

**130.** *Researches on Acetylenic Compounds. Part XVI. The Preparation, Reactions, and Light-absorption Properties of Some 2:5-Dihydroacetophenones and Related Compounds (Studies in Light Absorption. Part V).*

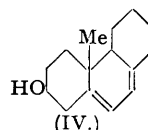
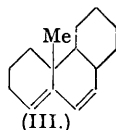
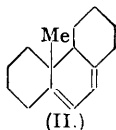
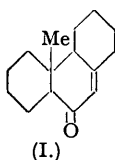
By E. A. BRAUDE, E. R. H. JONES, F. SONDHEIMER, and J. B. TOOGOOD.

2:5-Dihydroacetophenones, various types of which have been prepared by Diels-Alder reactions between butadienes and acetylenic ketones, have been found to dehydrogenate too readily to permit of their utilisation for the synthesis of perhydrophenanthrene ketones by Michael-type reactions with *cyclohexanone*. The sole products which could be isolated from such reactions were *cyclohexylideneacetophenones*.

The isolated ethylenic linkage in these dihydroacetophenones can be converted into an epoxide group, with perbenzoic acid, and also hydrogenated, using a palladium catalyst, without affecting the  $\alpha\beta$ -unsaturated ketone grouping in either case. The 4-ethoxy-compound is readily isomerised to the conjugated 4-ethoxy-2:3-dihydroacetophenone on treatment with alcoholic potassium hydroxide.

The ultra-violet light-absorption properties of the various compounds are recorded and compared with those of acetyl*cyclohexene*. The unexpectedly large influence of the "isolated" 3:4-double bond and of 2-alkyl substituents on both the location and intensity of the maxima is discussed in terms of steric and hyperconjugation effects.

THE work described in this paper was undertaken initially with the object of synthesising model substances similar to the provitamins of the D group. In 1938 Huber (*Ber.*, **71**, 725), employing the general conditions of Rapson and Robinson (*J.*, 1935, 1285), succeeded in effecting a Michael condensation between *cyclohexanone* and 1-acetyl-2-methyl*cyclohexene*, obtaining a non-crystalline ketone to which the structure (I) was assigned. Ponndorf reduction, followed by direct dehydration or elimination of benzoic acid from the benzoate, gave the required provitamin D analogue (II) invariably admixed with isomeric hydrocarbons such as (III), from which it could

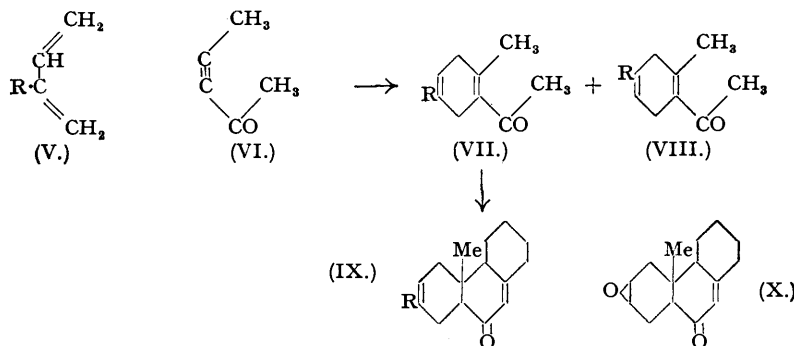


not be separated. Bagchi and Banerjee (*J. Indian Chem. Soc.*, 1946, **23**, 397) carried out a similar condensation with a more complex cyclic ketone, but the product also was non-crystalline.

It seemed to us that repetition of this work in such a manner as to obtain a product [*e.g.*, (IV)] containing a hydroxyl group not only represented a closer approach to the structure of the D provitamins but also afforded the opportunity of obtaining the model compound in a pure condition, since it was to be expected that purification of the anticipated mixture of isomers *via* the dinitrobenzoates or other derivatives would not present any great difficulty.

It has been shown in these laboratories by Bowden and Jones (*J.*, 1946, 52) that acetylenic ketones react readily with conjugated dienes to give dihydrobenzene ketones. Thus methyl ethynyl ketone and butadiene at 120° give 2:5-dihydroacetophenone in 75% yield. From a diene such as (V; R = EtO or AcO) and pent-3-yn-2-one (VI), a mixture of the two ketones (VII) and (VIII) should result. Separation of these two products, followed by Michael condensation of the former with *cyclohexanone*, should give the compound (IX), leading to the desired model compound (IV) after hydrolysis, followed by reduction and preferential dehydration.

An alternative route required the ketone-epoxide (X) which appeared to be obtainable from 2-methyl-3:6-dihydroacetophenone (VII; R = H), either by condensation with *cyclohexanone* followed by treatment of the perhydrophenanthrene ketone with perbenzoic acid, or preparation of the oxide and condensation of this with *cyclohexanone*. By treating (X) with appropriate reagents the oxide ring could be opened up, leading as before to compounds of type (IV).

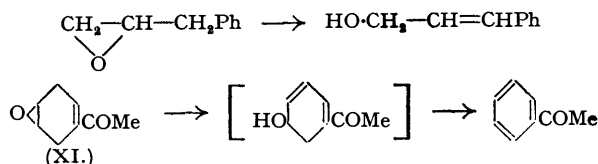


Unfortunately it has been found that these 2:5-dihydroacetophenones [*e.g.*, (VII)] cannot be made to undergo the normal Michael reaction with *cyclohexanone*, apparently because of their extremely ready dehydrogenation to acetophenones, and consequently the desired hydrophenanthrene ketones could not be obtained. Alternative routes to these compounds are being investigated.

When 2:5-dihydroacetophenone was condensed with sodiocyclohexanone (from *cyclohexanone* and sodamide) by the method of Rapson and Robinson (*loc. cit.*), a complex mixture resulted which could not have contained more than traces of the required ketone (IX; R = H, and without the Me group). The use of Huber's catalyst (potassium *isopropoxide* and pyridine) gave a crude product which consisted essentially of *cyclohexylideneacetophenone*, identical with the substance prepared by Farrow and Kon (*J.*, 1926, 2128) from *cyclohexanone* and acetophenone. The formation of this substance is attributed to the oxidation of the dihydroacetophenone by means of the *cyclohexanone*-potassium *isopropoxide* combination (the former being reduced to the alcohol as in the Oppenauer method), the resulting acetophenone then condensing with the excess of *cyclohexanone* under the influence of the basic catalyst.

This ready dehydrogenation of 2:5-dihydroacetophenones has been demonstrated in several other ways. Thus when 2:5-dihydroacetophenone was heated in a metal autoclave at 175° for 12 hours there was obtained, besides much polymer, a 20% yield of acetophenone (isolated as its 2:4-dinitrophenylhydrazone), and no trace of the starting material could be recovered. This probably explains the fact that, when Bowden and Jones (*loc. cit.*) heated 2:5-dihydrobutyrophenone with butadiene at 170–180°, no secondary adduct could be obtained; the "unchanged" dihydrobutyrophenone recovered was probably butyrophenone.

By treating 2:5-dihydroacetophenone with perbenzoic acid, 4:5-epoxy-1-acetylcyclohexene (XI), m. p. 35°, was obtained in 55% yield. A certain amount of dehydrogenation had again taken place, as the lower boiling fractions contained much acetophenone. When an attempt was made to condense this oxide with sodiocyclohexanone hardly any high-boiling product was formed, and from the preliminary fractions acetophenone (25% yield) was again isolated. Similarly, when the oxide was treated with sodamide in ether, acetophenone (20% yield) was produced together with much water-soluble material. It was shown by Haynes, Heilbron, Jones, and Sondheimer (*J.*, 1947, 1583) that when phenylpropylene oxide was treated with sodamide (in liquid ammonia) it was rearranged to cinnamyl alcohol. A similar rearrangement of the oxide probably occurs in this case, the intermediate carbinol dehydrating to give acetophenone.



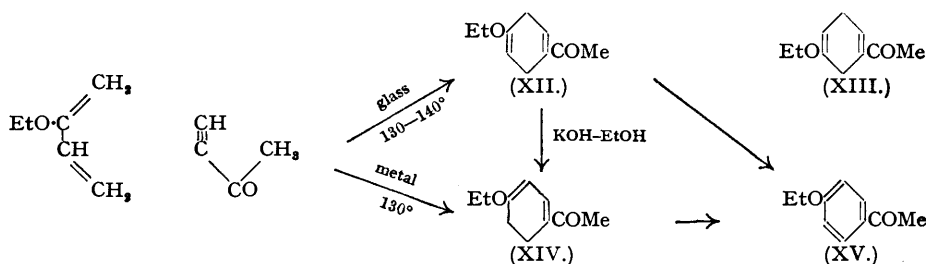
Hydration of the oxide (XI) with dilute sulphuric acid gave 4 : 5-dihydroxy-1-acetylcyclohexene, m. p. 77°, in excellent yield.

Pent-3-yn-2-one (VI) was prepared originally by Yvon (*Compt. rend.*, 1925, **180**, 748) by condensing sodiopropyne (made by passing propyne into an ethereal suspension of sodamide) with acetyl chloride. This method gives unsatisfactory yields, and the reaction between propyne and sodamide is very slow. Several attempts were made to prepare (VI) by adding an ethereal suspension of propynemagnesium chloride to excess of acetic anhydride at  $-30^\circ$  (cf. Kroeger and Nieuwland, *J. Amer. Chem. Soc.*, 1936, **58**, 1861; Bowden, Heilbron, Jones, and Weedon, *J.*, 1946, 39), but again only poor yields of the ketone were obtained; the product always contained some of the tertiary carbinol formed by further reaction of the ketone with the Grignard reagent. A satisfactory method was finally found by condensing propynemagnesium bromide with acetaldehyde (cf. Iotsitch, Cholokhof, Andereg, and Levinson, *J. Russ. Phys. Chem. Soc.*, 1909, **41**, 529) and then oxidising the pent-3-yn-2-ol so formed with chromium trioxide in acetone to give pent-3-yn-2-one (VI) in 70% yield. The structure of this ketone was rigidly established by its light-absorption properties and by complete hydrogenation to methyl propyl ketone. It was found to be much less reactive than methyl ethynyl ketone towards butadiene, and after 6 hours' heating at 125—135° only a 20% yield of 2-methyl-3 : 6-dihydroacetophenone (VII; R = H) was obtained; however, all the unreacted acetylenic ketone could be recovered. The structure of (VII; R = H) was confirmed by spectrographic data and dehydrogenation to *o*-methylacetophenone. From an attempted Michael condensation with cyclohexanone, using a potassium isopropoxide-pyridine catalyst, the only higher-boiling material which could be isolated was cyclohexylidene-*o*-methylacetophenone, which was also synthesised independently from *o*-methylacetophenone and cyclohexanone. The methyl-dihydroacetophenone (VII; R = H) behaved in the same way as the unsubstituted compound towards perbenzoic acid, giving an epoxide, although only in 20% yield.

Butadiene was condensed with oct-3-yn-2-one (Kroeger and Nieuwland, *loc. cit.*; Bowden, Heilbron, Jones, and Weedon, *loc. cit.*), and at 120—130° a 35% yield of 2-*n*-butyl-3 : 6-dihydroacetophenone was obtained, most of the unchanged ketone again being recoverable. The ready conversion of these dihydroacetophenones into benzenoid compounds is again illustrated by the formation of *o*-*n*-butylacetophenone (75% yield) on treatment of the dihydro-compound with excess of chromium trioxide in acetone.

Not only can the isolated ethylenic linkage in these dihydroacetophenones be oxidised preferentially with perbenzoic acid, but it can also be hydrogenated without affecting the  $\alpha\beta$ -unsaturated ketone system. By using a palladium-calcium carbonate catalyst, 2 : 5-dihydroacetophenone can be converted into acetylcyclohexene (80% yield); its homologue (VII; R = H) gives 1-acetyl-2-methylcyclohexene (75%), and 2-*n*-butyl-3 : 6-dihydroacetophenone gives the corresponding 1-acetyl-2-*n*-butylcyclohexene (70%).

The condensation of 2-ethoxy-1 : 3-butadiene (V; R = OEt) (prepared from butadiene according to Petrov, *Acta Univ. Voronegiensis*, 1935, **8**, 68) with methyl ethynyl ketone has also been studied; different products are obtained according to the experimental conditions employed.



The straightforward Diels-Alder reaction between these two compounds could yield the two isomeric ketones (XII) and (XIII), but if (XIII) was produced at all it could only have been in very small yield. When equimolecular amounts of the two reactants were heated at 130—140° in a "Pyrex" tube, a semi-solid product resulted from which a 55% yield of the crystalline 4-ethoxy-2 : 5-dihydroacetophenone (XII) was isolated. Otherwise identical experiments carried out in a metal autoclave gave only yields of up to 15% of the same product (XII), the main bulk of the material in these cases, and the minor proportion when the reaction was carried out in glass, being the isomeric 4-ethoxy-2 : 3-dihydroacetophenone (XIV). The last substance was subsequently found to be formed from the unconjugated isomer (XII) by treatment in the cold

with alcoholic potassium hydroxide. The structures of these two isomers are confirmed by their light-absorption properties, and they gave identical yields of *p*-ethoxyacetophenone (XV) on dehydrogenation with chloranil. When the addition reaction in the metal autoclave was carried out at a higher temperature (150°), some *p*-ethoxyacetophenone (25% estimated by light-absorption measurements) was formed; its presence was confirmed by its isolation as the 2 : 4-dinitrophenylhydrazone. This result was not unexpected in view of the behaviour of 2 : 5-dihydroacetophenone in an autoclave at 175°.

When 4-ethoxy-2 : 5-dihydroacetophenone (XII) was condensed with cyclohexanone, using a potassium isopropoxide-pyridine catalyst, *p*-ethoxycyclohexylideneacetophenone, m. p. 75°, was the only product which could be isolated.

The ultra-violet light-absorption properties of the various compounds described in this paper, which present a number of points of interest, are collected together in the Table. An inspection of the data shows that the selective absorption of the  $\alpha\beta$ -unsaturated ketone system present in the parent compound, acetylcyclohexene (*a*), is considerably altered by alkyl substituents in the 2-position, as well as by the introduction of a double bond in the "isolated" 3 : 4-position. The effects observed can be summarised as follows :

(i) A 2-methyl substituent (*b*) increases  $\lambda_{\max}$ , by *ca.* 150A., and lowers  $\epsilon_{\max}$ , by nearly 50%. The effect of a 2-*n*-butyl substituent (*c*) is very similar, the lowering of  $\epsilon_{\max}$ , being slightly greater.

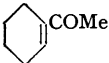
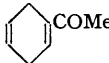
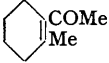



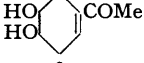
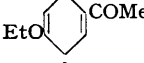
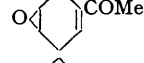
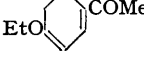
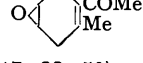
(ii) Two hydroxyl substituents in the 3 : 4-positions (*d*) or a 3 : 4-oxido-ring (*e* and *f*) have only negligible effects.

(iii) Introduction of a 3 : 4-double bond into acetylcyclohexene itself, to give 2 : 5-dihydroacetophenone (*g*), again increases  $\lambda_{\max}$ , by *ca.* 150 A. and lowers  $\epsilon_{\max}$ , by *ca.* 50%. However, introduction of a 3 : 4-double bond into 1-acetyl-2-methyl- or -2-butyl-cyclohexene (*h* and *i*) has little further effect, nor is any effect observed if a 4-ethoxyl substituent is present (*j*).

(iv) Introduction of a double bond in the conjugated 4 : 5-position (*k*) results in the expected larger bathochromic displacement of  $\lambda_{\max}$ .

The observations grouped under (i) and (iii) are at first sight somewhat surprising, since the effect of an alkyl group attached to a conjugated system is normally confined to a small bathochromic displacement, while an "isolated" ethylenic bond is usually assumed to be without influence (cf. Braude, *Ann. Reports*, 1945, **42**, 105). There can be hardly any reason to doubt that the structures assigned to the present compounds are correct and that they have been obtained in a pure condition.

Considering first the effect of a 2-alkyl substituent, the pronounced lowering in intensity is exactly analogous to that observed in *o*-alkylstyrenes, diphenyls, and related systems (Rodebush and Feldman, *J. Amer. Chem. Soc.*, 1946, **68**, 896, and earlier papers; Carlin and Constantine,

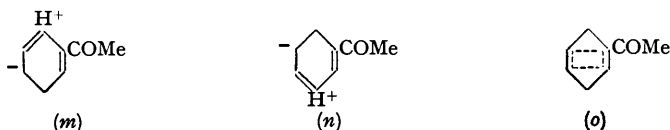
	$\lambda_{\max}$ , A.	$\epsilon_{\max}$ .		$\lambda_{\max}$ , A.	$\epsilon_{\max}$ .
(a) 	2320	12,500	(g) 	2450	4,000
(b) 	2450 2490 *	6,500 6,000	(h) 	2450	5,000
(c) 	2450	4,000	(i) 	2430	6,500
(d) 	2300 2360 *	11,500 10,500	(j) 	2280	11,500
(e) 	2290	13,000	(k) 	3360	13,000
(f) 	2440	5,000			

\* Inflexion.

*ibid.*, 1947, **69**, 50), and is undoubtedly due to the steric interference, shown by scale models, between the 2-alkyl substituent and the methyl group of the -COMe side chain. This steric interference decreases the planarity of the molecule, thus reducing the extent of resonance in the conjugated system and therefore decreasing the probability of the electronic transition giving rise to the high-intensity band. The occurrence of this effect in benzenoid systems is now well established, but the existence of this type of resonance inhibition in non-aromatic compounds

has only recently been recognised. Further examples will be reported in Part VI of the Light Absorption series (Braude, Jones, Koch, Richardson, Sondheimer, and Toogood) where a more detailed discussion will be presented. The small increase in  $\lambda_{\max}$ , also associated with the introduction of a 2-alkyl substituent is fully to be expected, being of the same order of magnitude as that observed with alkyl substitution of aliphatic  $\alpha\beta$ -unsaturated carbonyl compounds (Woodward, *J. Amer. Chem. Soc.*, 1941, **63**, 1123; Evans and Gillam, *J.*, 1941, 815; 1945, 432).

The interpretation of the effect of the "isolated" 3:4-ethylenic bond is less straightforward. The somewhat abnormal light-absorption properties of 2:5-dihydroacetophenones have already been noted (Bowden and Jones, *loc. cit.*), and clearly indicate considerable electronic interaction between the isolated double bond and the main chromophoric system. This interaction could be a direct "spatial" one, acting across the centre of the 6-membered ring, or could take place *via* the methylene groups separating the two ethylenic linkages. In other words, the interaction either (a) depends on the geometrical alignment of the ethylenic linkages in the *cyclohexa-1:4*-diene ring, or (b) depends on strong hyperconjugation of the *cyclomethylene* groups, with contributions from resonance forms such as (m) and (n). Hypothesis (a) appears intrinsically less likely in view of the directional properties of the  $\pi$ -electron orbitals and the comparatively large distance (*ca.* 2.5 Å.) between opposite sides of the *cyclohexadiene* ring, and would amount to the incursion of ring-chain tautomerism as represented in (o). The occurrence of this type of



interaction in dibromophorone and in hexa-1:5-diene-1:1:3:3:4:4:6:6-octacarboxylic esters has been postulated (Ingold and Shoppee, *J.*, 1928, 365; Ingold, Parekh, and Shoppee, *J.*, 1936, 142), but has been disproved in the latter case (Bateman and Jeffrey, *J.*, 1945, 211; Bateman and Koch, *J.*, 1945, 216). In the present instance, interaction between the 1:2- and 3:4-ethylenic bonds as represented in (o) would be expected to result in some inertness of the 3:4-ethylenic bond towards addition reactions, whereas, in fact, hydrogenation and epoxidation of this bond appear to proceed with normal ease. Hypothesis (b), on the other hand, seems quite plausible and bears an obvious relationship to the pronounced hyperconjugation known to exist (Mulliken, *J. Chem. Physics*, 1939, **7**, 121, 339) in *cyclopentadiene* ( $\lambda_{\max}$ , 2440 Å.) where it results in a highly "activated" methylene group and in the displacement of maximal absorption by *ca.* 200 Å. with respect to the open-chain analogue, methylbutadiene ( $\lambda_{\max}$ , 2235 Å.) (Pickett, Paddock, and Sackter, *J. Amer. Chem. Soc.*, 1941, **63**, 1073; Booker, Evans, and Gillam, *J.*, 1940, 1453). In *cyclohexa-1:3*-diene ( $\lambda_{\max}$ , 2560 Å. Henri and Pickett, *J. Chem. Physics*, 1939, **7**, 439) the bathochromic displacement is even greater. A similar effect should be operative in *cyclohexa-1:4*-diene and also in 1:4-dihydronaphthalene. The former has been little studied, since the selective absorption lies below 2000 Å. (as would be expected even if the hyperconjugation effect were considerable). 1:4-Dihydronaphthalene has been examined by Morton and Gouveia (*J.*, 1934, 911) who found that its absorption showed only small differences from that of tetralin. Similarly, the location of the high-intensity band of indene is identical with that of  $\beta$ -methylstyrene. The hyperconjugating effect is thus evidently much more pronounced with the more highly polarisable unsaturated ketone system present in 2:5-dihydroacetophenone than with the benzene chromophore.

Although hyperconjugation in the *cyclohexa-1:4*-diene ring readily accounts for the increase in  $\lambda_{\max}$ , the decrease in  $\epsilon_{\max}$ , still remains to be explained. This cannot be a simple steric effect as in the case of a 2-alkyl substituent, nor is it likely to be brought about by the very small change in valency angles due to the introduction of the 3:4-double bond. It could be understood in terms of spatial double-bond interaction as in (o) but, as is shown above, such a hypothesis is not supported by other evidence. It therefore appears that the lowering of  $\epsilon_{\max}$ , must also be due in some way to the increased conjugation of the acetyl side-chain with the ring system, and although this effect is surprisingly large, it is somewhat analogous to the decrease in intensity generally associated with increasing cyclic symmetry of a chromophore. The idea of increased hyperconjugation in *cyclohexa-1:4*-dienes as compared with *cyclohexenes* is amenable to a number of experimental tests which it is hoped to carry out as soon as opportunity permits.

The non-operation of the effect of a 3:4-ethylenic bond in the presence of a 2-alkyl substituent must again be due to the steric displacement of the acetyl side-chain out of the plane

of the ring, thus preventing contributions from co-planar resonance forms such as (*m*) and (*n*), while, in the presence of a 4-ethoxyl group, conjugation of the double bond with the latter presumably takes preference over interaction with the methylene groups.

#### EXPERIMENTAL.

(All light-absorption data were determined in alcoholic solution unless otherwise stated.)

*Condensation between 2:5-Dihydroacetophenone and cycloHexanone.*—Potassium (22 g.), in small pieces, was suspended in dry ether (800 c.c.), and isopropyl alcohol (110 c.c.) was added with stirring in nitrogen during  $\frac{1}{2}$  hour. When all the potassium had dissolved, a mixture of 2:5-dihydroacetophenone (50 g.; Bowden and Jones, *J.*, 1946, 52), cyclohexanone (45 g.), and pyridine (200 c.c.) was gradually added, and the solution was kept under nitrogen for 46 hours. Decomposition with dilute sulphuric acid, followed by working up with ether, gave a product from which by fractionation cyclohexylideneacetophenone (21.3 g.), b. p. 117—122°/0.01 mm., was obtained. After regeneration from the semicarbazone (plates from aqueous methanol, m. p. 124°) it had b. p. 97—98°/10<sup>-3</sup> mm.,  $n_D^{20}$  1.5502. Light absorption: Maximum, 2420A.;  $\epsilon$  = 13,500. The 2:4-dinitrophenylhydrazones crystallised from ethanol in orange plates, m. p. 165° (Found: C, 63.5; H, 5.6. Calc. for C<sub>20</sub>H<sub>20</sub>O<sub>4</sub>N<sub>4</sub>: C, 63.15; H, 5.3%). The m. ps. of the derivatives were not depressed on admixture with authentic samples from cyclohexylideneacetophenone prepared by the method of Farrow and Kon (*loc. cit.*) (these workers give b. p. 176—178°/17 mm.,  $n_D^{18}$  1.5589, for the ketone, and m. p. 120—121° for the semicarbazone; Marvel and Walton, *J. Org. Chem.*, 1942, 7, 88, give m. p. 163—164° for the 2:4-dinitrophenylhydrazone).

4:5-Epoxy-1-acetylcyclohexene (XI).—2:5-Dihydroacetophenone (33.1 g.) was added to an ice-cooled chloroform solution of perbenzoic acid (770 c.c.; Braun, *Org. Synth.*, Coll. Vol. I, p. 431), containing  $3.87 \times 10^{-4}$  g.-atoms of active oxygen per c.c. (10% excess). The mixture was allowed to reach room temperature and it was then kept for 18 hours in the dark. Isolation gave 4:5-epoxy-1-acetylcyclohexene (27.2 g.), b. p. 69—71°/0.05 mm.,  $n_D^{21}$  1.5122, as a mobile liquid, which rapidly solidified. Crystallisation from ether-light petroleum (b. p. 40—60°) gave plates (21.0 g.), m. p. 33—34°, which by further crystallisation was increased to 35° (Found: C, 69.5; H, 7.35. C<sub>8</sub>H<sub>10</sub>O<sub>2</sub> requires C, 69.55; H, 7.3%). Light absorption: see Table. The semicarbazone crystallised in needles from ethanol, m. p. 228° (Found: N, 21.9. C<sub>9</sub>H<sub>13</sub>O<sub>2</sub>N<sub>3</sub> requires N, 21.55%). The use of permonophthalic acid instead of perbenzoic acid considerably decreased the rate of epoxidation.

When an ethereal solution of the oxide was stirred for some hours with either sodamide or the sodio-derivative of cyclohexanone, acetophenone was isolated in about 20% yield. It was characterised as the 2:4-dinitrophenylhydrazone, m. p. (and mixed m. p.) 248°.

4:5-Dihydroxy-1-acetylcyclohexene.—4:5-Epoxy-1-acetylcyclohexene (2.0 g.) was dissolved in water (15 c.c.), and concentrated sulphuric acid (3 drops) was added. The solution was then heated on the steam-bath under reflux for 12 hours, and the sulphuric acid was removed by adding barium hydroxide solution, the excess of which was precipitated by saturation with carbon dioxide. The inorganic salts were filtered off, the solvent was evaporated, and the residue was distilled to give 4:5-dihydroxy-1-acetylcyclohexene (1.85 g.; 82%) as a very viscous liquid, b. p. 153°/0.1 mm., which after several days at room temperature set to a solid, m. p. 73—75°. Crystallisation from ethyl acetate-benzene or nitroethane gave needles, m. p. 77° (Found: C, 61.45; H, 7.85. C<sub>8</sub>H<sub>12</sub>O<sub>3</sub> requires C, 61.55; H, 7.75%). Light absorption: see Table. The 2:4-dinitrophenylhydrazones crystallised from ethanol in orange hexagonal plates, m. p. 246—248° (Found: N, 16.6. C<sub>14</sub>H<sub>16</sub>O<sub>6</sub>N<sub>4</sub> requires N, 16.65%).

Pent-3-yn-2-one (VI).—A solution of chromium trioxide (172 g.) in concentrated sulphuric acid (146 c.c.) diluted to 860 c.c. with water was added during 3 hours to a stirred solution of pent-3-yn-2-ol (195 g.) (prepared by the method of Iotsitch *et al.*, *loc. cit.*) in acetone (300 c.c.) at 5—10°. After a further 30 minutes' stirring, the mixture was diluted with water to 2500 c.c., and the product was isolated with ether; distillation then gave pent-3-yn-2-one (130 g.) as a somewhat lachrymatory liquid, b. p. 73.5—74.5°/95 mm.,  $n_D^{25.5}$  1.4380 [Yvon, *loc. cit.*, gives b. p. 132.5—133.5°,  $n_D^{20}$  1.1411 (probably a misprint)] (Found: C, 73.05; H, 7.55. Calc. for C<sub>5</sub>H<sub>8</sub>O: C, 73.15; H, 7.4%). Light absorption: Maximum, 2210A.;  $\epsilon$  = 7500. The 2:4-dinitrophenylhydrazones formed yellow needles, m. p. 149°, from alcohol (Found: N, 21.4. C<sub>11</sub>H<sub>10</sub>O<sub>4</sub>N<sub>4</sub> requires N, 21.4%). Light absorption: Maximum, 3600 A.;  $\epsilon$  = 30,000.

A solution of the ketone (0.46 g.) in methyl alcohol (30 c.c.) was shaken with platonic oxide (10 mg.) and hydrogen until absorption was complete, 260 c.c. of hydrogen being absorbed at 13°/763 mm., corresponding to 1.0 triple bond. Removal of the catalyst and solvent gave methyl propyl ketone, which gave a 2:4-dinitrophenylhydrazones, m. p. 141.5°, undepressed on admixture with an authentic specimen.

2-Methyl-3:6-dihydroacetophenone (VII; R = H).—A mixture of pent-3-yn-2-one (8.8 g.) and butadiene (8.0 g.), after being heated in a stainless steel autoclave at 125—135° for 6 hours, gave on distillation, recovered ketone (6.8 g.) and 2-methyl-3:6-dihydroacetophenone (3.0 g.), b. p. 81—82°/8 mm.,  $n_D^{20}$  1.5084 (Found: C, 79.4; H, 9.1. C<sub>9</sub>H<sub>12</sub>O requires C, 79.4; H, 8.9%). Light absorption: see Table. The 2:4-dinitrophenylhydrazones formed orange needles, m. p. 155°, from alcohol (Found: N, 17.9. C<sub>15</sub>H<sub>16</sub>O<sub>4</sub>N<sub>4</sub> requires N, 17.7%). Light absorption (in chloroform): Maximum, 3690 A.;  $\epsilon$  = 22,000. The ketone (2.1 g.) was heated with chloranil (5.4 g.) in boiling xylene (17 c.c.) for 4 hours; the mixture was filtered, and, after removal of solvent under reduced pressure, distillation of the residue gave *o*-methylacetophenone (1.1 g.), b. p. 73°/6 mm.,  $n_D^{18}$  1.5370 (Auwers, *Annalen*, 1915, 408, 242, gives b. p. 92—93°/17 mm.,  $n_D^{20}$  1.5320). The 2:4-dinitrophenylhydrazones crystallised from alcohol in orange plates, m. p. 161° (Borsche and Wagner-Roemmich, *Annalen*, 1941, 546, 273, give m. p. 161°). Light absorption (in chloroform): Maximum, 3660 A.;  $\epsilon$  = 21,500.

*Condensation between 2-Methyl-3:6-dihydroacetophenone and cycloHexanone.*—(a) Potassium (2.2 g.), in small pieces, was stirred under nitrogen in sodium-dry ether (100 c.c.), isopropyl alcohol (11 c.c.) was

added during 20 minutes, and after an hour's stirring, 2-methyl-3:6-dihydroacetophenone (5 g.) and cyclohexanone (4.8 g.) were added in dry pyridine (20 c.c.). After 67 hours' stirring, the pyridine was washed out with dilute sulphuric acid, the washed and dried ethereal solution was evaporated, and the residue was distilled to give cyclohexylidene-*o*-methylacetophenone (2.5 g.), b. p. 120—125°/10<sup>-2</sup> mm.,  $n_D^{20}$  1.5475. Light absorption: Maximum, 2430 Å.;  $\epsilon = 10,000$ . The 2:4-dinitrophenylhydrazone formed orange needles, m. p. 187°, from aqueous alcohol (Found: C, 64.3; H, 5.85. C<sub>21</sub>H<sub>22</sub>O<sub>4</sub>N<sub>4</sub> requires C, 63.95; H, 5.6%).

(b) *o*-Methylacetophenone (3.75 g.) and cyclohexanone (2.9 g.) were added to a sodium ethoxide solution (15 c.c.; 5%). After 72 hours, ether was added and the ethereal solution was washed and dried. Evaporation and distillation gave cyclohexylidene-*o*-methylacetophenone (0.8 g.), b. p. 120—125°/10<sup>-2</sup> mm.,  $n_D^{23}$  1.5442. The 2:4-dinitrophenylhydrazone, crystallised as above, formed orange plates, m. p. 187—188°, undepressed on admixture with the sample prepared above.

4:5-Epoxy-1-acetyl-2-methylcyclohexene.—2-Methyl-3:6-dihydroacetophenone (5.4 g.) was kept in the dark for 66 hours with a solution of perbenzoic acid in chloroform (360 c.c. containing 1.12 × 10<sup>-4</sup> g.-atoms of active oxygen per c.c.). Washing with dilute sodium hydrogen carbonate solution, drying, and distillation, gave starting material (2.45 g.) and 4:5-epoxy-1-acetyl-2-methylcyclohexene (1.35 g.), b. p. 71—72°/10<sup>-1</sup> mm.,  $n_D^{25}$  1.5030 (Found: C, 70.4; H, 7.7. C<sub>9</sub>H<sub>12</sub>O<sub>2</sub> requires C, 71.0; H, 7.95%). Light absorption: see Table.

2-*n*-Butyl-3:6-dihydroacetophenone.—A mixture of oct-3-yn-2-one (6 g.) and butadiene (2.7 g.), after being heated in a stainless steel autoclave at 120—130° for 9 hours, gave on distillation the original ketone (3 g.) and 2-*n*-butyl-3:6-dihydroacetophenone (3 g.), b. p. 53—53.5°/10<sup>-2</sup> mm.,  $n_D^{20}$  1.4982 (Found: C, 80.5; H, 10.2. C<sub>13</sub>H<sub>18</sub>O requires C, 80.85; H, 10.2%). Light absorption: see Table. The semicarbazone formed needles, m. p. 145—146°, from alcohol (Found: N, 17.7. C<sub>13</sub>H<sub>21</sub>ON<sub>3</sub> requires N, 17.9%). Light absorption: Maxima, 2290 and 2410 Å.;  $\epsilon = 12,000$  and 11,000 respectively.

A solution of chromium trioxide (2.0 g.) in concentrated sulphuric acid (1.8 c.c.), made up to 10 c.c. with water, was added slowly to a cooled solution of the ketone (4.65 g.) in acetone (10 c.c.). The mixture, after 30 minutes' stirring, was diluted to 100 c.c., and the product was isolated with ether; distillation then gave *o*-*n*-butylacetophenone (3.45 g.), b. p. 63°/10<sup>-2</sup> mm.,  $n_D^{21}$  1.5076. Light absorption: Maximum, 2420 Å.;  $\epsilon = 7,500$  (Found: C, 81.9; H, 9.2. C<sub>12</sub>H<sub>16</sub>O requires C, 81.8; H, 9.15%). The semicarbazone formed needles, m. p. 121°, from methyl alcohol (Found: N, 18.2. C<sub>13</sub>H<sub>19</sub>ON<sub>3</sub> requires N, 18.0%). Light absorption: Maximum, 2450 Å.;  $\epsilon = 12,000$ . The 2:4-dinitrophenylhydrazone crystallised from ethanol in orange plates, m. p. 82° (Found: C, 60.6; H, 5.75; N, 16.2. C<sub>18</sub>H<sub>20</sub>O<sub>4</sub>N<sub>4</sub> requires C, 60.65; H, 5.65; N, 15.75%). Light absorption (in chloroform): Maximum, 3680 Å.;  $\epsilon = 24,000$ .

1-Acetylcyclohexene.—A solution of 2:5-dihydroacetophenone (5.0 g.) in methyl acetate (30 c.c.) was hydrogenated at 17°/769 mm., using a palladium-calcium carbonate catalyst (0.8 g.; 0.3% Pd), until 983 c.c. of gas had been absorbed. Removal of catalyst and solvent, followed by fractionation of the residue, gave 1-acetylcyclohexene (4.0 g.), b. p. 77—79°/14 mm.,  $n_D^{20}$  1.4883. Light absorption: Maximum, 2330 Å.;  $\epsilon = 11,000$ . (An authentic sample had b. p. 84—85°/18 mm.,  $n_D^{25}$  1.4919. Light absorption: Maximum, 2320 Å.;  $\epsilon = 12,000$ .) The 2:4-dinitrophenylhydrazone, large red needles from ethyl acetate, had m. p. 202°, undepressed on admixture with an authentic specimen (m. p. 202°).

1-Acetyl-2-methylcyclohexene.—A solution of 2-methyl-3:6-dihydroacetophenone (1.76 g.) in methyl alcohol (20 c.c.) was shaken with palladium on calcium carbonate (0.2 g.; 3% Pd) in hydrogen until 310 c.c. of gas had been absorbed at 18°/760 mm., corresponding to 1.0  $\bar{F}$ . Removal of the catalyst and solvent gave 1-acetyl-2-methylcyclohexene (1.33 g.), b. p. 89—91°/14 mm.,  $n_D^{21}$  1.4842. Light absorption: Maximum, 2440 Å.;  $\epsilon = 6000$ . (An authentic sample had b. p. 98°/25 mm.,  $n_D^{25}$  1.4854. Light absorption: Maximum, 2450 Å.;  $\epsilon = 6500$ . Inflexion, 2490 Å.;  $\epsilon = 6,000$ .) The 2:4-dinitrophenylhydrazone crystallised in bright red plates, m. p. 120°, raised to 124—125° by chromatographic purification (Found: N, 17.75. C<sub>11</sub>H<sub>16</sub>O<sub>4</sub>N<sub>4</sub> requires N, 17.6%). Light absorption (in chloroform): Maximum, 3750 Å.;  $\epsilon = 24,000$ . No depression in m. p. was observed on admixture with a sample (m. p. 125°) prepared from the authentic ketone.

1-Acetyl-2-*n*-butylcyclohexene.—A solution of the dihydroacetophenone (4.55 g.) in methyl alcohol (20 c.c.) was shaken with a palladium-calcium carbonate catalyst (0.4 g.; 3% Pd) in hydrogen until 610 c.c. of gas had been absorbed at 22°/764 mm. corresponding to 1.0  $\bar{F}$ . Removal of the catalyst and solvent gave 1-acetyl-2-*n*-butylcyclohexene (3.1 g.), b. p. 65—66°/10<sup>-2</sup> mm.,  $n_D^{21}$  1.4756 (Found: C, 80.2; H, 11.3. C<sub>12</sub>H<sub>20</sub>O requires C, 79.95; H, 11.2%). Light absorption: see Table. The semicarbazone formed needles, m. p. 154°, from methyl alcohol (Found: N, 18.0. C<sub>13</sub>H<sub>23</sub>ON<sub>3</sub> requires N, 17.7%). Light absorption: Maximum, 2260 Å.;  $\epsilon = 12,000$ . The 2:4-dinitrophenylhydrazone crystallised from ethanol in dark red plates, m. p. 116° (Found: N, 15.55. C<sub>18</sub>H<sub>24</sub>O<sub>4</sub>N<sub>4</sub> requires N, 15.55%). Light absorption (in chloroform): Maximum, 3690 Å.;  $\epsilon = 25,500$ .

2-Ethoxy-1:3-butadiene (V; R = OEt).—This was prepared by the method of Petrov (*loc. cit.*) with the following modifications: The iodine, instead of being added in 3 portions, was slowly added during 4 hours, so as to keep the temperature at -10°; when dehydrohalogenating, the finely ground potassium hydroxide was added gradually, with water cooling, so as to keep the violent reaction under control; the reaction was finally completed by refluxing for 1 hour. In this way there was obtained, from butadiene (324 g.), mercuric oxide (518 g.), ethyl alcohol (368 g.), and iodine (1016 g.), 2-ethoxy-1:3-butadiene (206.5 g.; 53% based on iodine), b. p. 94.5—95.5°,  $n_D^{18}$  1.4400 (Petrov, *loc. cit.*, gives b. p. 92.5—93.5°,  $n_D^{15}$  1.443; Dykstra, *J. Amer. Chem. Soc.*, 1935, 57, 2255, gives b. p. 96.5°,  $n_D^{20}$  1.4401).

4-Ethoxy-2:5-dihydroacetophenone (XII).—A mixture of 2-ethoxy-1:3-butadiene (9.8 g.), methyl ethynyl ketone (6.8 g.), Bowden, Heilbron, Jones, and Weedon, *J.*, 1946, 39), and a trace of quinol was heated in a "Pyrex" glass tube at 130—140° for 4 hours. The dark red semi-solid product was distilled; the fraction (13.5 g.), b. p. 86—93°/0.1 mm., on crystallisation from pentane gave 4-ethoxy-2:5-dihydroacetophenone (9.0 g.) as long needles, m. p. 59° (Found: C, 72.05; H, 8.2. C<sub>16</sub>H<sub>14</sub>O<sub>2</sub> requires C, 72.25; H, 8.5%). Light absorption: see Table. The compound is rather unstable, and even at 0° in the absence of air and light soon turns to a brown gum. The residue from the mother liquors, after removal of solvent, had light absorption: Maxima, 2230 and 3360 Å.;  $\epsilon = 6000$  and 5000 respectively.

The solid ketone (3.5 g.) was heated with chloranil (7.8 g.) in boiling xylene (30 c.c.) for 4 hours; the mixture was filtered, and the solvent was removed under reduced pressure. Distillation of the residue gave *p*-ethoxyacetophenone, b. p. 94–95°/0.1 mm., which partly solidified, and after crystallisation from pentane gave plates (1.75 g.), m. p. 36°. These on admixture with an authentic sample (b. p. 90–91°/0.05 mm., m. p. 36°), made from phenetole and acetyl chloride, gave no depression in m. p.

4-Ethoxy-2 : 3-dihydroacetophenone (XIV).—(a) 4-Ethoxy-2 : 5-dihydroacetophenone (1.7 g.) in dry ethanol (5 c.c.) was added to a solution of potassium hydroxide (0.34 g.) in dry ethanol (8 c.c.), and after 15 minutes at room temperature the dark red solution was saturated with carbon dioxide. Water and ether were added, and the aqueous layer was thoroughly extracted with more ether; from the ether extract there was obtained by distillation 4-ethoxy-2 : 3-dihydroacetophenone (1.3 g.), b. p. 78°/0.03 mm.,  $n_D^{20}$  1.5490, as a light yellow mobile liquid (Found : C, 72.1; H, 8.4.  $C_{10}H_{14}O_2$  requires C, 72.25; H, 8.5%). Light absorption : see Table. The 2 : 4-dinitrophenylhydrazone was precipitated as a purple powder, but attempted crystallisation from hot solvents resulted in extensive decomposition. However, by precipitation from a solution in cold chloroform by the addition of methanol, it was obtained as purple prisms, m. p. 193–194° (Found : N, 16.55.  $C_{16}H_{18}O_5N_4$  requires N, 16.2%).

When the reaction time was increased to 40 minutes, the light absorption of the product was : Maximum 3350 A.;  $\epsilon = 9000$ , while after 15 hours the intensity had dropped to  $\epsilon = 8000$ .

(b) A mixture of 2-ethoxy-1 : 3-butadiene (8.2 g.), methyl ethynyl ketone (5.7 g.), and a trace of quinol was heated in a small stainless steel autoclave at ca. 130° for 4 hours. Distillation of the residue gave a fraction (9.0 g.), b. p. 83–88°/0.1 mm.,  $n_D^{20}$  1.5485, which had light absorption : Maximum, 3380 A.;  $\epsilon = 12,500$ , and consequently consisted almost entirely of 4-ethoxy-2 : 3-dihydroacetophenone. The 2 : 4-dinitrophenylhydrazone, crystallised as described above, formed purple prisms, m. p. 192–193°, undepressed on admixture with the sample prepared before. When the liquid ketone was dehydrogenated with chloranil, as described above, there was obtained a 58% yield of *p*-ethoxyacetophenone, m. p. 35°; the 2 : 4-dinitrophenylhydrazone had m. p. 229°. Neither of these m. p.s was depressed on admixture with authentic samples (m. p.s 36–37° and 229° respectively).

On repeating the Diels-Alder reaction in the metal autoclave several times, it was found that complete rearrangement did not always occur, and yields of up to 15% of the unrearranged solid ketone could be obtained.

When the temperature at which this reaction was carried out in the metal autoclave was increased to 150°, there was obtained a 50% yield of a product, b. p. 83–86°/0.1 mm., which showed light absorption : Maxima, 2690, 3350 A.;  $\epsilon = 4000$  and 8500 respectively. That this again mainly consisted of the rearranged ketone was shown by the fact that it gave an unstable purple 2 : 4-dinitrophenylhydrazone, m. p. (and mixed m. p.) 192–193°. However, refluxing the crude dinitrophenylhydrazone with ethyl acetate, concentrating the filtrate, and crystallising the residue from ethyl acetate, gave the 2 : 4-dinitrophenylhydrazone of *p*-ethoxyacetophenone, dark red prisms, m. p. 227°, undepressed on admixture with an authentic sample (m. p. 229–230°). This explains the first maximum in the light absorption of the ketone mixture above, as a sample of authentic *p*-ethoxyacetophenone had light absorption : Maxima, 2700, 2790 A.;  $\epsilon = 18,000$  and 17,000 respectively.

*p*-Ethoxycyclohexylideneacetophenone.—(a) A solution of potassium isopropoxide (from 3.5 g. potassium and 20 c.c. isopropyl alcohol) in dry ether (200 c.c.) was made as described above. A mixture of 4-ethoxy-2 : 5-dihydroacetophenone (10.0 g.), cyclohexanone (6.2 g.), and pyridine (40 c.c.) was added slowly, and the mixture was then stirred under nitrogen for 64 hours. Working up and removal of starting materials by distillation gave a liquid, b. p. 140–190°/0.01 mm., which partly solidified, and crystallisation from ether-pentane gave *p*-ethoxycyclohexylideneacetophenone (1.25 g.) as plates, which after further crystallisation had m. p. 75° (Found : C, 78.6; H, 8.3.  $C_{16}H_{20}O_2$  requires C, 78.65; H, 8.25%). Light absorption : Maximum, 2740 A.;  $\epsilon = 12,000$ . The 2 : 4-dinitrophenylhydrazone crystallised from ethyl acetate in scarlet prisms, m. p. 181° (Found : C, 61.95; H, 5.8; N, 13.0.  $C_{22}H_{24}O_5N_4$  requires C, 62.25; H, 5.7; N, 13.2%).

(b) Ethanol (6 c.c.) in which sodium (0.32 g.) had been dissolved was added to a mixture of *p*-ethoxyacetophenone (2.2 g.), cyclohexanone (1.32 g.), and ethanol (0.5 c.c.), with ice-cooling. The solution was kept at 20° for 48 hours, and was then worked up. Removal of starting material by distillation left a residue which partly solidified, and crystallisation from aqueous methanol gave *p*-ethoxycyclohexylideneacetophenone (0.72 g.) which after further crystallisation had m. p. 75°. The 2 : 4-dinitrophenylhydrazone had m. p. 180°, and neither this derivative nor the ketone showed any depression in m. p. on admixture with the samples prepared as in (a).

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