The Reactions of Ester with Acyl Chloride in the Presence of Aluminum Chloride. V. Reaction Mechanism of the Benzoylation of Diethyl Malonate

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In a previous paper[1] it was reported that triacylated methanes were obtained in addition to diacylated compounds when diethyl malonate was treated with two or three molecular equivalents of benzoyl chloride or *p*-substituted benzoyl chlorides in the presence of three molecular equivalents of aluminum chloride. This paper describes attempts to achieve a more fundamental understanding of the reaction mechanism of the benzoylation of diethyl malonate.

Reaction of Ethyl Dibenzoylacetate with Aluminum Chloride.—These reactions resulted in the formation of acetophenone, dibenzoylmethane, aluminum chelate of dibenzoylmethane, tribenzoylmethane and benzoic acid (Table I). In every reaction, an appreciable amount of dibenzoylmethane was obtained with tribenzoylmethane. This fact shows that ethyl dibenzoylacetate gives dibenzoylmethane by decarbethoxylation and simultaneously decomposes to benzoyl chloride and ethyl benzoylacetate, which converts into acetophenone. On the other hand, tribenzoylmethane is formed by the benzoylation of the dibenzoylmethane which is formed.

$$(C_6H_5CO)_2CHCOOC_2H_5 \rightarrow C_6H_5COCH_2COOC_2H_5 + C_6H_5COCl + (C_6H_5CO)_2CH_2$$

$$(C_6H_5CO)_2CH_2 + C_6H_5COCl \rightarrow (C_6H_5CO)_3CH$$

$$C_6H_5COCH_2COOC_2H_5 \rightarrow C_6H_5COCH_3 + C_2H_5Cl + CO_2$$

Reactions of Dibenzoylmethane-*O*-benzoate with Aluminum Chloride.—The products of these reactions (Table I) were dibenzoylmethane, tribenzoylmethane and benzoic acid. From this table, it can be noted that dibenzoylmethane-*O*-benzoate is fairly stable in the presence of a small amount of aluminum chloride, but is decomposed to dibenzoylmethane in the presence of a large amount of aluminum chloride.

Reactions of Tribenzoylmethane with Aluminum Chloride.—In every case (Table I) tribenzoylmethane is decomposed to dibenzoylmethane, but it is difficult to decompose it to dibenzoylmethane with only a small amount of aluminum chloride.

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[1] H. Kaneyuki, This Bulletin, 35, 523 (1962).

TABLE I. REACTIONS OF ALUMINUM CHLORIDE WITH ACYLATED COMPOUNDS
Solvent : Nitrobenzene 8 ml.**, 4 ml.

Reactant			Reaction condition		Product and yield							
	mol. $\times 10^{-2}$	$AlCl_3$ mol. $\times 10^{-2}$	°C	hr.	AP a) %	DBM b) %	DBM-Al c) %	TBM d) %	TBM-O-B e) %	DBA f) %	DBM-O-B g) %	BA h) %
DBA	0.33	0.49	60	8	12.5	46.0	2.1	Trace		4.6*		24.3
	0.33	0.67	30	5	12.5	37.0	16.5	1.3		2.5*		24.3
DBM-*O*-B	0.30	0.30	30	5		20.6	42.5	4.0				54.0
	0.30	0.04	45	26		Trace	32.4	3.5			50.0*	13.5
TBM	0.30	0.7	45	5		44.0	28.1	10.0*				67.6
	0.30	0.3	45	5		20.6	37.8	22.0*				57.0
	0.30	0.1	30	90		20.6		71.0*				26.0
TMB-*O*-B	0.23	0.22	45	5		9.0	40.7	33.0	6.0*			58.4
DBM**	0.22	0.22	65	8		22.0*	75.0					

* Recovered material.
a) AP ; Acetophenone
b) DBM ; Dibenzoylmethane
c) DBM-Al ; Aluminum chelate of dibenzoylmethane
d) TBM ; Tribenzoylmethane
e) TBM-*O*-B ; Tribenzoylmethane-*O*-benzoate
f) DBA ; Ethyl dibenzoylacetate
g) DBM-*O*-B ; Dibenzoylmethane-*O*-benzoate
h) BA ; Benzoic acid

Reaction of Tribenzoylmethane-*O*-benzoate with Aluminum Chloride.—It is to be noted that tribenzoylmethane-*O*-benzoate is easily converted into tribenzoylmethane and then further decomposed to dibenzoylmethane (Table I).

Reaction of Dibenzoylmethane with Aluminum Chloride.—Dibenzoylmethane seemed to be stable in the presence of aluminum chloride, for it is recovered in substantial quantities with its aluminum chelate (Table I).

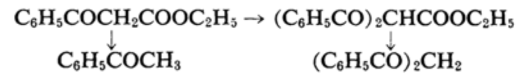
Benzoylation of Ethyl Dibenzoylacetate.—In these reactions (Table II), the yield of dibenzoylmethane is good at a higher temperature, but the yield of tribenzoylmethane is good when a larger amount of aluminum chloride is used. It is fairly difficult to benzoylate ethyl dibenzoylacetate ; a considerable amount of this material is recovered unchanged.

Benzoylation of Dibenzoylmethane and its Aluminum Chelate.—In these reactions (Table II), the yield of tribenzoylmethane is small when one molecular equivalent of aluminum chloride is used and is lower at a higher reaction temperature. Using 0.1 molecular equivalent of aluminum chloride, the yield of tribenzoylmethane is much increased. In the absence of aluminum chloride, the yield of tribenzoylmethane is very good, however, aluminum chelate of dibenzoylmethane gives it in a 12% yield. Therefore, it can be seen that the formation of tribenzoylmethane by the benzoylation of dibenzoylmethane is hindered to some extent by the presence of aluminum chloride.

Benzoylation of Tribenzoylmethane.—In every case (Table II), the yield of tribenzoylmethane-*O*-benzoate is low and the decomposition of tribenzoylmethane is greatest at a high temperature.

Benzoylation of Diethyl Malonate in the Presence of a Small Amount of Aluminum Chloride.—After diethyl malonate was warmed at 70°C with 1/3 molecular equivalent of aluminum chloride for 2 hr., one molecular equivalent of benzoyl chloride was added to the reaction mass, and then the mixture was kept at 70°C. When the reaction time is 8 hr., diethyl benzoylmalonate is the only product, but after a reaction of 24 hr., its yield is decreased, and instead small amounts of ethyl benzoylacetate, ethyl dibenzoylacetate and traces of acetophenone, dibenzoylmethane are obtained (Table III). In considering these results, diethyl benzoylmalonate seems to be converted slowly by decarbethoxylation into ethyl benzoylacetate, which is partly changed to acetophenone and ethyl dibenzoylacetate. Therefore, the following reaction sequences may be considered :

$$C_6H_5COCH(COOC_2H_5)_2 \rightarrow C_6H_5COCH_2COOC_2H_5$$



$$\begin{array}{ccc} C_6H_5COCH_2COOC_2H_5 & \rightarrow & (C_6H_5CO)_2CHCOOC_2H_5 \\ \downarrow & & \downarrow \\ C_6H_5COCH_3 & & (C_6H_5CO)_2CH_2 \end{array}$$

It can be concluded that the isolation of ethyl

TABLE II. BENZOYLATION OF SOME ACYLATED COMPOUNDS

Solvent : Nitrobenzene 8 ml., **25 ml.

Reactant				Reaction condition		Product*** and yield				
	mol. $\times 10^{-2}$	C_6H_5COCl mol. $\times 10^{-2}$	$AlCl_3$ mol. $\times 10^{-2}$	°C	hr.	DBM[a)] %	DBM-Al[b)] %	TBM[c)] %	TBM-*O*-B[d)] %	DBA[e)] %
DBA	0.33	0.35	0.67	60	5	43.7	17.8	21.6	2.0	4.0*
			0.37	60	5	14.5	51.0	2.7	Trace	25.0*
			0.37	30	5	20.0	6.3	3.6		54.0*
			0.06	30	56		3.8			95.0*
DBM	0.45	0.43	0.45	70	5	13.0*	75.0	2.4	2.6	
			0.45	30	5	25.0*	62.5	6.5	4.5	
			0.04	30	93	Trace*	23.0	71.5	0.5	
			0	30	90	17.5*		78.0		
DBM-Al**	0.04	0.21	0	30	90	24.2	63.4*	11.8		
TBM	0.30	0.64	0.60	70	8	56.0	8.9	9.5*	6.0	
		0.35	0.37	45	5	40.0	Trace	32.0*	5.7	

* Recovered material.

*** Benzoic acid was obtained in each case.

a) DBM ; Dibenzoylmethane

b) DBM-Al ; Aluminum chelate of dibenzoylmethane

c) TBM ; Tribenzoylmethane

d) TBM-*O*-B ; Tribenzoylmethane-*O*-benzoate

e) DBA ; Ethyl dibenzoylacetate

TABLE III. BENZOYLATION OF DIETHYL MALONATE WITH BENZOYL CHLORIDE

Reactant : Diethyl malonate 3.1×10^{-2} mol., benzoyl chloride 3.1×10^{-2} mol., $AlCl_3$ 1.0×10^{-2} mol.

Reaction temp. : 70°C. Solvent : Nitrobenzene 16 ml.

Reaction time	Product and yield					
	BME[a)]	BAE[b)]	AP[c)]	DBA[d)]	DBM[e)]	BA[f)] recovered
hr.	%	%	%	%	%	%
8	52					21
24	25	4	Trace	5	Trace	16

Yield : Calculated from benzoyl chloride.

a) BME ; Ethyl benzoylmalonate

b) BAF ; Ethyl benzoylacetate

c) AP ; Acetophenone

d) DBA ; Ethyl dibenzoylacetate

e) DBM ; Dibenzoylmethane

f) BA ; Benzoic acid

benzoylacetate is due to the difficulty of the benzoylation of itself because of the small amount of aluminum chloride. Like these reaction products, ethyl *p*-nitrobenzoylacetate and *p*-nitroacetophenone were also obtained when diethyl malonate was treated with *p*-nitrobenzoyl chloride[1].

Discussion

The acylation of an active methylene group with acid chloride has been generally accomplished by means of a basic reagent. On the other hand, using an acidic reagent boron trifluoride, Meerwein[2] and Hauser[3] prepared β-diketone by the acylation of ketone with acid anhydride. Hauser has suggested that the acylation of ketone probably involves the conversion, by boron trifluoride, of both the anhydride and the ketone to reactive intermediates which condense. Therefore, the anhydride is presumably converted into carbonium ion, and the ketone is apparently converted into an enol form.

As shown in the experimental part of this paper, by treating diethyl malonate with benzoyl chloride in the absence of a catalyst, only a 4% yield of diethyl benzoylmalonate was obtained. Consequently, it may be considered that in the presence of a proper amount of aluminum chloride, diethyl malonate and β-keto-ester are activated much more effectively than acid chloride. From this standpoint, the

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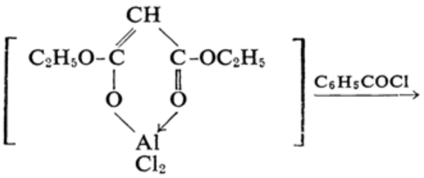
[2] H. Meerwein and D. Vossen, *J. prakt. Chem.*, **141**, 149 (1934).

[3] R. Hauser and T. Adams, *J. Am. Chem. Soc.*, **66**, 345 (1944).

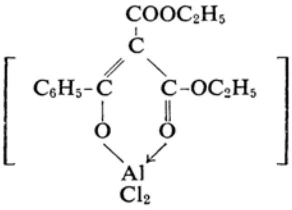
following mechanism is postulated for the benzoylation of diethyl malonate in the presence of aluminum chloride: Diethyl malonate reacts with aluminum chloride to give the aluminum chloride complex (I). The reaction of I with benzoyl chloride leads to diethyl benzoylmalonate which soon becomes an aluminum chloride complex of diethyl benzoylmalonate (II).

$$CH_2(COOC_2H_5)_2 \xrightarrow{AlCl_3}$$



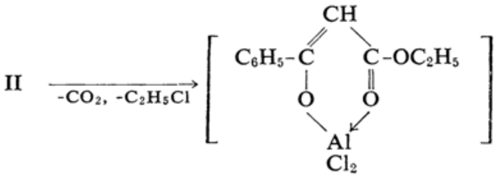
I

$$C_6H_5COCH(COOC_2H_5)_2 \xrightarrow{AlCl_3}$$



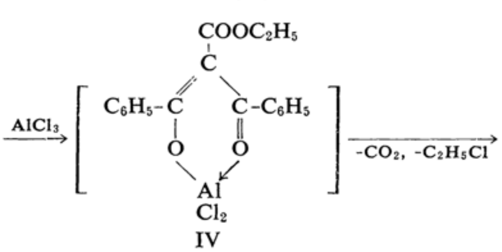
II

II is converted into an aluminum chloride complex of ethyl benzoylacetate (III) by decarbethoxylation. III will react immediately with benzoyl chloride to give ethyl dibenzoylacetate, which soon becomes an aluminum complex of ethyl dibenzoylacetate (IV). By slow decarbethoxylation, IV would be converted into an aluminum chloride complex of dibenzoylmethane (V).

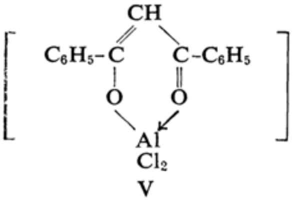


III

$$\xrightarrow{C_6H_5COCl} \begin{matrix} C_6H_5CO \\ C_6H_5CO \end{matrix} \rangle CHCOOC_2H_5$$



IV



V

The fact that water-insoluble dibenzoylmethane is precipitated from the clear aqueous layer containing aluminum chloride by heating, as has been described in the experimental part of this paper, may show that dibenzoylmethane exists as V or VI in the presence of aluminum chloride. Because dibenzoylmethane and VII were always obtained in any of these experiments, it may be considered that dibenzoylmethane, V, VI and VII are in equilibrium.

$$(C_6H_5CO)_2CH_2 \underset{HCl}{\overset{AlCl_3}{\rightleftarrows}} V \rightleftarrows \underset{VI}{[(C_6H_5CO)_2CH]_2AlCl} \rightleftarrows \underset{VII}{[(C_6H_5CO)_2CH]_3Al}$$

When tribenzoylmethane was treated with aluminum chloride only, 22% of tribenzoylmethane was recovered, while dibenzoylmethane-*O*-benzoate gave a small amount of tribenzoylmethane under similar conditions (Table I). Therefore, the formation of tribenzoylmethane is not due to the isomerization of dibenzoylmethane-*O*-benzoate, but to the benzoylation of dibenzoylmethane or such complexes as V, VI and VII. As a similar example with the above reactions, it has been known that a copper complex of β-diketone reacts with *p*-nitrobenzoyl chloride to give copper chelate of triketone⁴⁾. Moreover, in the presence of a large amount of aluminum chloride (Table II), the direct conversion of ethyl dibenzoylacetate into tribenzoylmethane may occur. Besides benzoylation, the reactions of aluminum chloride are complicated by such side reactions as decarbethoxylation, debenzoylation and the cleavage of ester linkage, as shown in Table I.

Owing to the above considerations, the following sequence has to be postulated:

$$CH_2(COOC_2H_5)_2 \longrightarrow C_6H_5COCH(COOC_2H_5)_2 \longrightarrow C_6H_5COCH_2COOC_2H_5 \longrightarrow (C_6H_5CO)_2\cdot CHCOOC_2H_5 \longrightarrow (C_6H_5CO)_2CH_2 \rightleftarrows (C_6H_5CO)_3CH \rightleftarrows (C_6H_5CO)_2C{=}\underset{OCOC_6H_5}{C}C_6H_5$$

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4) W. J. Barry, *J. Chem. Soc.*, **1960**, 670.

Experimental

Reaction methods were the same as in the previous paper[1]. The treatment of the reaction mixture was also the same; that is, it was separated into the aqueous layer containing aluminum chloride, sodium bicarbonate extract, sodium hydroxide extract, water extract and residual solution. Descriptions overlapping with those of the previous paper are omitted here. Reaction conditions are shown in the above tables.

Reaction of Ethyl Dibenzoylacetate with Aluminum Chloride.—Precipitates were deposited with a small amount of an oily substance when the aqueous layer containing aluminum chloride was warmed and allowed to stand. The precipitates were collected, washed with petroleum ether and recrystallized from methanol to afford dibenzoylmethane. 2, 4-Dinitrophenylhydrazone derived from the petroleum ether soluble substance was recrystallized from ethanol to yield crystals, m. p. 245~248°C, which showed no depression of melting point on admixture with 2,4-dinitrophenylhydrazone of acetophenone.

Reaction of Dibenzoylmethane-*O*-benzoate with Aluminum Chloride.—Dibenzoylmethane-*O*-benzoate was prepared according to the procedure of the literature[5]. By removing the solvent from the residual solution separated from the reaction mixture, dibenzoylmethane-*O*-benzoate was recovered.

Benzoylation of Diethyl Malonate with Benzoyl Chloride in the Presence of a Small Amount of Aluminum Chloride.—An oily substance was precipitated with some solid from the aqueous layer containing aluminum chloride, as has been described above. The solid was collected by filtering, washed with water and recrystallized from methanol to afford dibenzoylmethane. The filtrate was extracted with ether, and the ethereal extract was shaken with a copper acetate solution. A small amount of the yellowish green precipitate formed was filtered. By treating this precipitate with hydrochloric acid, dibenzoylmethane was obtained. After removal of ether from the ethereal solution, a green semi-solid I was obtained. The semi-solid was filtered and washed with ethanol. The ethanol wash was concentrated to yield crystals of copper chelate of diethyl benzoylmalonate. The mother liquor was subjected to steam distillation, and from the distillate 2,4-dinitrophenylhydrazone was prepared and identified as that of acetophenone by the mixed melting point method. The sodium hydroxide extract was acidified and extracted with ether. After concentrating the ether extract, crystallized ethyl dibenzoylacetate was filtered off. From the ethereal filtrate, copper chelate of diethyl benzoylmalonate was prepared, as has been mentioned above.

Copper Chelate of Ethyl Benzoylacetate.—The solid I was recrystallized from benzene as light green needles, 0.35 g., m. p. 178~184°C, reported m. p. 180°C, 182~183°C[6].

Found: C, 59.53; H, 4.87. Calcd. for $C_{22}H_{22}O_6Cu$: C, 59.25; H, 4.97%.

Reaction of Diethyl Malonate with Benzoyl Chloride.—Diethyl malonate (3.4 g., 0.021 mol.) and benzoyl chloride (3.0 g., 0.021 mol.) were dissolved in nitrobenzene (15 ml.) and kept at 65°C for 8 hr. The treatment of the reaction mixture was the same as has been mentioned above. Benzoic acid (2.3 g.) was obtained on acidifying the sodium bicarbonate extract. The oily substance obtained by acidification of the sodium hydroxide extract and water extract was converted into copper chelate, 0.25 g., m. p. 178~179°C; this was identified as copper chelate of diethyl benzoylmalonate by the mixed melting point method.

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[5] L. Claisen and E. Hasse, *Ber.*, **36**, 3674 (1903).

[6] "Beilsteins Handbuch der Organischen Chemie", H., **10**, 678 (1927).