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The Transacylation between β-Diketone and Ester in the Presence of Aluminum Chloride

Kiyotada MATSUI and Masatoshi MOTOI

Department of Industrial Chemistry, Faculty of Technology, Kanazawa University, Kodatsuno, Kanazawa

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The reaction of acetylacetone with an equivalent of phenyl benzoate in the presence of 2 equivalents of aluminum chloride in nitrobenzene afforded benzoylacetone (26% yield), dibenzoylmethane (4%), and phenyl acetate (37%), together with small amounts of phenolic ketones at 45°C. The total yield, based on the acyl groups introduced into the β-diketones, is similar to the yield of the ester newly formed. Such a similarity, suggestive of a transacylation, was also observed both on the use of *p*-nitrophenyl benzoate and on the treatment of benzoylacetone with phenyl benzoate or on that of dibenzoylmethane with *p*-nitrophenyl acetate. The non-formation of triacylmethanes is a strong evidence for the transacylation reaction, in which β-diketones and some esters exchange acyl groups directly. The analogous treatment of acetylacetone with α-naphthyl benzoate produced phenolic ketones, such as 2-acetyl- and 4-acetyl-1-naphthol, and the same benzoylated ketones as above in yields of 30 and 32% respectively. The considerably higher ratio of the 2-acetyl to the 4-acetyl isomer than that from the Fries rearrangement of α-naphthyl acetate indicates that another transacylation is accompanied by a rearrangement proceeding through complexes different from those in the Fries rearrangement.

In the course of studies[1] of the aluminum chloride-catalyzed acylation reaction of active methylene compounds with acid chlorides, the use of *p*-nitrophenyl benzoate, which is known to react only as an acylating agent for the Friedel-Crafts reaction,[2] was tried in the acylation of acetylacetone (I) in order to obtain insight into the mechanism of this acylation reaction. Thus, benzoylated ketones, such as benzoylacetone (II) and dibenzoylmethane (III), and *p*-nitrophenyl acetate were both obtained in about the same yields:

$$(CH_3CO)_2CH_2 + p\text{-}O_2NC_6H_4OOCC_6H_5 \longrightarrow CH_3CO\text{-}CH_2COC_6H_5 + (C_6H_5CO)_2CH_2 + p\text{-}O_2NC_6H_4OOCCH_3$$

This seems to imply that a transacylation between the reactants is involved in this unusual acylation reaction. The purpose of this paper is to report on such reactions between β-diketones and some esters.

The reaction of I with an equivalent of phenyl benzoate in the presence of an equivalent of aluminum chloride in nitrobenzene at 45°C for 3 hr gave II and phenyl acetate in low yields, as is shown in Table 1. The increase in the condensing agent to 2 equivalents afforded III in addition to the foregoing products, all in noticeably high yields, together with small amounts of phenolic ketones, such as *o*-hydroxy-, *p*-hydroxyacetophenone, and *p*-hydroxybenzophenone. The formation of III can be explained as being due to the benzoylation of the II formed, because the similar benzoylation of II gave III and phenyl acetate in about the same yields. The yields of the main prod-

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2) E. H. Man and C. R. Hauser, *J. Org. Chem.*, **17**, 397 (1952).

Table 1. Reactions of β-diketone with ester and of diacetylbenzoylmethane with phenol

Reactant: Substrate (10 mmol)	Reactant: Acylating agent mol ratio	Reaction time (hr)	Product (%): II	III	PhOAc	1-HO-2-Ac-C_6H_4	1-HO-4-Ac-C_6H_4	1-HO-4-Bz-C_6H_4	PhOBz
I	PhOBz 1[a)]	3	7	—	13				(81)
I	PhOBz 1	3	26	4	37	0.3	1.2	2.1	(55)
I	PhOBz 1[a')]	3	28	4	37	0.7	4.0	2.2	(57)
I	PhOBz 1	1	15	—	23	tr	tr	tr	(76)
I	PhOBz 1	20	40	15	57	2.7	11.7	5.8	(19)
I	PhOBz 1	3[c)]	32	7	47	1.0	4.2	2.3	(44)
I	PhOBz 2	3	31[d)]	5[d)]	47[d)]	0.7	0.6	1.2	(75)
II	PhOBz 1	3	(45)	30	33	0.4	1.2	1.5	(64)
I	PhOBz 1[b)]	3	9	tr	12	tr	tr	tr	(85)
I	PhOBz 1[b)]	20	19	1	29	0.4	0.7	0.6	(67)
$(Ac_2CH)_3Al$ (10/3 mmol)	PhOBz 3	3	3	—	4	tr	tr	tr	(93)
PhOH	Ac_2CHBz 1	3	57	—	64		2.4		[e)]
III	PhOAc 1	3	0	(97)	(79)	0.8	4.7	0	0
					p-NO_2-C_6H_4OAc				*p*-NO_2-C_6H_4OBz
I	*p*-NO_2-C_6H_4OBz 1[a)]	3	tr	0	0				(99)
I	*p*-NO_2-C_6H_4OBz 1	3	39	20	76				(5)
III	*p*-NO_2-C_6H_4OAc 1	3	14	(86)	(43)				14
					p-Me-C_6H_4OAc				*p*-Me-C_6H_4OBz
I	*p*-MeC_6H_4OBz 1	3	21	1	33		[f)]		(67)
					o-Me-C_6H_4OAc				*o*-Me-C_6H_4OBz
I	*o*-MeC_6H_4OBz 1	3	17	1	23		[f)]		(70)
			p-$NO_2C_6H_4CO$-CH_2Ac		PhOAc				$PhOCOC_6H_4$-NO_2-*p*
I	$PhOCOC_6H_4NO_2$-*p* 1	3	3	—	4				(98)

$AlCl_3$: mol ratio 2, a) 1, a') 3; solvent: $C_6H_5NO_2$ 7 ml, b) $(ClCH_2)_2$ 7 ml; reaction temp.: 45°C, c) 55°C; d) The yields based on I, the others based on phenylbenzoate; ( ): the yields of recovered materials; e) 8 and 30% yields of diacetylbenzoylmethane and of phenol respectively; f) Identification of the phenolic ketones could not be effected because of small amounts.

ucts were not increased adequately by the increase either in the condensing agent to 3 equivalents or in the acylating agent to 2 equivalents. The rise in the reaction temperature to 55°C led to some increase in yields, and the extension of the reaction time to 20 hr, giving relatively higher yields of the benzoylated ketones, resulted in an increase in the phenolic ketones at the expense of both phenyl acetate and recovered benzoate. The other products isolated were phenol, benzoic acid (both in 1—8% yields), and the unchanged I and phenyl benzoate; no triacylmethane was isolated, in contrast with the results of a similar acylation with acid chlorides.[1c)] However, there is one common feature—the acylation with either the ester or the *n*-butyryl chloride[1a)] requires 2 equivalents of aluminum chloride in order to obtain a satisfactory yield. Such a requirement for the condensing agent was also observed, more markedly, in the reaction of I with *p*-nitrophenyl benzoate. On the other hand, the similarity of the total yield based on the benzoyl groups introduced into the β-diketones (*e.g.*, the yield of III obtained from I, noted in Table 1, should be doubled) to the yield of phenyl acetate is suggestive of a transacylation during the reaction.

Table 2. Fries rearrangement of ester and reaction between phenol and acyl chloride at 45°C

Reactant (10 mmol)	Product (%): 1-HO-2-Ac-C_6H_4	1-HO-4-Ac-C_6H_4	1-HO-4-Bz-C_6H_4	PhOAc	PhOBz
PhOAc	7	9		(75)	
PhOH+AcCl	14	50		30	
PhOBz			4		(89)
PhOH+BzCl			22		72

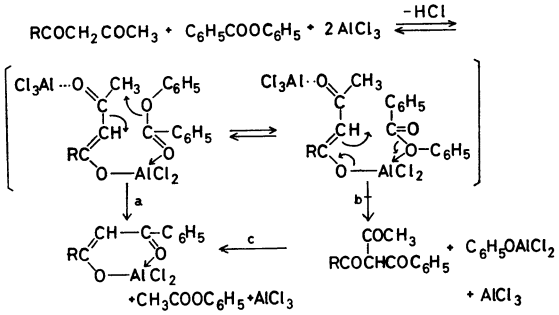
$AlCl_3$: 10 mmol; solvent: $C_6H_5NO_2$ 7 ml; reaction time: 3 hr; ( ): the yield of recovered material.

The esters present in the reacting mixture are subject to some extent to the rearrangement to yield phenolic ketones, but it is a question whether or not the formation of these products is due to acyl chlorides, which may be generated as intermediates because of the similarity of the conditions to those for the acylation with acyl chloride.[1c)] Therefore, the reaction of phenol

with acid chloride and the Fries rearrangement of the phenyl ester were carried out under conditions similar to those used for the present reaction. In consequence, in the reaction between I and phenyl benzoate, the slight yields of hydroxyacetophenones, contrasting with the moderate yield of the phenyl acetate, are due to the Fries rearrangement of the phenyl acetate formed, not to the reaction of phenol with acetyl chloride (Table 2). Similarly, as compared with the moderate yield of the benzoylated ketones or of the unaltered benzoic ester, the low yield of *p*-hydroxybenzophenone is ascribable to the Fries rearrangement of the phenyl benzoate used, not to the reaction of phenol with benzoyl chloride. Judging from these facts, not only the phenolic ketones, but also the acetic ester and β-ketones obtained, do not seem to be formed by the action of the acyl chlorides suspected of being intermediates.

With the benzoylation of aluminum trisacetylacetonate, the use of benzoyl chloride gave II, III, and tribenzoylmethane in considerably high yields, similar to those from the analogous benzoylation of I,[1c] whereas the use of phenyl benzoate gave only II in a 3% yield (Table 1). The use of *p*-nitrobenzoyl chloride for the acylation of I afforded di-*p*-nitrobenzoylmethane in a high yield, while a similar acylation with phenyl *p*-nitrobenzoate gave a less acylated product, *p*-nitrobenzoylacetone, in a low yield. The ester as acylating agent seems to follow a course differing substantially from that of acid chloride.

In the aluminum chloride-catalyzed reaction between synthesized diacetylbenzoylmethane and phenol (Scheme 1, Path c, R=CH_3), II and phenyl acetate were obtained in relatively high yields (Table 1), but the triacylmethane, which has not been isolated, was recovered and the phenol remained unchanged in a considerably higher yield than that from the present acylation reaction. This suggests that the triacylmethane capable of behaving as an acylating agent, if formed as an intermediate, can survive the reaction of I with phenyl benzoate. However, not even the isolation of stable tribenzoylmethane was accomplished. The above findings indicate that the present acylation, predominating over the Fries rearrangement, proceeds by transacylation between I (or II) and phenyl benzoate (Path a), without forming triacylmethane (Path b). The transacylation can be explained in terms of an intramolecular condensation of a complex which is generated by the ability of the carbonyl oxygen of the ester to coordinate with the metal atom of the dichloroaluminum β-diketonate complex proposed previously.[1a] The reaction mechanism is illustrated in Scheme 1.



R=CH_3 or C_6H_5

Scheme 1.

This mechanism is also supported by the idea that the acylation of I with an ester, giving higher yields of β-diketones in nitrobenzene than those in ethylene chloride, seems to proceed by some charge separation in the transition state.

The acylation of I with different benzoic esters showed that, except for ethyl benzoate which failed to react, the substituted phenyl benzoates gave decreasing yields of β-diketones in this order: *p*-nitrophenyl>phenyl>*p*-cresyl>*o*-cresyl benzoate. With acetic esters, phenyl acetate failed to react with III, whereas *p*-nitrophenyl acetate did react to give equimolar amounts of II and *p*-nitrophenyl benzoate.

Table 3. Reaction of acetylacetone with naphthyl benzoate, Fries rearrangement of naphthyl ester, and reaction of naphthol with acyl chloride at 45°C

Reactant (10 mmol)	Product (%)						
	II	III		1-HO-2-Ac-$C_{10}H_6$	1-HO-4-Ac-$C_{10}H_6$	1-HO-4-Bz-$C_{10}H_6$	α-$C_{10}H_7$-OBz
I+α-$C_{10}H_7OBz$[a]	26	3		21	9	21	(30)
α-$C_{10}H_7OAc$				50	41		
α-$C_{10}H_7OH$+AcCl				33	44		
α-$C_{10}H_7OBz$						46	
α-$C_{10}H_7OH$+BzCl						66	
			β-$C_{10}H_7$-OAc			2-HO-1-Bz-$C_{10}H_6$	β-$C_{10}H_7OBz$
I+β-$C_{10}H_7OBz$[a]	22	2	16			13	(47)
β-$C_{10}H_7OAc$			(79)				
β-$C_{10}H_7OH$+AcCl			90				
β-$C_{10}H_7OBz$						37	(55)
β-$C_{10}H_7OH$+BzCl						72	21

$AlCl_3$: mol ratio 1, a) .2; solvent: $C_6H_5NO_2$ 7 ml; reaction time: 3 hr; ( ): the yield of recovered material.

These facts indicate that the transacylation is facilitated by electron-attracting groups in the phenol portion of the ester and rendered somewhat difficult by electron-donating groups. With substituted benzoic esters other than that described above, phenyl *p*- and *o*-toluate also gave slight amounts of copper complexes from the β-diketone fraction separated from the reaction mixture; therefore, further studies were not undertaken.

α-Naphthyl benzoate and its β-isomer, when used, were subjected to the Fries rearrangement to form relatively large amounts of 4-benzoyl-1- and 1-benzoyl-2-naphthol respectively, giving both the foregoing β-diketones. Simultaneously, the latter ester gave β-naphthyl acetate, whereas the former gave 2-acetyl- and 4-acetyl-1-naphthol, instead of the acetic ester (Table 3). Here again, the two yields of the benzoylated ketones and of acetyl-1-naphthols are similar to each other. The Fries rearrangement of α-naphthyl acetate and the acylation of α-naphthol with acetyl chloride, when carried out under conditions comparable to those of the present reaction, gave isomeric mixtures of acetyl-1-naphthols in the 2-acetyl/4-acetyl ratios of 1.2 and 0.8 respectively. The higher isomer ratio of 2.3 obtained from the reaction of I with α-naphthyl benzoate suggests that, independently of the intermediate α-naphthyl acetate as well as of acetyl chloride, the acetyl-1-naphthols form by way of complexes different from those in the Fries rearrangement.[3] It can be deduced that an acetylium ion to be formed from a coordination complex as is illustrated in Scheme 1, concurrent with the closure of the chelate ring of the new β-diketonate, can uniquely complex with a leaving α-naphthoxide ion without becoming free; then it can migrate more easily to the 2 position in the nucleus to give the isomeric mixture.

Experimental

Materials. The following benzoic esters were prepared from the corresponding phenols and benzoyl chloride according to the Schotten-Baumann method: phenyl (mp 70—71°C (lit,[4] 70°C)), α-naphthyl (mp 57.5—58.5°C (lit,[5] 56°C)), β-naphthyl (mp 109—109.5°C (lit,[6] 106°C)), and *o*-cresyl benzoate (bp 301°C (lit,[7] 307—308°C/728 mmHg)). *p*-Nitrophenyl (mp 147.5—148.5°C (lit,[8] 142.5°C)), *p*-cresyl benzoate (mp 73°C (lit,[9] 71.5°C)), phenyl *p*-nitrobenzoate (mp 131—132°C (lit,[10] 129°C)), and *p*-nitrophenyl acetate (mp 77.5—78°C (lit,[11] 81—82°C)) were prepared from the corresponding phenols and acid chlorides. α-Naphthyl and β-naphthyl acetate were prepared from the corresponding naphthols and acetic anhydride in the presence of a catalytic amount of concentrated sulfuric acid, which melted at 45.5—46°C (lit,[12] 46°C) and 70—70.5°C (lit,[13] 70°C) respectively.

Reaction Method and Separation Procedure. Both were the same as in our previous paper[1c] except for the use of esters as acylating agents and the following points.

a) Product from the Reaction with Phenyl Benzoate: The reaction mixture, quenched, was shaken with cold hydrochloric acid and ether, and then separated into two layers. The upper layer was freed from benzoic acid with a sodium bicarbonate solution, dried over sodium sulfate, concentrated, and then distilled under reduced pressures (16—20 mmHg). At a later stage of the distillation, a small amount of nitrobenzene was supplied in order to remove the volatile substances completely. From the distillate phenol, phenyl acetate and *o*-hydroxyacetophenone (sometimes a slight amount of acetophenone also) were determined by glpc analysis on a column (0.3×200 cm) packed with polyethylene succinate (30%) on celite (hydrogen flow, 40 ml/min), using dimethyl azelate as the internal standard at 200°C. From the remaining distillate, acetyl- and benzoyl-acetone were obtained as their respective copper chelates according to our fractionation method.[1c,14] This method was also applied to the pot residue to obtain three extracts. The first extract, in ether, was shaken with a copper acetate solution; then the solvent was replaced with a small amount of ether–petroleum ether (1:2) to crystallize a copper chelate of benzoylacetone. The mother liquor was evaporated to leave a crude *p*-hydroxyacetophenone. The same treatment of the second extract gave the same chelate, along with a crude *p*-hydroxybenzophenone. The third extract and extracted residue were combined, evaporated, and then steam distilled *in vacuo* to remove the nitrobenzene. The trituration of the residue with ether gave an ether-insoluble aluminum chelate[1c] of dibenzoylmethane. The resulting ether solution was freed from dibenzoylmethane with a copper acetate solution; it was then evaporated to give phenyl benzoate, which was recrystallized from ethanol. The crude *p*-hydroxy-acetophenone and -benzophenone were treated individually with a dilute sodium hydroxide solution to remove slight amounts of the copper chelates; then they were purified according to the fractional extraction method described in a previous paper.[14] The former melts at 110—111°C, the latter, at 135—136°C. Both melting points were undepressed on admixture with authentic samples.

b) Product from the Reaction with p-*Nitrophenyl Benzoate*: The separation procedure was the same as above except for the following. From the pot residue, much of the *p*-nitrophenyl acetate was removed by crystallizing it from benzene–petroleum ether. The mother liquor was concentrated and then chromatographed on a column packed with silica gel. The eluents used, benzene–petroleum ether (1:1), the same (2:3), benzene, and benzene–ether (3:1), eluted successively dibenzoylmethane, *p*-nitrophenyl benzoate, a mixture, and *p*-nitrophenol respectively. The mixture (weighed) in ether was extracted with successive, small portions of a 0.1N sodium hydroxide solution to obtain benzoylacetone; then it was concentrated to crystallize *p*-nitrophenyl acetate; mp 78—79°C, undepressed on admixture with an authentic sample.

c) Product from the Reaction with o- *or* p-*Cresyl Benzoate*: The mixture distilled with nitrobenzene, after glpc analysis for determining cresyl acetates and cresols, was separated into acetyl- and benzoyl–acetone according to the fractionation method. The pot residue was treated with benzene–

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petroleum ether (1: 3) to crystallize *p*-cresyl benzoate. The mother liquor was concentrated and chromatographed using benzene–petroleum ether (1: 1) and benzene–ether (1: 1), which gave *p*-cresyl benzoate and benzoylacetone respectively. *o*-Cresyl benzoate, when used, was determined by a glpc analysis of the pot residue. From the remainder, benzoylacetone was separated by alkaline extraction.

d) Product from the Reaction with α-Naphthyl Benzoate: The pot residue was chromatographed similarly using benzene–petroleum ether (2: 3), the same (1: 1), and benzene–ether (1: 1), which gave three effluents successively. The evaporation of the first effluent gave α-naphthyl benzoate, which was then recrystallized from ether–petroleum ether; mp 58—59°C. The solvent of the second effluent was replaced with ether, freed from dibenzoylmethane as described above, and then extracted fractionally with the 0.1N sodium hydroxide solution to separate 2-acetyl-1-naphthol, which was then recrystallized from petroleum ether–ether; mp 100—101°C (lit,[15] 100—101°C). The concentration of the remaining ether solution gave α-naphthyl benzoate; mp 57—58°C. The third effluent was made up to about 100 ml by the addition of ether; then it was treated as above with the 0.1N sodium hydroxide solution to separate 4-acetyl-1-naphthol, which was subsequently recrystallized from benzene–ethanol; mp 204—206°C (lit,[15] 200—201°C). The solvent of the remaining solution was replaced with benzene to crystallize 4-benzoyl-1-naphthol; mp 165—166°C, (lit,[15] 163—164°C). The mother liquor was separated into 4-acetyl-, 4-benzoyl-1-naphthol, and benzoylacetone according to the fractional extraction method. The melting points of the three acylated naphthols were undepressed on admixture with authentic samples.

e) Product from the Reaction with β-Naphthyl Benzoate: The pot residue was chromatographed using as eluents benzene–petroleum ether (1: 1), the same (3: 1), benzene, and ether; this gave β-naphthyl benzoate, a mixture, β-naphthol, and benzoylacetone respectively. The ether solution of the mixture was freed from dibenzoylmethane as above and then evaporated to leave a solid. This solid in a small amount of benzene was chromatographed using benzene–petroleum ether (3: 2); this gave β-naphthyl acetate (mp 69.5—70°C (ether–petroleum ether)) and 1-benzoyl-2-naphthol (mp 144—145°C (benzene), (lit,[15] 140—141°C)). Both were undepressed on admixture with authentic samples.

f) Product from the Reaction with Phenyl p-*Nitrobenzoate*: The separation procedures were the same as in the case of *a*). The alkaline extract from the ether solution of the pot residue and the ether extract from the aqueous solution containing aluminum chloride both gave *p*-nitrobenzoylacetone. This was then recrystallized from methanol; it melts at 113—114°C, undepressed on admixture with an authentic sample.

g) Product from the Reaction between Diacetylbenzoylmethane and Phenol: The mixture distilled with nitrobenzene, the ethereal extract from the aqueous layer containing aluminum chloride, and the pot residue were separated individually by the usual fractionation method into copper chelates of diacetylbenzoylmethane and of benzoylacetone. However, the former chelate from the pot residue was contaminated with *p*-hydroxyacetophenone, which was isolated by alkaline extraction.

Acylation of Phenol with Acid Chlorides and the Fries Rearrangement of Esters. For the former reaction, phenol was dissolved in a solution of aluminum chloride in nitrobenzene; then acid chloride was added. For the Fries rearrangement, the ester was added to the nitrobenzene solution of aluminum chloride. Each product obtained was treated according to the appropriate separation procedure described above.

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