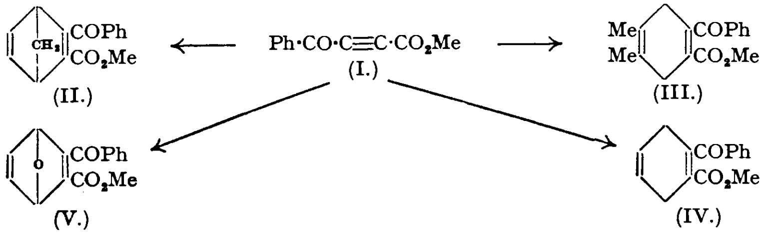
359. *Researches on Acetylenic Compounds. Part XXIV. Diels–Alder Reactions with Acetylenic Keto-esters.*

By T. Y. Shen and M. C. Whiting.

Addition reactions between αβ-acetylenic γ-keto-esters and various conjugated dienes give a series of 2-acyl-3 : 6-dihydrobenzoic esters, some of which are readily dehydrogenated to the corresponding aromatic compounds. The light-absorption properties of the adducts are compared with those of analogous adducts obtained from ethynyl ketones, and with those of acylbenzoic esters.

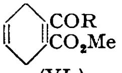
In Part III of the present series (Bowden and Jones, *J.*, 1946, 52) the application of the Diels–Alder reaction to ethynyl ketones was described. It was to be expected that the recently available αβ-acetylenic γ-keto-esters (Nineham and Raphael, *J.*, 1949, 118; Jones, Shen, and Whiting, *J.*, 1950, 236) would undergo similar diene additions and, because of possible applications of the method to the synthesis of fused-ring systems, and the interest aroused by the anomalous light-absorption properties of the adducts obtained from ethynyl ketones, this reaction has been examined.

The acetylenic keto-esters proved rather more reactive as dienophils than the corresponding ethynyl ketones, but their lower stability made the reaction conditions more critical. Thus methyl benzoylpropiolate (I) combined smoothly with *cyclo*pentadiene and 2 : 3-dimethylbutadiene, at room temperature and *ca.* 70° respectively, to give the adducts (II) and (III) in

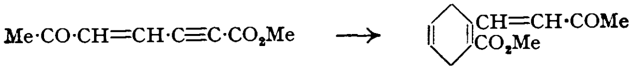


good yields. The reaction with butadiene, however, required very careful temperature control. At 20° very little reaction took place during seven days even when an excess of the hydrocarbon was used as solvent, but in an autoclave at 45° a good yield of (IV) was obtained after 6—18 hours. On the other hand heating to 60° resulted in the formation of a dark, uncrystallisable product from which only methyl *o*-benzoylbenzoate could be isolated on distillation. Similar difficulties were encountered in the reaction with furan, a fair yield of the adduct (V) being obtained when the reaction temperature was 50°.

Reactions between butadiene and the aliphatic keto-esters, methyl β-acetyl- and β-butyryl-propiolates, were next examined. The expected adducts (VI; R = Me and Pr respectively)

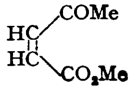


(VI.)

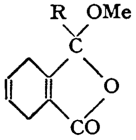


(VII.) (VIII.)

(IX.)



(X.)



(XI.)

were obtained in good yields at 50°. The vinylacetylenic keto-ester (VII) also combined with butadiene at 50° to give a small yield of a high-boiling liquid formulated as (VIII), although analytical data indicated that it was not pure. Its light-absorption (see below) resembled that of a typical doubly-unsaturated conjugated ketone and its 2 : 4-dinitrophenylhydrazone analysed well, after chromatographic purification, for a derivative of (VIII) and showed the expected light-absorption. It has already been found (Bowden, Braude, Jones, and Weedon, *J.*, 1945, 45) that hex-3-en-5-yn-2-one gives amine-adducts in which only the acetylenic linkage is involved, and therefore the formation of (VIII) is not unexpected.

It was shown by Bowden and Jones (*loc. cit.*) and by Braude, Jones, Sondheimer, and Toogood (*J.*, 1949, 607) that 2 : 5-dihydroacetophenone and analogous substances are converted into the corresponding aromatic ketones by a variety of oxidising agents and also by heating to *ca.* 175°. Similar behaviour was encountered with the present series of dihydrobenzene derivatives. Thermal dehydrogenation obviously occurred in the butadiene reaction at 60° described above, and oxidation with chromic acid in acetic acid readily converted the esters (III) and (IV) into the corresponding benzenoid compounds.

The adducts derived from methyl β-benzoylpropiolate closely resemble acetophenone in their light-absorption properties and these are not very different from those of the *o*-benzoylbenzoic esters which have been examined (*e.g.*, see Fig. 1). It is probable that the absorption of the benzoyl group is predominant in these cases. On the other hand, the spectra of the adducts (VI; R = Me or Pr) from butadiene and methyl β-acetyl- and β-butyryl-propiolates (the curves for these two substances almost coincide) are quite different from that of methyl acetophenone-*o*-carboxylate (Fig. 2); indeed the intensity of absorption in the former cases is so low that it was at first considered possible that these esters had a cyclic structure such as (XI). This hypothesis was supported by the fact that they failed to form 2 : 4-dinitrophenylhydrazones, even under the drastic conditions necessary for the preparation of these derivatives from the benzoyldihydrobenzoic esters. Further consideration of the light-absorption data, however, reveals that these are not incompatible with the structures assigned. 2 : 5-Dihydroacetophenone has already been found by Bowden and Jones (*J.*, 1946, 52; cf. Braude, Jones, Sondheimer, and Toogood, *J.*, 1949, 607) to exhibit abnormally low intensity light-absorption, and a carbomethoxyl group in the *o*-position would be expected to produce a further reduction in intensity by virtue of its steric effect, which would tend to prevent the αβ-unsaturated ketone grouping from assuming its preferred coplanar configuration (cf. Braude, Jones, Koch, Richardson, Sondheimer, and Toogood, *J.*, 1949, 1890). In the absence of through-conjugation (see below) the carbomethoxyl group might lead to a hypsochromic displacement of the maximum, and a combination of these effects might well result in absorption such as is indicated in curve *B* (Fig. 2). This reasoning was tested in the following manner. It was shown by Braude, Jones, Sondheimer, and Toogood (*loc. cit.*) that 2 : 5-dihydroacetophenone could be

Fig. 1.

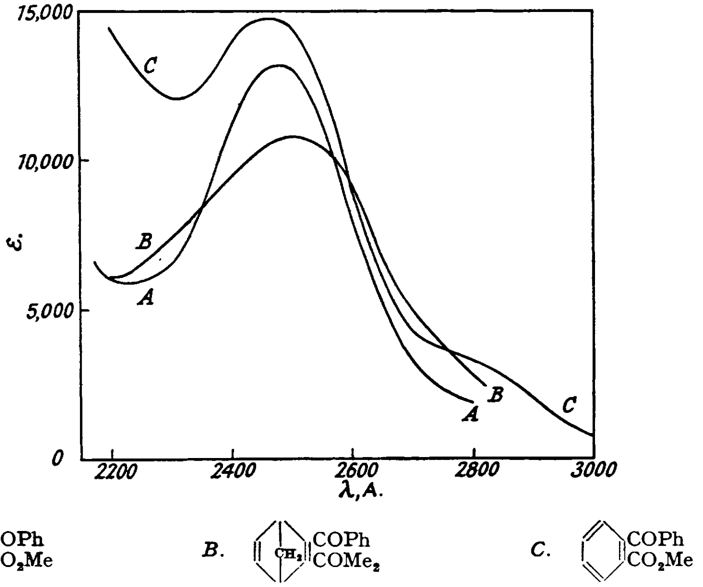
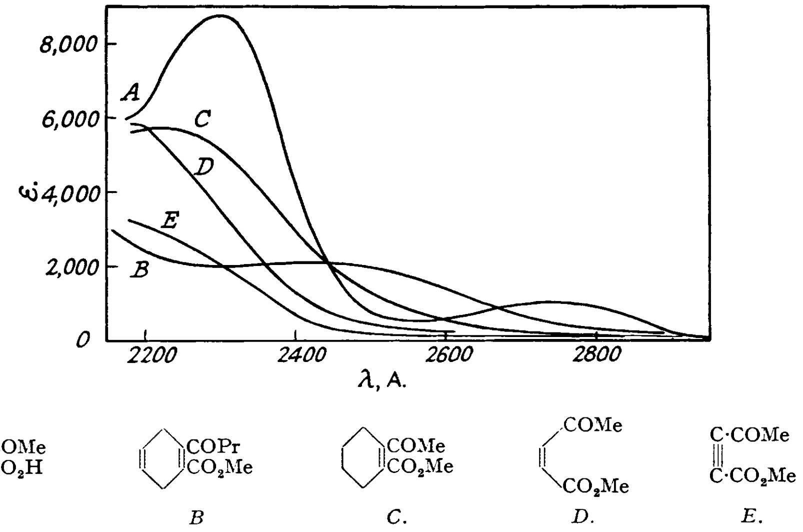


Fig. 2.



converted, by partial hydrogenation of the isolated double bond, into 1-acetyl*cyclo*hexene which showed no light-absorption abnormalities. Partial hydrogenation of the keto-ester (VI; R = Me) gave an apparently homogeneous product (IX) which showed much more intense absorption (*C*; Fig. 2) than did the parent compound (VI; R = Me); the other effects mentioned above are still apparent, however, in that the intensity is still appreciably lower than that of acetyl*cyclo*hexene ($\lambda_{\text{max.}}$ 2320—2330 A., ε = 13,500). The two cases thus appear to be analogous and it is clear that the keto-ester has the normal rather than the cyclic structure, as would indeed by expected in view of the method of preparation.

In order to make available another *cis*-β-acylacrylic ester having an unambiguous structure, the parent compound, methyl *cis*-β-acetylacrylate (X) was prepared by semihydrogenation of the acetylenic ester. Its light-absorption (*D*; Fig. 2) was similar to that of (IX), the latter absorbing at longer wave-lengths, as expected from the alkyl substitution of ethylenic bond. The acetylenic ester itself showed similar but less intense absorption (*E*; Fig. 2) (cf. methyl vinyl and methyl ethynyl ketones; Bowden, Heilbron, Jones, and Weedon, *J.*, 1945, 39). The results obtained for the various γ-keto-αβ-unsaturated esters are thus consistent; they show that the system is cross-conjugated, as would be expected in view of the opposed polarities of the keto- and carbomethoxyl groups and by analogy with maleic and fumaric esters ($\lambda_{\text{max.}}$ 1927 and 2087 A., log ε = 4·34 and 4·52 respectively; Sörensen, *Annalen*, 1941, **546**, 57) and with pyruvic ester ($\lambda_{\text{max.}}$ 3287 A., log ε = 0·73, and end absorption with log ε = 2·88 at 2144 A.; Bielecki and Henri, *Ber.*, 1914, **47**, 1690). Nevertheless it must be borne in mind that in all the cases examined the double bond had a *cis*-configuration and " through " conjugation would in any case be hindered sterically. Further work on the light-absorption of γ-keto-acids and -esters in connection with their tautomeric behaviour is in progress in these laboratories.

EXPERIMENTAL.

(Light-absorption data were determined using alcohol as solvent with a Beckman Model B spectrophotometer.)

Methyl 2-*Benzoyl*-3 : 6-*dihydrobenzoate* (IV).—A mixture of methyl benzoylpropiolate (Nineham and Raphael, *loc. cit.*) (3 g.), butadiene (2 c.c.), and a trace of quinol was heated in a small steel autoclave (capacity 50 c.c.) at 45° for 18 hours. After cooling and removal of excess of butadiene the residue solidified, and crystallisation from light petroleum (b. p. 40—60°) gave the *keto*-ester (3·1 g.) as rhombic prisms, m. p. 65° (Found: C, 74·55; H, 5·75; $C_{15}H_{14}O_3$ requires C, 74·35; H, 5·8%). The 2 : 4-*dinitrophenylhydrazone*, prepared by refluxing the compound with methanolic 2 : 4-dinitrophenylhydrazine sulphate solution for 12 hours, separated from ethyl acetate–ethanol in red prismatic needles, m. p. 208° (Found: C, 60·0; H, 4·45. $C_{21}H_{18}O_6N_4$ requires C, 59·7; H, 4·3%).

Methyl 2-*Benzoyl*-4 : 5-*dimethyl*-3 : 6-*dihydrobenzoate* (III).—A mixture of methyl benzoylpropiolate (3 g.) and 2 : 3-dimethylbutadiene (2·5 g.) was heated under reflux for 18 hours. Crystallisation of the resultant solid from benzene–light petroleum (b. p. 40—60°) gave the *keto*-ester as prisms, m. p. 103—104° (Found: C, 75·25; H, 6·75. $C_{17}H_{18}O_3$ requires C, 75·55; H, 6·7%). The 2 : 4-*dinitrophenylhydrazone*, obtained by interaction with methanolic 2 : 4-dinitrophenylhydrazine sulphate for 4 days at room temperature, crystallised from ethyl acetate–ethanol in orange-red flat needles, m. p. 224—226° (decomp.) (Found: C, 61·0; H, 4·9. $C_{23}H_{22}O_6N_4$ requires C, 61·3; H, 4·95%).

Methyl 2-*Benzoyl*-3 : 6-endo*methylene*-3 : 6-*dihydrobenzoate* (II).—*cyclo*Pentadiene (2 g.; freshly redistilled) was added to methyl benzoylpropiolate (2 g.), and the resultant exothermic reaction was moderated by external cooling. After a few minutes at room temperature removal of excess of diene and distillation at 85—90° (bath temp.)/10^{-4} mm. gave the *keto*-ester (2·3 g.) as a light-yellow, very viscous liquid, n_{D}^{16} 1·5686 (Found: C, 75·55; H, 5·65. $C_{16}H_{14}O_3$ requires C, 75·6; H, 5·55%). The 2 : 4-*dinitrophenylhydrazone*, formed comparatively readily, crystallised from ethyl acetate–ethanol in orange-red rhombic plates, m. p. 207° (Found: C, 60·75; H, 4·2. $C_{22}H_{18}O_6N_4$ requires C, 60·8; H, 4·2%).

Methyl 3 : 6-endo-*Oxido*-2-*benzoyl*-3 : 6-*dihydrobenzoate* (V).—A mixture of methyl benzoylpropiolate (3 g.) and furan (1·5 g.) was heated in a small autoclave to 50° for 6 hours. Distillation of the resultant dark syrup after the removal of more volatile material gave the *keto*-ester (1·6 g.), b. p. 80° (bath temp.)/10^{-4} mm., n_{D}^{20} 1·5666 (Found: C, 70·05; H, 4·75. $C_{15}H_{12}O_4$ requires C, 70·5; H, 4·7%). The 2 : 4-dinitrophenylhydrazone, m. p. 178°, could not be obtained analytically pure.

Methyl 2-*Acetyl*-3 : 6-*dihydrobenzoate* (VI; R = Me).—A mixture of methyl acetylpropiolate (Jones, Shen, and Whiting, *loc. cit.*) (2 g.), butadiene (2 c.c.) and a trace of quinol was heated in a small autoclave to 50° for 18 hours. After the removal of excess of diene distillation gave the *keto*-ester as a liquid, b. p. 81—82°/0·02 mm., n_{D}^{20} 1·5008, which when kept solidified and had m. p. 32° (Found: C, 66·95; H, 7·05. $C_{10}H_{12}O_3$ requires C, 66·65; H, 6·7%). It did not form a 2 : 4-dinitrophenylhydrazone even under vigorous conditions.

Methyl 2-*Butyryl*-3 : 6-*dihydrobenzoate* (VI; R = Pr^n).—A mixture of methyl butyrylpropiolate (Jones, Shen, and Whiting, *loc. cit.*) (1·1 g.) and butadiene (1 c.c.) was heated in a small autoclave at 50° for 18 hours. After removal of excess of diene and cooling, the residue solidified, and crystallisation from light petroleum (b. p. 40—60°) gave the *keto*-ester (1·0 g.) as needles, m. p. 55° (Found: C, 69·45; H, 7·75. $C_{12}H_{16}O_3$ requires C, 69·2; H, 7·8%). It did not form a 2 : 4-dinitrophenylhydrazone even under drastic conditions.

4-(2-*Carbomethoxy*-3 : 6-*dihydrophenyl*)*but*-4-*en*-2-*one*.—A mixture of methyl 5-ketohex-3-en-1-yne-

1-carboxylate (Jones, Shen, and Whiting, *loc. cit.*) (1·0 g.) butadiene (1 c.c.), and a trace of quinol was heated in a small autoclave at 50° for 6 hours. Removal of the excess of diene, followed by distillation at 80—100° (bath temp.)/10^{-4} mm., gave the crude *keto*-ester (0·4 g.) as an oil, n_D^{21} 1·5206 (Found : C, 67·8; H, 6·65. $C_{12}H_{14}O_3$ requires C, 69·9; H, 6·85%). Light absorption : Maximum, 2810 A.; ε = 9,500. As insufficient material was available for purification it was converted into its 2 : 4-*dinitrophenylhydrazone* which, after chromatography and crystallisation from ethyl acetate, formed red prismatic needles, m. p. 186° (Found : C, 56·25; H, 4·95. $C_{18}H_{18}O_6N_4$ requires C, 55·95; H, 4·7%). Light absorption : Maxima, 2560, 3080 and 3950 A.; ε = 14,500, 11,500, and 32,500 respectively.

o-*Benzoylbenzoic Acid.*—Methyl 2-benzoyl-3 : 6-dihydrobenzoate (0·5 g.) was dissolved in glacial acetic acid (20 c.c.) and treated with 6N-chromic acid (1·0 c.c.). Isolation with ether followed by hydrolysis with aqueous-methanolic potassium hydroxide solution at room temperature gave *o*-benzoylbenzoic acid (0·35 g.), m. p. 126°, undepressed on admixture with an authentic specimen.

An attempted dehydrogenation with chromic acid in acetone (Braude, Jones, Sondheimer, and Toogood, *loc. cit.*) gave a heterogeneous product.

2-*Benzoyl*-4 : 5-*dimethylbenzoic Acid and Methyl Ester.*—A solution of the corresponding dihydro-ester (1·1 g.) in glacial acetic acid (30 c.c.) was treated with 6N-chromic acid (1·8 c.c.) added slowly. Dilution with water gave a precipitate which was crystallised from light petroleum (b. p. 40—60°) to give the keto-ester (1·0 g.) as rhombic prisms, m. p. 124° (Found : C, 75·8; H, 5·65. Calc. for $C_{17}H_{16}O_3$: C, 76·1; H, 6·0%). The 2 : 4-*dinitrophenylhydrazone* separated from ethyl acetate in orange-yellow plates, m. p. 249° (Found : C, 61·4; H, 4·35. $C_{23}H_{20}O_6N_4$ requires C, 61·6;. H, 4·5%). Hydrolysis of the ester (0·15 g.) with methanolic potassium hydroxide gave the acid (0·1 g.), which after crystallisation from benzene–light petroleum (b. p. 40—60°) formed plates, m. p. 197° (Found : C, 75·55; H, 5·9. Calc. for $C_{16}H_{14}O_3$: C, 75·6; H, 5·55%) (Fieser and Fieser, *J. Amer. Chem. Soc.*, 1935, **57**, 1679 give m. p. 123·5° and 197·5° for the methyl ester and the acid, respectively).

Methyl 2-*Acetyl*cyclo*hexene*-1-*carboxylate.*—A solution of methyl 2-acetyl-3 : 6-dihydrobenzoate (2·0 g.) in methyl acetate (25 c.c.) was shaken in hydrogen in the presence of a palladium–calcium carbonate catalyst (10%; 75 mg.). When the theoretical amount of hydrogen had been absorbed (278 c.c. at 22°/755 mm.) the catalyst was separated and the solvent removed under reduced pressure at room temperature. Distillation of the residue gave *methyl* 2-*acetyl*cyclo*hexene*-1-*carboxylate* (1·3 g.), b. p. 110—112°/2 mm., n_D^{21} 1·4834 (Found : C, 66·3; H, 7·75. $C_{10}H_{14}O_3$ requires C, 65·9; H, 7·75%).

Methyl cis-*β*-*Acetylacrylate.*—A solution of methyl acetylpropiolate (2·0 g.) in methyl acetate (25 c.c.) was shaken in hydrogen in the presence of a palladium–calcium carbonate catalyst (50 mg.; 10%). When the theoretical amount of hydrogen had been absorbed (400 c.c. at 762 mm./23°) the catalyst was filtered off and the solvent removed under reduced pressure at room temperature. Distillation of the residue gave *methyl* cis-*β*-*acetylacrylate* (1·1 g.), b. p. 85°/22 mm., n_D^{20} 1·4390.

It readily formed a 2 : 4-*dinitrophenylhydrazone* which, after chromatographic purification on alumina and recrystallisation from benzene–light petroleum (b. p. 60—80°), formed orange-yellow plates, m. p. 195° (Found: C, 53·95; H, 3·65. $C_{16}H_{14}O_6N_4$ requires C, 53·6; H, 3·95%).

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