derivative crystallised from benzene–hexane in orange needles, m. p. 152—153° (K) (Found : C, 54·8; H, 6·6; N, 16·0. $C_{16}H_{22}O_5N_4$ requires C, 54·8; H, 6·3; N, 16·0%). Light absorption in $CHCl_3$: Max. at 2560, 2900, and 3780 Å; inflection at 2800 Å; ε = 20,000, 12,300, 30,600, and 14,700 respectively. This derivative, when allowed to stand with solvent, after crystallisation changed slowly to light red needles, m. p. 152—153°, undepressed by the orange form and showing light absorption properties in chloroform and analytical data similar to those of the orange form. On recrystallisation the red reverted to the orange form. The 2 : 4-dinitrophenylhydrazones of (XIV) and of its ethyl ether were also obtained by treating (VIII) with 2 : 4-dinitrophenylhydrazine in aqueous-ethanolic sulphuric acid. When aqueous-methanolic sulphuric acid was used the 2 : 4-*dinitrophenylhydrazone* of the methyl ether of (XIV) was prepared. It crystallised from benzene–hexane in orange prisms, m. p. 168—170° (K) (Found: C, 53·9; H, 6·1; N, 16·7. $C_{15}H_{20}O_5N_4$ requires C, 54·0; H, 6·0; N, 16·7%). Light absorption in $CHCl_3$: Main max. at 3780 Å; ε = 27,500.

Ozonolysis of 5-*Hydroxy*-3 : 5-*dimethylhex*-3-*en*-2-*one* (XIV).—Ozonolysis of (XIV) (0·9 g.) by the method of Church, Whitmore, and McGrew (*J. Amer. Chem. Soc.*, 1932, **54**, 3710; 1934, **56**, 176) and conversion of the carbonyl compounds formed into their 2 : 4-dinitrophenylhydrazones afforded the derivative of α-hydroxy*iso*butyraldehyde, which after chromatography from chloroform on alumina, crystallised from benzene-hexane in yellow needles (75 mg.), m. p. 188—191° (K) undepressed on admixture with an authentic specimen prepared as described below.

There was also obtained the *bis*-2 : 4-*dinitrophenylhydrazone* of diacetyl which crystallised from ethanol–nitrobenzene in orange needles (90 mg.), m. p. 346—349° (K) (Matthiessen and Hagedorn, *Mikrochem. Mikrochim. Acta*, 1941, **29**, 60, give m. p. 335—338° but report no analytical data), undepressed by an authentic sample (Found: C, 43·3; H, 3·5; N, 24·9. $C_{16}H_{14}O_8N_8$ requires C, 43·1; H, 3·2; N, 25·1%). Light absorption in $CHCl_3$: Max. at 3950 and 4360 Å; ε = 40,000 and 37,000 respectively.

α-*Hydroxy*iso*butyraldehyde*.—Addition of bromine to a solution of freshly distilled *iso*butyraldehyde (51 g.), b. p. 63—64° ($\lambda_{max.}$ in hexane 2900 Å, ε = 15·5), in carbon disulphide (700 ml.) was continued until the bromine colour persisted. The carbon disulphide was removed by distillation and the residue was further distilled, to give almost pure α-bromo*iso*butyraldehyde (cf. Franke, *Monatsh.*, 1900, **21**, 205, 210). The middle fraction had b. p. 86·5—92°/310 mm., n_D^{20} 1·4738. Light absorption in hexane : Max. at 2980 Å; ε = 35·0. A mixture of α-bromo*iso*butyraldehyde (29 g.) and water (400 ml.) was refluxed until homogeneous. After cooling and neutralisation with 2N-sodium hydroxide the product was extracted with ether. The extract was dried (Na_2SO_4) and the ether removed. Fractionation of the residue gave α-hydroxy*iso*butyraldehyde as a colourless liquid, b. p. 88—95°/140 mm., n_D^{19} 1·4424 (cf. Franke, *ibid.*, pp. 213 and 1127). Light absorption in hexane: Max. at 2710 and 2810 Å; ε = 22. The 2 : 4-*dinitrophenylhydrazone* was chromatographed on alumina from benzene–chloroform and crystallised from benzene–chloroform or benzene–hexane in yellow needles, which sublimed and had m. p. 188—191° (K) (Found: C, 45·1; H, 4·7; N, 21·0. $C_{10}H_{12}O_5N_4$ requires C, 45·1; H, 4·5; N, 19·9%). Light absorption in $CHCl_3$: Main max. at 3530 Å; ε = 24,000. Campbell (*J. Amer. Chem. Soc.*, 1937, **59**, 1980) reports orange-red needles, m. p. 142°, which did not give satisfactory analyses.

Di-(2 : 3 : 5 : 5-*tetramethyl*-2 : 5-*dihydro*-2-*furyl*) *Ether* (XVI) *and* 3 : 5-*Dimethylhexa*-3 : 5-*dien*-2-*one* (XVII).—3-Hydroxy-3 : 5-dimethylhex-4-en-2-one (6 g.) and 1% (v/v) aqueous sulphuric acid (200 ml.) were kept at 65° for 26 hr. Isolation of the products as in the preparation of 5-hydroxy-3 : 5-dimethylhex-3-en-2-one afforded two fractions. The first was impure 3 : 5-dimethylhexa-3 : 5-dien-2-one (XVII), a colourless oil (0·5 g.), b. p. 77°/10 mm., n_D^{17} 1·4830. Light absorption in EtOH : Max. 2510, 2580, and 2650 Å; ε = 5200, 5200 and 6800 respectively. The 2 : 4-*dinitrophenylhydrazone*, after chromatography on alumina with benzene–ethyl acetate, crystallised from benzene–hexane in red prisms, m. p. 176° (K) (Found: C, 55·3; H, 5·6; N, 18·2. $C_{14}H_{16}O_4N_4$ requires C, 55·3; H, 5·3; N, 18·4%). Light absorption in $CHCl_3$: Max. at 2580, 2670, 2810, 2920, and 3870 Å; ε = 17,000, 17,000, 14,300, 14,300, and 33,500 respectively. The main fraction (2·2 g.) was *di*-(2 : 3 : 5 : 5-*tetramethyl*-2 : 5-*dihydro*-2-*furyl*) *ether*, a colourless viscous oil, b. p. 107—110°/0·6 mm., n_D^{17} 1·4710 [Found: C, 72·1; H, 9·8%; *M* (Rast), 240. $C_{16}H_{26}O_3$ requires C, 72·2; H, 9·8%; *M*, 266]. Light absorption in hexane : Max. at 2280 Å; inflection at 2640 Å; ε = 1480 and 320 respectively. Some crystals were slowly deposited, which crystallised from pentane–ether in colourless needles, m. p. 178—181° (K) (Found: C, 71·5; H, 10·0%; *M*, 243). The ether gave no effervescence with a solution of methylmagnesium iodide in ether and did not form a 2 : 4-dinitrophenylhydrazone in the cold. Several attempts to isolate the 2 : 3 : 5 : 5-tetramethyl-2 : 5-dihydrofuran-2-ol itself, by carrying out the cyclisation with a more dilute solution of the rearranged hydroxy-ketone (XIV) (*e.g.*, 1%), were unsuccessful, only the dienone (XVII) and the ether (XVI) being obtained (cf. Braude, Fawcett, and Newman, *J.*, 1950, 793).

Fission and Dehydration of Di-(2 : 3 : 5 : 5-*tetramethyl*-2 : 5-*dihydro*-2-*furyl*) *Ether*.—The ether (XVI) (1·4 g.) was added to an aqueous solution (14 ml.) of 85% phosphoric acid (4 ml.) and the mixture was steam-distilled (cf. Woods and Temin, *J. Amer. Chem. Soc.*, 1950, **72**, 139). From the steam-distillate 3 : 5-dimethylhexa-3 : 5-dien-2-one was isolated as the 2 : 4-dinitrophenylhydrazone, which after chromatographic purification and crystallisation (135 mg.) had m. p. 172—173° (K) undepressed by the specimen obtained as a by-product in the preparation of the ether (XVI).

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