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The Reversible Acylation of β-Diketone with Acyl Chloride in the Presence of Aluminum Chloride

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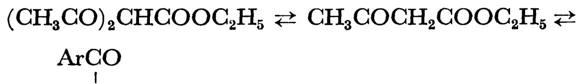
The treatment of acetylacetone (I) with *n*-butyryl chloride in the presence of aluminum chloride in nitrobenzene gave *n*-butyrylacetone and di-*n*-butyrylmethane at 45°C. The same products were obtained, along with *n*-butyric acid, when *n*-butyrylacetone or di-*n*-butyrylmethane was treated with acetyl chloride under analogous conditions. The reactions between I and benzoyl chloride and between benzoylacetone or dibenzoylmethane and acetyl chloride gave products consisting of I, benzoylacetone, dibenzoyl-, diacetylbenzoyl-, acetyldibenzoyl-, tribenzoyl-methane, and benzoic acid. These findings show that β-diketone can reversibly react with acyl chloride to form new β-diketones by way of the mixed triacylmethanes. The acylation mechanism is discussed.

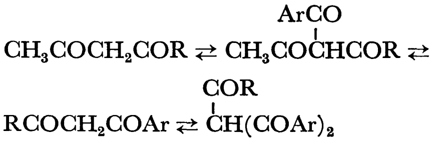
In our previous papers[1] it was shown that the aluminum chloride-catalyzed acylation of ethyl acetoacetate with aroyl chloride, accompanied by deacylation, involves the following sequence of four-step equilibria among the substrate and products in the presence of aroyl and acetyl chlorides:



$$(CH_3CO)_2CHCOOC_2H_5 \rightleftarrows CH_3COCH_2COOC_2H_5 \rightleftarrows$$
$$CH_3CO\overset{\overset{ArCO}{|}}{C}HCOOC_2H_5 \rightleftarrows ArCOCH_2COOC_2H_5 \rightleftarrows$$
$$(ArCO)_2CHCOOC_2H_5$$

The similar acylation[2] of acetylacetone (I) with *n*-butyryl chloride was established to proceed by the coordination of the acyl chloride with the metal atom of the β-diketone complex. The purpose of this paper is to give more information on the reaction of β-diketones with acid chlorides other than the *n*-butyryl chloride.

As is shown in Table 1, the butyrylation of I with *n*-butyryl chloride and the acetylation of *n*-butyrylacetone or di-*n*-butyrylmethane with acetyl chloride in the presence of aluminum chloride in nitrobenzene all gave the same products—I, *n*-butyrylacetone, di-*n*-butyrylmethane, and *n*-butyric acid—at 45°C. The latter acid obviously results from the hydrolysis of the *n*-butyryl chloride derived from the starting butyrylated ketones except when *n*-butyryl chloride is used. The products resulting from either the benzoylation of I or the acetylation of benzoylacetone or dibenzoylmethane consisted of I, benzoylacetone, dibenzoylmethane, and benzoic acid; also, triacylmethanes and aluminum chelate of dibenzoylmethane, $[(C_6H_5CO)_2CH]_3Al$, were obtained under certain conditions. Tribenzoylmethane was isolated in every case, while acetyldibenzoyl- and diacetylbenzoyl-methane were not always isolated. The latter was obtained particularly, along with the former in small amounts, when I was benzoylated in a stream of dry nitrogen gas for a shorter reaction time in order to avoid the effect of the hydrogen chloride formed. Both mixed triacylmethanes were also obtained from aluminum trisacetylacetonate, which could undergo benzoylation without liberating a large amount of hydrogen chloride because of its enolate structure. From these facts, it appears that the mixed triacylmethanes tend to decompose more easily into β-diketones and acyl chlorides as the amount of hydrogen chloride formed is increased. The acid chlorides thus formed can react with any β-diketones present in the reacting mixture to yield the triacylmethanes. Among these, the mixed triacylmethanes act as intermediates for the formation of the new β-diketones. Apparently, there is the following equilibrium in the presence of the acyl chlorides and aluminum chloride:



$$CH_3COCH_2COR \rightleftarrows CH_3CO\overset{\overset{ArCO}{|}}{C}HCOR \rightleftarrows$$
$$RCOCH_2COAr \rightleftarrows \overset{\overset{COR}{|}}{C}H(COAr)_2$$

$R = CH_3$ or Ar

Triacetylmethane, though not isolated, seems to take part in this equilibrium, because it is known to be synthesized by the aluminum chloride-catalyzed reaction of I with acetyl chloride.[3]

In the presence of various amounts of aluminum chloride, I was benzoylated with 2 equivalents of benzoyl chloride under comparable conditions. The use of a 0.3 equivalent of the condensing agent afforded the benzoylated ketones (including tribenzoylmethane) and the aluminum chelate of dibenzoylmethane in a relatively low and a high yield respectively, but the former were obtained in high yields at the expense of the latter on the increase of the condensing agent to a 0.5 or 0.7 equivalent. Accordingly, it seems that the increase in the condensing agent allows the benzoylation to proceed with a high yield by hindering the formation of the stable aluminum chelate. The control of the chelate-ring formation by aluminum chloride has also been visualized as spectral evidence for the action of aluminum chloride on I[2] or aluminum trisacetylacetonate.[4] The above variation in yield with the amount of aluminum chloride was also observed with the butyrylation reaction.[2] In this case,

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[1] K. Matsui and T. Nojiri, *Nippon Kagaku Zasshi*, **86**, 531 (1965); T. Nojiri and K. Matsui, *ibid.*, **87**, 880 (1966).

[2] T. Nojiri, I. Hashimoto, M. Motoi, and K. Matsui, This Bulletin, **42**, 3359 (1969).

[3] L. Birkenbach, K. Kellermann, and W. Stein, *Ber.*, **65**, 1075 (1932).

[4] T. Nojiri, M. Motoi, and I. Hashimoto, This Bulletin, **44**, 850 (1971).

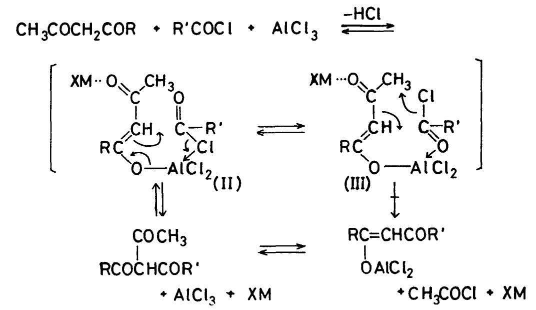
Table 1. Reaction of β-diketone with acyl chloride

Substrate (15 mmol)	Reactant RCOCl (mol ratio)	$AlCl_3$ (mol ratio)	Reaction time (hr)	Product (%)				
				I	$BtCH_2Ac$	Bt_2CH_2		BtOH
I	BtCl 2	0.5	1	(34)	22	0		
I	BtCl 1	1	1	(25)	33	5		
$BtCH_2Ac$	AcCl 1	1	1	25	(34)	6		21
Bt_2CH_2	AcCl 1	1	1	7	36	(29)		20
					$BzCH_2Ac$	Bz_2CH_2	Bz_3CH	BzOH
I	BzCl 2	2	3	(4)	23	33 0	4	
I	BzCl 2	1.2	3	(4)	32	34 [1]	5	
I	BzCl 2	0.7	3	(5)	40	36 [1]	8[c]	
I	BzCl 2	0.5	3	(4)	46	36 [2]	6[c]	
I	BzCl 2	0.3	3	(5)	47	20 [9]	3[c]	
I	BzCl 2	0.5	1	(5)	50	29 [1]	4	
I	BzCl 1	0.5	1.5, N_2	(8)	43	7 [4]	tr[d]	
I	BzCl 1	0.5	3	(13)	29	6 0	tr	
$BzCH_2Ac$	BzCl 1	0.5	3	tr	(23)	43 [29]	3	
$BzCH_2Ac$	AcCl 1.2	0.5	3	12	(39)	10 [tr]	tr[c]	5
Bz_2CH_2	AcCl 1.2	0.5	3	tr	24	(53) [36]	tr	21
$(Ac_2CH)_3Al$ (5 mmol)	BzCl 6	1.5	3	3	27	41 [11]	4[e]	
Ac_2CHBz	BzCl 1	0.5	3	tr	35	35 [12]	2[f]	
I	BzCl 2	2	5[b]		12	37 [6]	1	
					p-NO_2Bz-CH_2Ac	$(p\text{-}NO_2Bz)_2CH_2$		
I	p-NO_2BzCl 2	0.5	3		29	44 [35]		
I	p-NO_2BzCl 2	2	5[b]		5	67 [40]		
I	p-NO_2BzCl 3	3	5[b]		2	85 [40]		
						$(ClAc)_2CH_2$		
I	ClAcCl 2	1[a]	3[b]			41		

Solvent: $C_6H_5NO_2$ 10 ml, a) $(ClCH_2)_2$ 5 ml; reaction temp.: 45°C, b) 55°C; N_2: The reaction was carried out in a stream of nitrogen gas. ( ): The yield of recovered material. [ ]: The yield of Al chelate of β-diketone (included in the yield of β-diketone). c) less than 1% yield of acetyldibenzoylmethane. d) both 1.7%, yields of diacetylbenzoyl- and acetyldibenzoyl-methane; e) 2.2, 0.2%. f) 2.3, 0.7% yields respectively.

however, relatively large amounts of aluminum chloride were required to give the products in a maximum yield, but no aluminum chelate was obtained, even when a small amount of aluminum chloride was used. On the other hand, the fact that the yields of the benzoylated ketones were decreased on the use of more than 1.2 equivalents of aluminum chloride suggests that the liberation of aluminum chloride causes the condensation to proceed, and that an excess of aluminum chloride tends to coordinate with the acyl chloride resulting from the coordination complex between acyl chloride and dichloroaluminum β-diketonate complex as was pointed out in a previous paper.[2] Such a coordination complex is in the forms of II and III (Scheme 1), which should be in a rapid mobile equilibrium because of the abilities of chlorine and carbonyl oxygen in the acyl chloride to coordinate with the metal atom of enolate. Complex II must be more favorable for the intramolecular condensation to form triacylmethane, which is then deacylated easily to give β-diketone as shown in Scheme I.

However, there is no denying an acyl exchange through Complex III. Moreover, when an ester was used as the acylating agent, a coordination complex corresponding to III proved to lead directly to a new β-diketonate. Such a transacylation will be reported in our next paper.[5]



MX=$AlCl_3$ or HCl; R=CH_3 or C_3H_7 where R'=C_3H_7; R=CH_3 or C_6H_5 where R'=C_6H_5

Scheme I.

In the reaction of benzoylacetone with benzoyl chloride or in that of dibenzoylmethane with acetyl chloride, the yields of dibenzoylmethane and especially of its aluminum chelate were far higher than those from the reaction of I with benzoyl chloride. The high yield of the aluminum chelate can be explained as being due mainly to high concentrations of dibenzoylmethane

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[5] K. Matsui and M. Motoi, This Bulletin, **46**, 565 (1973).

compared with those of aluminum chloride in the reacting mixture. However, in the reaction of I with p-nitrobenzoyl chloride the high yields of di-p-nitrobenzoylmethane and its aluminum chelate seem to be ascribable to the susceptibility of certain intermediates to acylation or deacetylation, as well as to the high stabilities of the final products.

From the standpoint of synthetic chemistry, this acylation of I is useful for preparing β-diketones, such as di-p-nitrobenzoylmethane and di-chloroacetylmethane, sensible to alkali. Their yields are shown in Table 1.

Experimental

Materials. The benzoylacetone[6] (mp 59°C) and the dibenzoylmethane[7] (mp 79—80°C) were prepared according to the literature. Commercial acetyl chloride was used after distillation; bp 51—52°C. The chloroacetyl[8] (bp 104—105°C), benzoyl[9] (bp 192°C) and p-nitrobenzoyl chlorides[9] (bp 160°C/26 mmHg), were prepared from the corresponding carboxylic acids, commercially obtained, according to the literature. The diacetylbenzoyl- and acetyldibenzoyl-methane were prepared by the benzoylation of acetyl- and benzoylacetone respectively, according to the Schotten-Baumann method; the former has mp of 30—31°C and bp of 107—108°C/2 mmHg, its copper chelate, mp 247—249°C (benzene), (lit,[10] mp 35°C, bp 167°C/22 mmHg, copper chelate mp 228°C), while the latter has mp of 106.5—107.5°C, (lit,[11] 99—101°C). The other materials were described previously.[2]

Acylation Method and Separation Procedure for Product. Both were the same as in the previous paper,[2] except for the following:

a) Butyrylated Product: For the estimation of n-butyric acid, the sodium bicarbonate extract was acidified with sulfuric acid and then extracted with ether. The ether extract was dried, evaporated carefully, and then analyzed, using acetophenone as the internal standard, by gas-liquid chromatography at 130°C.

b) Benzoylated Product: The reaction mixture, quenched with crushed ice and hydrochloric acid, was shaken with ether to separate it into 2 layers. The lower layer was extracted with ether 2 days later; then, after 5 or more days, the dibenzoylmethane which gradually crystallized out was collected by filtration. The upper layer, freed from aluminum chloride, was occasionally shaken with an aqueous sodium bicarbonate solution until the Beilstein test for benzoyl chloride became negligible. The partial distillation of the aqueous extract gave a distillate containing a slight amount of acetophenone (obtained as its 2,4-dinitrophenylhydrazone). The pot residue was acidified to give benzoic acid. The above organic layers were combined and separated successively into a crude copper chelate of each, diacetylbenzoylmethane, acetylacetone, acetyldibenzoylmethane, and benzoylacetone, according to our usual fractionation method,[12] which consists of fractional extraction (the step-by-step extraction of an acid with small, successive portions of alkali, followed by thin-layer chromatographic test of the acidified extracts) and subsequent treatment with a copper acetate solution. The remaining organic layer was steam-distilled *in vacuo* to remove the nitrobenzene. The residual solid was triturated with ether, and then an aluminum chelate of dibenzoylmethane was filtered off.[13] The ethereal filtrate was shaken with a copper acetate solution to give a copper chelate of dibenzoylmethane. This chelate is insoluble in ether after drying.

The copper chelates suspended in their ether solution, when consisting mainly of the copper chelates of the first three substances above, were freed from the chelate of acetylacetone by washing them with aqueous acetic acids (3%); then the ether was replaced with a small amount of benzene to crystallize a chelate of acetyldibenzoylmethane, which was collected by filtration. The solvent of the filtrate was replaced with a small amount of ether to crystallize the chelate of diacetylbenzoylmethane. The ethereal mother liquor gave a slight amount of the chelate of benzoylacetone on concentration. The above aqueous acetic acid washings and the copper acetate solution used for the chelate preparation were shaken with methylene chloride in order to obtain the chelate of acetylacetone.

Acetyldibenzoylmethane: Its copper chelate was shaken with ether and hydrochloric acid; the ether layer was then evaporated to leave colorless crystals; mp 106—107°C (ligroin).

Diacetylbenzoylmethane: Its copper chelate, slightly soluble in ether, was recrystallized from benzene to give cobalt-blue crystals (mp 246—248°C), which were decomposed as above to give an oil.

Tribenzoylmethane: This substance, present in both free and copper chelate forms, was present mainly in the crude copper chelates of benzoylacetone and of dibenzoylmethane. Each crude chelate (weighed) was decomposed as above to give a solid, which was dissolved in acetone–ethyl acetate; then, after 24 hr, the solvent was replaced with ether to give tribenzoylmethane in an ether-insoluble form (mp 235—237°C (acetone)). This tribenzoylmethane does not form its copper chelate directly.

Acetylacetone: Its copper chelate was decomposed to give a liquid. Its 2,4-dinitrophenylhydrazone has mp of 125—126°C (lit,[14] 122°C).

Benzoylacetone: The recrystallization of the copper chelate from methanol gave greenish-blue needles; mp 200—202°C (lit,[15] 195—196°C). This chelate was decomposed as above to give colorless needles; mp 60—61°C (petroleum ether).

Dibenzoylmethane: The decomposition of its copper or aluminum chelate gave light yellow needles; mp 80—81°C (methanol).

All the above substances were identified by the mixed-melting point method and/or by means of their similarity in thin-layer chromatographic behavior with authentic samples, except for impossible cases. Each yield other than that of tribenzoylmethane was calculated from the weight of the copper chelate.

c) p-*Nitrobenzoylated Product*: The reaction mixture quenched was shaken with a small amount of ether; then

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6) G. T. Morgan and R. W. Thomason, *J. Chem. Soc.*, **125**, 754 (1924).

7) A. Magnani and S. M. McElvain, "Organic Syntheses," Coll. Vol. III. p. 251 (1955).

8) W. J. Hickinbottom, "Reactions of Organic Compounds," Longmans, Green and Co. Inc., New York (1957), p. 292.

9) R. Adams and R. L. Jenkins, "Organic Syntheses," Coll. Vol. I. p. 394 (1956).

10) J. U. Nef, *Ann. Chem.*, **277**, 59 (1894).

11) L. Claisen, *ibid.*, **291**, 25 (1896).

12) K. Matsui, T. Nojiri, M. Motoi, and R. Takatsuka, *Yuki Gosei Kagaku Kyokai Shi*, **28**, 943 (1970).

13) H. Kaneyuki, This Bulletin, **35**, 523 (1962).

14) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "Systematic Identification of Organic Compounds," 4th ed. John Wiley & Sons, Inc., New York (1956), p. 316.

15) W. Wislicenus and W. Stoebner, *Ber.*, **35**, 539 (1902).

it was separated into two layers with a centrifuge. From the organic layer a solid was filtered off and then washed with ether. The solid was dissolved in tetrahydrofuran and acidified with hydrochloric acid to give di-*p*-nitrobenzoylmethane; mp 248°C (tetrahydrofuran). The combined organic solution was freed from *p*-nitrobenzoic acid with a sodium bicarbonate solution; then it was steam-distilled *in vacuo*. The pot residue was triturated with ether, and then di-*p*-nitrobenzoylmethane was filtered off. The ethereal filtrate, after it had been shaken with a copper acetate solution, was evaporated to dryness and triturated with methanol; then a copper chelate was filtered off. This, when decomposed, gave *p*-nitrobenzoylacetone; mp 115—116°C (methanol). (lit,[16] 112—113.5°C), (Found: N, 7.1%). The concentration of the methanolic filtrate gave a small amount of *p*-nitroacetophenone; mp 80—81°C (ethanol). These substances were identified by the mixed-melting-point method with authentic samples.[13]

d) Dichloroacetylmethane: The reaction mixture, quenched, was shaken with ether. After washing with water, the ether layer was shaken with a copper acetate solution; then it was filtered and washed with ether to give a crystalline copper chelate. The upper layer of the filtrate was washed with dilute acetic acid and subsequently concentrated to give the same chelate as above. Dilute sulfuric acid (10%) was added in portions to the mixture of the copper chelates and fresh ether with stirring until the ether layer became colorless. The ether layer was then dried over sodium sulfate, concentrated, and cooled to give colorless needles; mp 41.5—42.5°C (ether–petroleum ether), (lit,[17] solid at 0°C). Found: C, 35.84; H, 3.56; Cl, 41.66%; mol wt (benzene), 168. Calcd for $C_5H_6Cl_2O_2$: C, 35.50; H, 3.55; Cl, 41.95%; mol wt, 169.

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[16] H. Burgess, *J. Chem. Soc.*, **1927**, 2017.

[17] A. Stieglits and O. Horn, *Chem. Ber.*, **84**, 607 (1951).