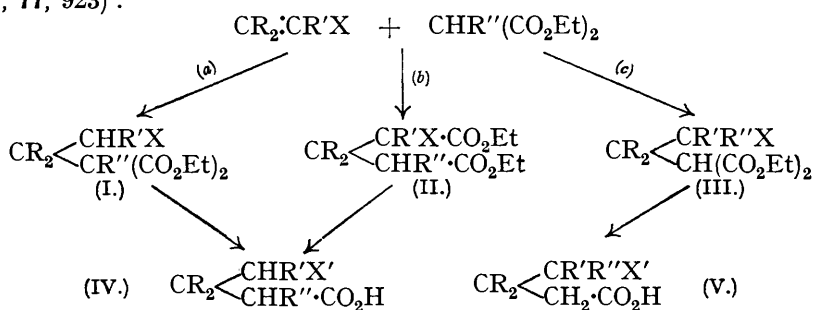


12. Studies on the Michael Reaction. Part III. General Considerations : The Addition of Alkylmalonic Esters to Some Unsaturated Diketones.

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Abnormal Michael reactions, *viz.*, those in which an apparent migration of an alkyl group occurs, can be explained on the basis of two different mechanisms. In Thorpe's mechanism the sodioalkylmalonic ester is held to split into alkyl and sodiomalonic residues during the addition, whereas according to Holden and Lapworth's mechanism the ester is believed to add normally as a sodium kation and an alkylmalonic ester anion, the abnormal product arising as a result of isomerisation of the primary normal product. It is shown, from general considerations, that experimental discrimination between these mechanisms is only possible when the unsaturated reactant is a ketone or an α -substituted ester. The condensation of ethyl benzylmalonate with dibenzoyl- and diacetyl-ethylenes is complicated by a side reaction, the nature of which is discussed; the condensation with dibenzoylethylene is shown to proceed normally under certain conditions.

THE products to be expected in the general case of the reaction between an alkylmalonic ester and a suitable unsaturated compound, according to the mechanism controlling the reaction, are set out in the following scheme, in which route (a) indicates the normal mechanism, route (b) the course of the reaction according to the mechanism of Holden and Lapworth (J., 1931, 2370), and route (c) the course required by Thorpe's mechanism (J., 1900, 77, 923) :



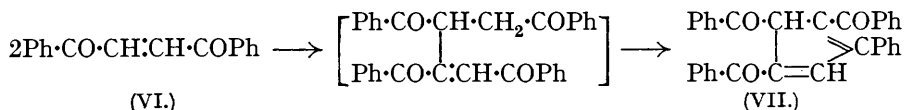
X is an activating group (such as CO_2Et , COR or CN), which passes into X' (*e.g.*, CO_2H , COR) on acid hydrolysis; (I), (II), and (III) are the expected condensation products, and (IV) and (V) the acids into which they pass on acid hydrolysis.

Inspection shows that routes (a) and (b) yield the same acid (IV). It is therefore evident that the corresponding mechanisms can only be differentiated by comparison of the condensation products (I) and (II) or the acids obtained from these by alkaline hydrolysis; such a comparison will also differentiate both of these routes from route (c). Such a comparison is, however, not always experimentally possible (*cf.* Part I, J., 1935,

420); for this reason, in a search for reactions proceeding by Thorpe's mechanism (route *c*), it is desirable so to choose the reactants that (IV) and (V) will be different. Now (IV) = (V) if $R'' = H$, hence substituted malonic esters must be used. With this proviso, (IV) and (V) are also identical if $X' = CO_2H$ ($X = CO_2Et$ or CN) and $R' = H$; we may thus distinguish between (IV) and (V) only if either $X' \neq CO_2H$ (*i.e.*, $X \neq CO_2Et$ or CN) or $R' \neq H$. That is to say, the most suitable reactions are those in which an alkylmalonic ester is added to an unsaturated ketone or to an α -substituted unsaturated ester. The present paper is concerned with the first class of reaction and Part IV (following paper) with the second.

Since it had been shown (Parts I and II) that the condensation of ethyl benzylmalonate with ethyl fumarate is abnormal (route *b* or *c*), it was decided to use ketonic analogues of the latter of the type $R \cdot CO \cdot CR' \cdot CR' \cdot COR$. The first diketone to be studied was $\alpha\beta$ -dibenzoyl ethylene (VI), the *trans*-modification of which is readily accessible (Conant and Lutz, *J. Amer. Chem. Soc.*, 1923, **45**, 1303). The earlier experiments showed the Michael reaction with this substance to be complicated by a side reaction, which was investigated.

At room temperature, dibenzoyl ethylene reacted with one equivalent of sodium ethoxide in alcoholic solution to give, as the principal product, a bright orange substance, $C_{32}H_{22}O_3$, m. p. 161°. This substance, although unsaturated, was very resistant to catalytic hydrogenation, and only benzoic acid could be isolated on oxidation with potassium permanganate. It is suggested that the reaction consists in an intermolecular condensation of two molecules of dibenzoyl ethylene (*cf.* ethyl crotonate; von Pechmann, *Ber.*, 1900, **33**, 3340), followed by the elimination of a molecule of water between the methylene group so formed and one carbonyl group, the orange material being 1 : 4 : 5-tribenzoyl-2-phenylcyclopentadiene (VII or a tautomeride of this) :

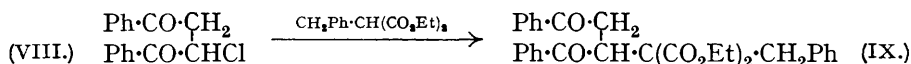


$\alpha\beta$ -Diacetyl ethylene (Armstrong and Robinson, *J.*, 1934, 1650) formed tarry products with sodium ethoxide; an attempt to condense this substance with ethyl sodiomalonate gave a small amount of a ketonic oil, the semicarbazone of which furnished the analytical figures required for the monosemicarbazone of a product similar to (VII).

If the above view of the mechanism of this side reaction is correct, an unsaturated diketone without hydrogen atoms on the ethylenic carbons should be stable towards sodium ethoxide. Such a diketone is $\alpha\beta$ -dibenzoylstilbene, $\text{Ph} \cdot \text{CO} \cdot \text{CPh} : \text{CPh} \cdot \text{COPh}$, and, in conformity with this view, it underwent no reaction on treatment with sodium ethoxide.

Bearing in mind this remarkable reactivity towards sodium ethoxide, we made experiments on the addition of ethyl benzylmalonate to *trans*- $\alpha\beta$ -dibenzoyl ethylene. Addition occurred rapidly and smoothly under the influence of alcoholic sodium ethoxide at -20° ; the product, m. p. 92°, was the expected addition compound.

The normal addition product was synthesised by condensation of α -chloro- $\alpha\beta$ -dibenzoyl ethane (VIII) (Paal and Schultze, *Ber.*, 1902, **35**, 171) with ethyl benzylmalonate :



Ethyl $\gamma\delta$ -dibenzoyl- α -phenylbutane- $\beta\beta$ -dicarboxylate (IX), so obtained, had m. p. 92°, unchanged on admixture with the condensation product from dibenzoyl ethylene and ethyl benzylmalonate; this addition, therefore, proceeds by route (*a*), *i.e.*, it is normal in mechanism.

All attempts to bring about the addition of ethyl benzylmalonate to *cis*- $\alpha\beta$ -dibenzoylstilbene were fruitless.

EXPERIMENTAL.

trans- $\alpha\beta$ -Dibenzoyl ethylene was prepared by the Friedel-Crafts reaction between fumaryl chloride and benzene (Conant and Lutz, *loc. cit.*).

Action of Sodium Ethoxide on Dibenzoyl ethylene.—2.5 G. of dibenzoyl ethylene were suspended in 50 c.c. of absolute alcohol, and sodium ethoxide [from sodium (0.25 g.) and absolute alcohol (10 c.c.)] added. The mixture immediately became deep red and the dibenzoyl ethylene dissolved. After 10 minutes the solution was poured into water; the buff-coloured precipitate, m. p. 65—68°, obtained was too intractable to allow of further study. Acidification of the deep red filtrate precipitated 1.5 g. of a dark red solid. Crystallisation from alcohol yielded bright orange needles, m. p. 161°, which were probably 1 : 4 : 5-tribenzoyl-2-phenylcyclopentadiene (VII) [Found : C, 84.0, 83.9; H, 5.0, 4.7; *M* (Rast), 444. $C_{35}H_{22}O_3$ requires C, 84.6; H, 4.8%; *M*, 454]. No hydrogen was absorbed when 1.0 g. of this material was shaken with 0.2 g. of Adams's platinum catalyst, suspended in acetic acid or alcohol, in an atmosphere of hydrogen for 3 days. 2.8 G. of powdered potassium permanganate were added to a mechanically stirred ice-cold solution of 0.7 g. of the product in acetone; only benzoic acid (0.4 g.; 53%) was isolated.

When dibenzoyl ethylene was refluxed with sodium ethoxide for several hours, only resinous products were obtained.

Addition of Ethyl Benzylmalonate to Dibenzoyl ethylene.—5 G. of ethyl benzylmalonate were added to a solution of 0.46 g. of sodium in 10 c.c. of absolute alcohol, and the mixture refluxed for 10 minutes. It was then cooled in an ice-salt freezing mixture, and a cooled suspension of 4.8 g. of dibenzoyl ethylene in 10 c.c. of alcohol added slowly. After about 10 minutes all the dibenzoyl ethylene dissolved and a white solid was precipitated. The mixture was left overnight, and the precipitate filtered off and washed with alcohol. The crude material (2.5 g.) was crystallised from light petroleum (b. p. 40—60°), yielding 2.0 g. (20%) of ethyl $\gamma\delta$ -dibenzoyl- α -phenyl-*n*-butane- $\beta\beta$ -dicarboxylate (IX) in clusters of prisms, m. p. 92°, mixed m. p. with the synthetic product (below) 92° (Found : C, 73.7; H, 6.0. $C_{30}H_{30}O_6$ requires C, 74.1; H, 6.2%).

Condensation of α -Chlorodibenzoyl ethane with Ethyl Benzylmalonate.—2.4 G. of pulverised sodium were suspended in dry ether, 25 g. of ethyl benzylmalonate added, and the solution refluxed until all the sodium had reacted. 27 G. of α -chlorodibenzoyl ethane (VIII) (Paal and Schultze, *loc. cit.*), suspended in ether, were added, and refluxing continued; the mixture was at first deep red, but the colour gradually lightened to a pale brown. The sodium chloride was removed, and the ethereal filtrate washed with water, dried over sodium sulphate, and evaporated. The viscous product deposited a solid, which was filtered off and washed with light petroleum. Three crystallisations of the crude yellow material (23 g.; 46%) from light petroleum (b. p. 60—80°) yielded ethyl $\gamma\delta$ -dibenzoyl- α -phenyl-*n*-butane- $\beta\beta$ -dicarboxylate (IX) in clusters of colourless prismatic needles, m. p. 92° (Found : C, 73.6; H, 5.9%). A substance, m. p. 133°, was also obtained, but in amount too small to allow of further investigation.

Ethyl Diacetylsuccinate.—The following is an improvement of the method of Knorr (*Ber.*, 1894, 27, 1155) and requires less solvent than the modification due to Bilton and Linstead (*J.*, 1937, 924) : 250 G. of ethyl acetoacetate, dissolved in 250 c.c. of dry ether, were run slowly (cooling when necessary) into a mechanically stirred suspension of 46 g. of "molecular" sodium in 750 c.c. of dry ether. When all the sodium had reacted, an ethereal suspension of 200 g. of finely powdered iodine was added slowly with stirring. When no further decolorisation of the iodine was observed, the sodium iodide was filtered off and washed with dry ether. The ethereal filtrate was evaporated, and the residue crystallised from 50% acetic acid, yielding 110 g. (42%) of pure ethyl diacetylsuccinate, m. p. 89—90°.

The ester was converted by Knorr's method (*Ber.*, 1900, 33, 1219) into acetylacetone; this was dehydrogenated to diacetyl ethylene, m. p. 77—78°, following Armstrong and Robinson (*loc. cit.*).

Attempted Condensation of Ethyl Malonate and Diacetyl ethylene.—1.7 G. of diacetyl ethylene, dissolved in 10 c.c. of absolute alcohol, were added to ethyl sodiomalonate (sodium, 0.35 g.; absolute alcohol, 5 c.c.; ethyl malonate, 2.4 g.). The solution became red and then brown; it was refluxed overnight, poured into water, and acidified. Resinous material (0.7 g.) was filtered off, and the filtrate extracted with ether. Distillation of the dried extract yielded 0.6 g. of a high fraction, b. p. 113—117°/1.5 mm., which gave a semicarbazone, m. p. 186—187° (Found : N, 16.1. $C_{13}H_{17}O_3N_3$ requires N, 16.0%).

Action of Sodium Ethoxide on Dibenzoyl stilbene.—2.0 G. of *cis*-dibenzoyl stilbene (Nadelung and Oberwegner, *Annalen*, 1931, 490, 234) were added to sodium ethoxide [from sodium (0.15 g.) and absolute alcohol (5 c.c.)], and the solution refluxed overnight. When it was poured into water, *cis*-dibenzoyl stilbene was reprecipitated, m. p. (after recrystallisation) and mixed m. p. 214°.

Attempted Addition of Ethyl Benzylmalonate to Dibenzoyl stilbene.—2.5 G. of ethyl benzyl-

malonate were added to sodium ethoxide (from 0.23 g. of sodium and 10 c.c. of absolute alcohol). A suspension of 3.8 g. of dibenzoylstilbene in absolute alcohol was added, and the mixture kept overnight. The dibenzoylstilbene remaining undissolved, the mixture was refluxed for 48 hours on the steam-bath. On cooling, a solid was precipitated (3.7 g.), m. p. 210—213°. Recrystallisation showed this to be unchanged *cis*-dibenzoylstilbene, m. p. and mixed m. p. 214°.

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