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Effects of Metal Chlorides on the Reaction of Acetylacetone with *n*-Butyryl Chloride[*1]

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Aluminum chloride-catalyzed acylation reactions of active methylene compounds such as diethyl malonate[1)] and ethyl acetoacetate[2)] with acid chlorides have been reported. These reactions are reversible and accompanied by deacetylation and/or decarbethoxylation reaction to give di- and triacylated methane derivatives. This prompted us to extend our studies to the acylation of acetylacetone (Ia) and also to search for any effective condensing agents other than aluminum chloride.

The reaction conditions for acylation of Ia with *n*-butyryl chloride and the yields of main products, *n*-butyrylacetone (IIa) and di-*n*-butyrylmethane (IIb), are summarized in Table 1.

The treatment of Ia in the presence of 0.5 equivalent of aluminum chloride in nitrobenzene at 45°C produced only IIa in about the same yield irrespective of the amount of acyl chloride used, while a similar treatment carried out with 1 equivalent of aluminum chloride gave IIa in a higher yield, together with IIb. Therefore, failure in the formation of IIb is ascribed to the insufficiency of the condensing agent. The formation of IIa will be explained by the mechanism proposed by Doolan and Gore[3)] for the Friedel-Crafts acetylation of

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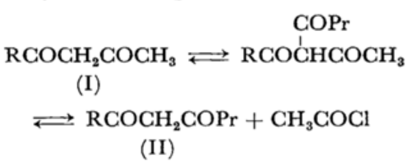
Table 1. Reaction of acetylacetone with *n*-butyryl chloride in the presence of metal chlorides

Reactant: $(CH_3CO)_2CH_2$ 1.5 g (0.015 mol)
C_3H_7COCl 3.2 g (0.03 mol) *1, **3 in mole ratio
Reaction temp.: 45°C, ***30°C
Solvent: Nitrobenzene 10 m*l*

Metal chloride	mole ratio	Reaction time, hr	Product and yield %				Neutral oil, g
			$PrCOCH_2$-$COCH_3$	$(PrCO)_2CH_2$	Total	Recovered $(CH_3CO)_2CH_2$	
$AlCl_3$	0	1	0	0	0	43	
	0.5*	1	21	0	21	48	a)
	0.5	1	22	0	22	34	a)
	1*	1	33	5	38	25	a)
	1	1	38	11	49	15	a)
	1	0.5	39	11	50	18	a)
	1	24	35	15	50	14	a)
	1	1***	38	11	49	17	a)
	2	1	40	19	59	18	a)
	2	1***	38	15	53	15	a)
	3	1	37	21	58	19	a)
	2**	1	45	25	70	15	a)
$TiCl_4$	1	1	31	13	44	26	a′)0.05b)
$SnCl_4$	1	1	21	7	28	9	a′)0.13c)
$ZnCl_2$	1	1	17	6	23	8	a′)0.21c)
$FeCl_3$	1	1	17	4	21	7	a′)0.38c)
$SbCl_5$	1	1	9	0	9	10	a′)0.29c)
$CuCl_2$	1	1	0	0	0	40	traceb)

a) Very small amounts of methyl propyl ketone and neutral oily substances.
a′) Very small amount of methyl propyl ketone.
b) Heterogeneous reaction.
c) Reacting mixture is heterogeneous at early stage.

aluminum trisacetylacetonate (III) of aromaticity or Ia (which is regarded as converting into III during the reaction) with aluminum chloride followed by decomposition of butyrylated III during separation process. However, the formation of IIb may be explained if IIa (or Ib) derived either by the butyrylation of Ia without ring-closure or by the ring-opening before or after butyrylation of III is further acylated during the course of the reaction.



$$\underset{\text{(I)}}{RCOCH_2COCH_3} \rightleftarrows RCO\overset{COPr}{\overset{|}{C}}HCOCH_3$$

$$\rightleftarrows \underset{\text{(II)}}{RCOCH_2COPr} + CH_3COCl$$

a: R=-CH_3; b: R=-C_3H_7=-Pr

In the presence of 1 equivalent of aluminum chloride the yields of IIa and IIb obtained by using 2 equivalents of *n*-butyryl chloride were hardly changed by the reaction periods, 0.5 and 1 hr, but the extended reaction period of 24 hr led to an increased yield of IIb at the expense of IIa. This means that the acylation reaction of Ia proceeds rapidly to reach an equilibrium in 0.5 hr, after which IIa is converted slowly into IIb. The fact that the yields afforded at 45°C are the same as those at 30°C is due to the insufficiency of eth condensing agent for the reaction at 45°C. This is also proved by the fact that the higher yields are provided by increasing only the condensing agent to 2 equivalents. The good yields, however, were lowered more or less both by the fall of reaction temperature and by the increase of the condensing agent to 3 equivalents, but increased by using 3 equivalents of *n*-butyryl chloride. These findings suggest that there is a suitable amount of aluminum

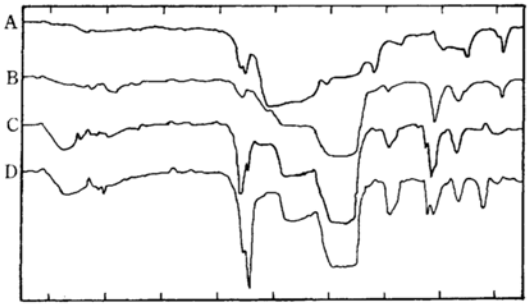
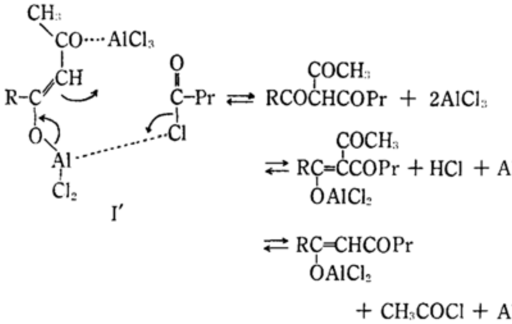


Fig. 1. Infrared spectrum of acetylacetone in nitrobenzene (A); with 0.3 (B); with 0.8 (C); and with 2 equivalents of $AlCl_3$ (D).

chloride for the acylation. Therefore, it can be expected that one half of the aluminum chloride enolizes one carbonyl group to form its enolate and the other half tends to coordinate with the other carbonyl group of the β-diketone. The infrared spectrum of Ia in the nitrobenzene solution of 2 equivalents of aluminum chloride shows strong carbonyl absorption peaks at 1710 and 1693 cm^{-1}, while such peaks are greatly reduced in intensity in the presence or absence of 0.3 equivalent of aluminum chloride in nitrobenzene (see Fig. 1). This is in substantial accord with expectations for the above experimental results. It follows then that it becomes difficult for the resulting species to close its chelate ring and it becomes susceptible to acylation with easy coordination of acyl chloride to the metal atom of enolate.

The above-mentioned fall of the yield caused by 3 equivalents of aluminum chloride suggests that the aluminum chloride competes with dichloroaluminum enolate for acyl chloride in order to coordinate, and that the reaction proceeds with liberation of aluminum chloride. The most predominant species, I′a and I′b, seem to react as follows:



a:R=$-CH_3$; b:R=$-C_3H_7$=-Pr

In order to compare the relative efficiencies of different metal chlorides several experiments were carried out using 1 equivalent of metal chloride, and the results in Table 1 were obtained. In nitrobenzene solution the order of decreasing efficiencies of metal chlorides on the basis of the yields is as follows:

$AlCl_3$, $TiCl_4 > SnCl_4 > ZnCl_2$, $FeCl_3 > SbCl_5 > CuCl_2$

Since this order differs from the one observed both for the Friedel-Crafts acetylation reaction of toluene[4] and for the addition of acid chloride to alkenes,[5] these reactions seem to be almost independent of the present acylation reaction.

Experimental

Materials. Acetylacetone[6] bp 136.5°C (lit bp 134—136°C), di-*n*-butyrylmethane[7] bp 82—84°C/11mmHg (lit[8] bp 101—102°C/20 mmHg), *n*-butyryl chloride,[9] bp 102°C, were prepared according to literature. *n*-Butyrylacetone was prepared from acetone and ethyl *n*-butyrate in yield of 20%, bp 55—56°C/11 mmHg (lit[6] bp 87—90°C/38 mmHg); copper chelate, mp 173—174°C (lit[10] mp 160—161°C), (Found: C, 52.80; H, 6.93%). Anhydrous aluminum chloride,[1] ferric chloride,[11] and cupric chloride[12] were prepared as described in a literature. Commercial anhydrous zinc chloride was used after fusion. The following commercial chemicals were distilled with exclusion of moisture: stannic chloride bp 113.5—113.8°C; titanium tetrachloride bp 135.5—136.5°C; antimony pentachloride bp 70.8—71.5°C/17 mmHg.

Acylation. As a typical example, to 10 m*l* of freshly distilled nitrobenzene in a 50-m*l* flask equipped with a calcium chloride tube was added the weighed amount of appropriate catalyst, and the mixture was cooled with ice water, then acetylacetone was added. After evolution of hydrogen chloride subsided the acid chloride was added to the resulting mixture with cooling, and then stirred vigorously with a magnetic stirrer.

Separation of the Product. The reaction mixture was put into crushed ice acidified with hydrochloric acid. After repeated extractions with ether, the aqueous layer was extracted again with ether next day, refluxed with ether for ten minutes, cooled, extracted with ether. The combined ether extract was washed with a saturated sodium bicarbonate solution, then extracted with 5% sodium hydroxide solution (four 15-m*l* portions) and with water. The combined sodium hydroxide and water extract, after acidification with hydrochloric acid, was extracted with ether repeatedly. The combined ether extract was dried over anhydrous sodium sulfate, then the solvent was removed by distillation through a column. The residue obtained was analyzed by gas-liquid chromatography. The organic layer containing nitrobenzene was steam distilled *in vacuo* to give neutral oily substance.

Gas-liquid Chromatographic Analysis. The analyses were carried out with gas-liquid chromatography on a Shimadzu GC-3AH, stainless steel column (0.3× 200 cm; high vacuum silicone grease (30%) on Celite; He carrier (50 m*l*/min)). The thermostat temperature was 130°C for analyses of methyl propyl ketone, acetyl-

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12) A. R. Pray, *ibid.*, Vol. V, ed. by T. Moeller, McGraw-Hill Book Co., Inc., New York (1957), p. 154.

acetone, and *n*-butyrylacetone, 155°C for di-*n*-butyrylmethane. The amounts of products were determined from the apparent peak area by using acetophenone as an internal standard.

Infrared Spectra. The infrared spectra were obtained with a Model DS-301 Spectrophotometer of Japan Spectroscopic Mfg. Co., Ltd. The spectra were obtained by compensation method with nitrobenzene. For preparation of specimen, 0.2 g of acetylacetone was dissolved in 10 m*l* of anhydrous nitrobenzene containing a given quantity of aluminum chloride (0.08, 0.21, 0.54 g), then allowed to stand for 0.5 hr at 45°C. The spectrum characteristic of nitrobenzene containing aluminum chloride (0.54 g in 10 m*l*) exhibits the broad band in the 1367—1315 cm^{-1} region and the sharp band at 852 cm^{-1}.

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