of 3,5-dibromoacetylmesitylene and 60 cc. of acetic acid in a three-necked flask surrounded by a water-bath. After one hour of stirring and heating, the solution was allowed to cool.

The crystalline material which appeared melted (after several crystallizations from alcohol) at 121–122°, and amounted to 5.7 g.

Anal. Calcd. for $C_{11}H_{10}OCl_2Br_2$: C, 33.9; H, 2.6. Found: C, 33.9; H, 2.7.

Summary

A satisfactory synthesis of 3,5-dichloroacetylmesitylene has been developed. It was found that the bromination of this acetophenone in acetic acid proceeded as in the case of 3,5-dibromoacetylmesitylene, giving a sharply melting product composed of the corresponding di- and tribromomethyl ketones. When 4-chloroacetophenone was brominated under the same conditions only α,α-dibromo-4-chloroacetophenone was isolated.

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The Michael Condensation. I. The Behavior of Diethyl Phenylmalonate in the Michael Condensation

BY RALPH CONNOR

The investigation of the reaction of diethyl phenylmalonate in the Michael condensation was undertaken for the purpose of studying the rearrangement which has been reported[1] in the reaction of diethyl methylmalonate, ethyl α-cyanopropionate and ethyl α-cyanobutyrate with α,β-unsaturated esters and ketones. This compound was selected because the tendency of an aryl group to migrate (according to the mechanism of Michael and Ross[1a,d]) or its influence upon the change in position of a carboethoxyl group (by the mechanism of Holden and Lapworth[1b]) might differ considerably from that of an alkyl group.

The first reaction carried out was that of diethyl phenylmalonate with ethyl crotonate in absolute alcohol containing a molecular equivalent of sodium ethoxide. Instead of the expected tribasic ester the products were diethyl carbonate and diethyl α-phenyl-β-methylglutarate (I). Similar results were obtained with ethyl tiglate, ethyl cinnamate and benzalacetophenone. It was also found that diethyl phenylmalonate in absolute alcohol with sodium ethoxide underwent alcoholysis to give diethyl carbonate and ethyl phenylacetate. This is analogous to the results obtained by Cope and McElvain[2] working with disubstituted malonic esters. Thus it

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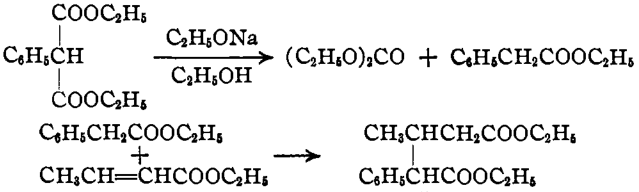
[1] (a) Michael and Ross, THIS JOURNAL, **52**, 4598 (1930); **53**, 1150 (1931). (b) Holden and Lapworth, *J. Chem. Soc.*, 2368 (1931). (c) Michael and Ross, THIS JOURNAL, **54**, 407 (1932). (d) Michael and Ross, *ibid.*, **55**, 1632 (1933).

[2] Cope and McElvain, *ibid.*, **54**, 4319 (1932).

appears that in the above reactions the phenylmalonic ester first underwent alcoholysis to give phenylacetic ester, which then added to the unsaturated esters and ketone.



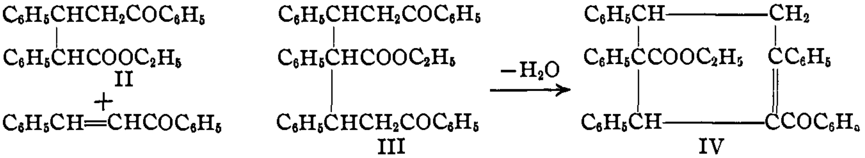
$$\begin{array}{c} COOC_2H_5 \\ | \\ C_6H_5CH \\ | \\ COOC_2H_5 \end{array} \xrightarrow[C_2H_5OH]{C_2H_5ONa} (C_2H_5O)_2CO + C_6H_5CH_2COOC_2H_5$$

$$\begin{array}{c} C_6H_5CH_2COOC_2H_5 \\ + \\ CH_3CH{=}CHCOOC_2H_5 \end{array} \longrightarrow \begin{array}{c} CH_3CHCH_2COOC_2H_5 \\ | \\ C_6H_5CHCOOC_2H_5 \end{array}$$

I

In the hope that condensation of the diethyl phenylmalonate might be accomplished under conditions such that alcoholysis could not occur, the reaction was carried out in other media. The catalysts employed were (a) one-sixth of a molecular equivalent of sodium ethoxide in ether and (b) in benzene, (c) one equivalent of sodium ethoxide in ether, (d) piperidine with no solvent other than the ester and (e) diethyl sodiophenylmalonate in benzene. In the runs in which alcohol had been used to dissolve the sodium there was isolated a small yield of product corresponding to the addition of ethyl phenylacetate to the unsaturated ester or ketone. The only other condensation product obtained was from the runs in which benzalacetophenone was used under conditions (b) and (e) above. In the latter case (e) there was isolated a 9% yield of a condensation product melting at 258°. A trace of the same compound was obtained in the other reaction (b).

The same high melting product was formed by the reaction of ethyl α,β-diphenyl-γ-benzoylbutyrate (II) with benzalacetophenone in the presence of sodium ethoxide. The product of this reaction might be either of two normal addition products or the cyclic compounds derived from them.[3]



$$\begin{array}{c} C_6H_5CHCH_2COC_6H_5 \\ | \\ C_6H_5CHCOOC_2H_5 \\ \text{II} \\ + \\ C_6H_5CH{=}CHCOC_6H_5 \end{array} \quad \begin{array}{c} C_6H_5CHCH_2COC_6H_5 \\ | \\ C_6H_5CHCOOC_2H_5 \\ | \\ C_6H_5CHCH_2COC_6H_5 \\ \text{III} \end{array} \xrightarrow{-H_2O} \begin{array}{ccc} C_6H_5CH & \text{———} & CH_2 \\ | & & | \\ C_6H_5CCOOC_2H_5 & & CC_6H_5 \\ | & & \| \\ C_6H_5CH & \text{———} & CCOC_6H_5 \\ & \text{IV} & \end{array}$$

The analysis of the product indicated that it was probably the cyclohexene (IV), although the carbon and hydrogen percentages of the cyclohexene and cyclohexanone are so close that analysis is not conclusive. However, the structure IV is confirmed by the fact that the compound does not undergo alcoholysis when treated with sodium ethoxide in alcohol. Michael and Ross[1d] have found that the cyclohexanone formed by the reaction of two moles of benzalacetophenone with one of malonic ester readily undergoes alcoholysis. The unknown did not form a pyryllium

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(3) The normal condensation products, 2,3,4-triphenyl-3-carbethoxyl-1,5-dibenzoylpentane and ethyl α,β,δ-triphenyl-γ,ϵ-dibenzoylcaproate may lose a molecule of water or alcohol, respectively, to give a cyclohexene or cyclohexanone derivative.[1d]

salt with ferric chloride in acetic anhydride.[4] Saponification gave α,β-diphenyl-γ-benzoylbutyric acid.[5] In view of these reactions the unknown has been assigned the structure IV.[6]

The Michael condensation has been considered a typical reaction of the active methylene group[7] and is known to take place readily with malonic ester[1] and phenylacetic ester.[8] On first thought, therefore, it was surprising that diethyl phenylmalonate, which contains an additional labilizing group, should fail to undergo the reaction. The explanation for this behavior may lie in the fact that the additional group causes enough steric hindrance to render the phenylmalonic ester unreactive. This is in agreement with the report[1a] that diethyl ethylmalonate gives a smaller yield of condensation product with crotonic ester than does diethyl methylmalonate.

The fact that substitution plays an important role in determining the reactivity of a compound in the Michael condensation has been confirmed by a study of the reaction with structures which contain only one labilizing group—*i. e.*, the simple ketones and esters. With these compounds the major difficulty encountered has been that they are so reactive that it is difficult to prevent the formation of products arising from the combination of two moles of α,β-unsaturated compound with one of the ketones[9] or esters. This phase of the reaction is now under further investigation.

Experimental

Preparation of Reagents.—Ethyl crotonate, b. p. 136–139°, and ethyl tiglate, b. p. 152–154°, were prepared by the hydrogenation of ethyl acetoacetate and ethyl α-methylacetoacetate[10] and dehydration of the β-hydroxy esters with phosphorus pentoxide.[11]

TABLE I

THE RESULTS OF THE REACTION OF DIETHYL PHENYLMALONATE WITH α,β-UNSATURATED COMPOUNDS IN ALCOHOL[a]

	Yield, %		
Reactant	$(C_2H_5O)CO$ 124–126°	$C_6H_5CH_2CO_2C_2H_5$ 119–122° (23 mm.)	Condensation product
$CH_3CH{=}CHCOOC_2H_5$	46[f]	..	80[b]
$CH_3CH{=}C(CH_3)COOC_2H_5$	50	20	70[c]
$C_6H_5CH{=}CHCOOC_2H_5$	..	62	35[d]
$C_6H_5CH{=}CHCOC_6H_5$	..	..	94[e]
None	61	86	..

[a] The reactions in alcohol were carried out according to the following general

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(4) Allen and Barker, THIS JOURNAL, **54**, 743 (1932).

(5) The loss of benzalacetophenone during hydrolysis is an example of the reversal of the Michael condensation [*cf.* Ingold and Powell, *J. Chem. Soc.*, **119**, 1976 (1921)]. Michael and Ross[1d] have found that the cyclohexene derivative obtained from the condensation of two moles of benzalacetophenone with one mole of malonic ester likewise loses benzalacetophenone during hydrolysis.

(6) The presence of the alcohol necessary to produce alcoholysis of the phenylmalonic ester to phenylacetic ester which then condensed to give IV may result from the action of sodium on phenylmalonic ester. It has been demonstrated that alcohol is formed by the action of sodium on esters [*cf.* Snell and McElvain, THIS JOURNAL, **53**, 2310 (1931)].

(7) Ionescu, *Bull. soc. chim.*, [4] **51**, 171 (1932).

(8) Borsche, *Ber.*, **42**, 4497 (1909); Meerwein, *J. prakt. Chem.*, **97**, 274 (1918).

(9) Kostanecki and Rossbach, *Ber.*, **29**, 1493 (1896).

(10) Adkins, Connor and Cramer, THIS JOURNAL, **52**, 5192 (1930).

(11) Courtot, *Bull. soc. chim.*, **35**, 111 (1906).

method. To 4.6 g. (0.2 mole) of sodium in 70 cc. of absolute ethanol was added 47.2 g. (0.2 mole) of diethyl phenylmalonate[12] and 0.2 mole of the α,β-unsaturated compound. The solution was refluxed on the steam-bath for eight hours in the runs with ethyl cinnamate and benzalacetophenone and for twenty-four hours in the other runs. It was then cooled, poured into 500 g. of ice-water containing 13 g. of acetic acid, extracted with ether and dried over sodium sulfate. The runs with ethyl crotonate, ethyl tiglate and with no unsaturated compound present were distilled through a 15-cm. Widmer column. Ethyl α,β-diphenyl-γ-benzoylbutyrate was isolated by crystallization from the reaction mixture, washing with water containing acetic acid and drying. It gave the reported melting point (152–154°) after one recrystallization from ethanol. Unchanged esters were distilled from the ethyl α,β-diphenylglutarate and the residue recrystallized from ethanol.

[b] Diethyl α-phenyl-β-methylglutarate, b. p. 156–158° (6 mm.). *Anal.*[13] Calcd. for $C_{16}H_{22}O_4$: C, 69.06; H, 7.91. Found: C, 68.90; H, 7.86.

[c] Diethyl α-phenyl-β,γ-dimethylglutarate, b. p. 157.5–159.5° (5 mm.). *Anal.*[13] Calcd. for $C_{17}H_{24}O_4$: C, 69.86; H, 8.21; saponification equivalent, 146. Found: C, 69.94; H, 8.23; saponification equivalent, 143.

[d] Diethyl α,β-diphenylglutarate, m. p. 92–93°.[14]

[e] Ethyl α,β-diphenyl-γ-benzoylbutyrate, m. p. 152–154°.[15]

[f] Diethyl carbonate was identified by the formation of triphenylcarbinol, m. p. 161–162°, when it was allowed to react with phenylmagnesium bromide. The melting point was unchanged when mixed with an authentic specimen of triphenylcarbinol.

TABLE II

THE BEHAVIOR OF DIETHYL PHENYLMALONATE IN MEDIA OTHER THAN ALCOHOL[a]

		Yield, %		
Reactant[b]	Solvent	Unreacted materials[c]	Compound II	Compound IV[m]
$C_6H_5CH{=}CHCOC_6H_5$[d]	....	97	0	0
$C_6H_5CH{=}CHCOC_6H_5$[e]	C_6H_6	84	9[f]	trace
$C_6H_5CH{=}CHCOC_6H_5$[g]	$(C_2H_5)_2O$	92	0	0
$C_6H_5CH{=}CHCOC_6H_5$[h]	$(C_2H_5)_2O$	85	5[f]	0
$C_6H_5CH{=}CHCOC_6H_5$[i]	C_6H_6	43[j]	0	9
$C_6H_5CH{=}CHCOOC_2H_5$[k]	C_6H_6	90	8[l]	0

[a] Benzoylacetic ester would be one of the products of condensation, rearrangement by the mechanism of Holden and Lapworth, and retrogression. In every distillate a test was made for benzoylacetic ester, using ferric chloride. There was never any color to indicate the presence of an enol.

[b] One-tenth mole of each of the reactants was used.

[c] Determined by distillation.

[d] This run was made with piperidine as a catalyst by the method of Kohler.[16]

[e] One-sixth of an equivalent of sodium was dissolved in 5 cc. of absolute alcohol, the reactants added and the mixture heated on the steam-bath with stirring for eight hours. Two-tenths gram of IV was filtered out and the filtrate treated in the usual manner.

[f] Ethyl α,β-diphenyl-γ-benzoylbutyrate, m. p. 152–154°.[15]

[g] The procedure of Michael and Ross[17] for the use of one-sixth of an equivalent of sodium ethoxide in ether was followed.

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(12) The author is indebted to Dr. V. H. Wallingford of the Mallinckrodt Chemical Works for a generous supply of diethyl phenylmalonate.

(13) These analyses were made by Mr. Ralph H. Wardlow.

(14) Avery and Maclay, THIS JOURNAL, **51**, 2833 (1929).

(15) Avery and Jorgensen, *ibid.*, **52**, 3628 (1930).

(16) Kohler, *Am. Chem. J.*, **46**, 482 (1911).

(17) Michael and Ross, THIS JOURNAL, **52**, 4605 (1930).

[h] Carried out in the presence of one equivalent of sodium ethoxide.[17]

[i] Diethyl sodiophenylmalonate was prepared from powdered sodium and diethyl phenylmalonate in 100 cc. of dry thiophene-free benzene, benzalacetophenone in 50 cc. of benzene added and the mixture refluxed gently with stirring for eight hours. A small amount of IV was filtered from the solution and the remainder of IV was obtained by washing the reaction mixture with aqueous acetic acid and concentrating the benzene layer. The solid was purified by suspension in hot ethanol and thorough washing with ether. It melted at 258° on the melting point bar[18] alone or mixed with the condensation product obtained by the reaction of ethyl α,β-diphenyl-γ-benzoylbutyrate with benzalacetophenone. Two grams was saponified with alcoholic potassium hydroxide. Acidification precipitated the solid acid, which after repeated recrystallization from benzene gave the lower melting isomer of α,β-diphenyl-γ-benzoylbutyric acid, m. p. 186.5–187.5°. The melting point was unchanged when mixed with an authentic sample of this acid.[15]

[j] The distillation residue was a stiff tarry material, evidently polymerized chalcone. It could not be crystallized.

[k] Diethyl sodiophenylmalonate was prepared and the procedure used as described under (*i*).

[l] Diethyl α,β-diphenylglutarate, m. p. 92–93°.[14]

[m] Compound IV was also prepared by the following method. To a solution prepared by dissolving 0.3 g. (0.013 mole) of sodium in 5 cc. of absolute ethanol was added 50 cc. of dry thiophene-free benzene and 5 g. (0.013 mole) of ethyl α,β-diphenyl-γ-benzoylbutyrate (II), followed by a solution of 2.7 g. (0.013 mole) of benzalacetophenone in benzene. The mixture was refluxed for eight hours, poured into 50 cc. of water containing 1 g. of acetic acid, the benzene layer separated and the solvent removed by distillation. The solid remaining was purified by suspending it in hot benzene, filtering and washing with ether. The material obtained melted at 258° on the melting point bar. The yield of pure material was 2.8 g. (38%). *Anal.*[13] Calcd. for $C_{40}H_{34}O_3$: C, 85.40; H, 6.04. Calcd. for $C_{38}H_{30}O_3$: C, 85.39; H, 5.62. Found: C, 85.15; H, 5.95.

An attempt to prepare a pyryllium salt[4] from 0.5 g. of this compound gave only unchanged material (m. p. 258°).

The conditions for alcoholysis used by Michael and Ross[19] for 1,5-diphenyl-2,6-dibenzoyl-4-carbethoxycyclohexanone-3 gave only unchanged material, even after standing for twenty hours (five times the time required for 60% alcoholysis of their compound).

Summary

It has been found that diethyl phenylmalonate does not undergo the Michael condensation. In alcohol solution diethyl carbonate and ethyl phenylacetate were formed and the latter condensed with α,β-unsaturated esters or ketones. In other media the only product isolated was a small amount of a cyclohexene derivative (IV) formed in benzene by the condensation of ethyl phenylacetate with two moles of benzalacetophenone. Since the failure of diethyl phenylmalonate to react suggested that increased substitution influences the reactivity of compounds in this reaction, a study of the simple ketones and esters has been undertaken.

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(18) Dennis and Shelton, THIS JOURNAL, **52**, 3128 (1930).

(19) Ref. 1d, p. 1624.