

[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

Ketones from Acyl Chlorides and Alkyl Aluminum Chlorides: A Selective Keto-ester Synthesis

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Convenient laboratory procedures are described for the preparation of methyl and ethyl aluminum dichlorides. Attempts to prepare propyl and butyl aluminum chlorides were unsuccessful. Methyl and ethyl aluminum dichlorides gave 65–90% yields of ketones by reaction with simple acid chlorides. A dibasic acid chloride, adipyl chloride, gave a 35% yield of 2,7-octanedione with methyl aluminum dichloride. The reactions of methyl and ethyl aluminum dichlorides with δ -carbomethoxyvaleryl and ω -carbomethoxypelargonyl chloride gave 92–95% yields of quite pure keto esters, while the reaction of methyl aluminum dichloride with β -carbomethoxypropionyl chloride gave a 36% yield of ethyl levulinate. The reaction of methyl aluminum dichloride with *p*-cyanobenzoyl chloride in benzene resulted in acylation of the benzene. These reactions represent convenient methods of preparation of methyl and ethyl ketones or keto esters from the corresponding acid chlorides, and are an improvement over reactions using diethyl and dimethyl cadmium.

This paper reports experiments with certain alkyl aluminum dichlorides with the view of developing selective syntheses of ketones and keto-esters with a variety of acyl chlorides.

The preparation, properties and analyses of alkyl aluminum halides have been described by Grosse and Mavity.³ These compounds are prepared by the action of alkyl halides on metallic aluminum. The product of the reaction is an alkyl aluminum sesquihalide ($R_3AlX \cdot RAlX_2$), which may be converted to the dihalide ($RAlX_2$) by treatment with the appropriate aluminum trihalide. These workers reported the preparation of methyl and ethyl aluminum sesquichlorides by the direct reaction of aluminum with methyl or ethyl chloride under pressure in a stirred autoclave, using a trace of aluminum chloride as a catalyst. Induction periods which sometimes amounted to several days were reported for this reaction.

When first tried in this Laboratory, methyl chloride could not be made to react with any available form of aluminum, and it was found that a fresh unoxidized surface was required for reaction in a reasonable time. The most satisfactory way found for preparing active aluminum was to make turnings under an inert atmosphere. It is sufficient merely to keep the area of cutting blanketed by a rapid stream of nitrogen, and then store the turnings under nitrogen. Aluminum prepared in this way was found to react very readily; for example: under a methyl chloride pressure of three atmospheres, the reaction started at 25° and was going rapidly in less than 30 minutes. Previous use of high pressure has been found unnecessary with active aluminum, and the use of lower pressures has permitted simplification of the equipment. The reaction with methyl chloride can be carried out at two to three atmospheres in a Pyrex pressure bottle of the type used in centrifuges, while the reaction with gaseous ethyl chloride can be carried out at atmospheric pressure in an ordinary flask.

Attempts were made to prepare the higher alkyl aluminum halides by reaction of *n*-propyl and butyl halides with aluminum, and by alkyl interchange of propyl and butyl halides with ethyl and methyl aluminum chlorides. These attempts were successful only in the case of the reaction of *n*-butyl

iodide and aluminum. From this reaction a 56% yield of butyl aluminum sesquiodide and a 15% yield of *n*-octane were obtained.

Reactions of Alkyl Aluminum Halides.—The reactions of alkyl aluminum halides with several acyl chlorides were investigated. The results are summarized in Table I. Apperson⁴ has reported the preparation of ketones by the reaction of benzoyl and acetyl chlorides with alkyl aluminum halides.

In the present work the acid chlorides of benzoic, butyric and 9-phenanthroic acids were found to give ketones in good yields when treated with a slight excess of methyl or ethyl aluminum dichloride. These reactions were usually carried out in benzene solution at slightly above room temperature. The initial product of these reactions was an addition complex, which on hydrolysis yielded the pure ketone.

The reaction of methyl aluminum dichloride with adipyl chloride gave the expected 2,7-octanedione, but in rather impure form, and in low yield (35%). A large amount of higher boiling material, probably resulting from further reaction of this ketone, was also obtained. Inasmuch as ethyl butyrate and ethyl benzoate were recovered unchanged after treatment with methyl aluminum dichloride, the synthesis of keto-esters from ester acid chlorides was studied. The use of ethyl and methyl aluminum dichlorides with δ -carbomethoxyvaleryl and ω -carbomethoxypelargonyl chlorides produced almost quantitative yields of quite pure keto esters. However, β -carbomethoxypropionyl chloride, when treated with methyl aluminum dichloride, gave a 24% yield of methyl levulinate, and β -carbomethoxypropionyl chloride gave a 36% yield of ethyl levulinate along with a 38% yield of ethyl β -benzoylpropionate, which resulted from acylation of the benzene solvent.

When *p*-cyanobenzoyl chloride was allowed to react with methyl aluminum dichloride in benzene solution, the only reaction occurring was acylation of the solvent with no evidence of cyanoacetophenone formation.

It is of interest to compare the results obtained with ethyl and methyl aluminum dichlorides to those with dimethylcadmium. Methyl aluminum dichloride gave 10–20% higher yields of purer products with ω -carbomethoxypelargonyl chloride and δ -carbomethoxyvaleryl chloride than those which have

(1) Deceased August 10, 1949.

(2) Standard Oil Company of Indiana Fellow, 1948; with Standard Oil Company of Indiana, Whiting, Indiana.

(3) A. V. Grosse and J. M. Mavity, *J. Org. Chem.*, **5**, 106 (1940).(4) L. D. Apperson, *Iowa State College J. Sci.*, **16**, 7 (1941).

TABLE I
 REACTIONS OF ALKYL ALUMINUM HALIDES

R Al halide	RCOCl, R is	Product	Yield, ^a %	B.p., °C.	Mm.	n _D ²⁰
CH ₃ AlCl ₂	C ₆ H ₅ -	C ₆ H ₅ COCH ₃ ^b	81	88-90	17	1.5323
C ₂ H ₅ AlCl ₂	C ₆ H ₅ -	C ₆ H ₅ COC ₂ H ₅ ^c	89	139-142	79	1.5253
CH ₃ AlCl ₂	n-C ₃ H ₇ -	n-C ₃ H ₇ COCH ₃ ^d	70	99-101	740
(CH ₃) ₂ AlCl	n-C ₃ H ₇ -	n-C ₃ H ₇ COCH ₃ ^d	65	99-101	740
CH ₃ AlCl ₂	C ₁₄ H ₉ - ^e	C ₁₄ H ₉ -COCH ₃ ^{f,g}	78	187	1
C ₂ H ₅ AlCl ₂	C ₁₄ H ₉ - ^e	C ₁₄ H ₉ -COC ₂ H ₅ ^{e,h}	86	185	1
CH ₃ AlCl ₂	-(CH ₂) ₄ -	CH ₃ CO(CH ₂) ₄ COCH ₃ ⁱ	35	115	13
CH ₃ AlCl ₂	-(CH ₂) ₅ CO ₂ C ₂ H ₅	CH ₃ CO(CH ₂) ₅ CO ₂ C ₂ H ₅ ^j	93	118-123	2	1.4398
C ₂ H ₅ AlCl ₂	-(CH ₂) ₅ CO ₂ C ₂ H ₅	C ₂ H ₅ CO(CH ₂) ₅ CO ₂ C ₂ H ₅ ^k	94	133-136	2	1.4411
CH ₃ AlCl ₂	-(CH ₂) ₂ CO ₂ C ₂ H ₅	CH ₃ CO(CH ₂) ₂ CO ₂ C ₂ H ₅ ^{l,m}	36	103-104	25	1.4214
		C ₆ H ₅ CO(CH ₂) ₂ CO ₂ C ₂ H ₅ ⁿ	38	125-127	2	1.5189
CH ₃ AlCl ₂	-(CH ₂) ₂ CO ₂ CH ₃	CH ₃ CO(CH ₂) ₂ CO ₂ CH ₃ ^o	24	80.5-81	12
CH ₃ AlCl ₂	-(CH ₂) ₄ CO ₂ C ₂ H ₅	CH ₃ CO(CH ₂) ₄ CO ₂ C ₂ H ₅ ^{p,q}	92-95	73	1	1.4304
CH ₃ AlCl ₂ (aq.)	-(CH ₂) ₄ CO ₂ C ₂ H ₅	CH ₃ CO(CH ₂) ₄ CO ₂ C ₂ H ₅	90	73	1	1.4308
C ₂ H ₅ AlCl ₂	-(CH ₂) ₄ CO ₂ C ₂ H ₅	C ₂ H ₅ CO(CH ₂) ₄ CO ₂ C ₂ H ₅ ^r	94	88-93	2	1.4329

^a Based on acid chloride. ^b Semicarbazone, m.p. 200-201°. ^c Semicarbazone, m.p. 177.5-178.5. ^d Semicarbazone, m.p. 109.5-110.5. ^e M.p. 72.2-73.2° cor. (Dornfeld, Callen and Coleman, *Org. Synth.*, **28**, 19 and 34). ^f C₁₄H₉ is 9-phenanthryl. ^g Oxime, m.p. 152.5-153.5° (recrystallized from ethanol) (Miller and Bachman, *THIS JOURNAL*, **57**, 766 (1935)). ^h M.p. 53.6-54.7° cor.; yield and m.p. after two recrystallizations from ethanol. Picrate after one recrystallization from ethanol, m.p. 104.5-105.5° (Bachmann and Struve, *ibid.*, **58**, 1659 (1936)). ⁱ M.p. 41-42.5° after recrystallization from petroleum ether and water; dioxime, m.p. 148-151° (Blaise and Koehler, *Bull. soc. chim.*, [4] **5**, 681 (1909)). ^j Sapn. equiv. calcd., 228; found, 228. Semicarbazone, m.p. 112.5-113.6° cor., isolated in 93.2% yield after one recrystallization from benzene (Cason and Prout, *THIS JOURNAL*, **66**, 46 (1944)). ^k Sapn. equiv. calcd., 240; found, 243. Semicarbazone of the free acid, m.p. 164.5-166° after recrystallization from ethanol (Paraskova, *Compt. rend.*, **198**, 1701 (1934)). ^l Sapn. equiv. calcd., 144; found, 141 (v. Grote, Kehrer and Tollens, *Ann.*, **206**, 221 (1880)). ^m 2,4-Dinitrophenylhydrazone, m.p. 100.5-101.5° (Cowley and Schuette, *THIS JOURNAL*, **55**, 3463 (1933)). ⁿ Sapn. equiv. calcd., 206; found, 204. Free acid, m.p. 116-118°. ^o Sapn. equiv. calcd., 130; found, 121 (R. Fittig, *Ann.*, **299**, 1 (1898), oxime of acid, m.p. 129.5-131.0° (W. Dollfus, *Ber.*, **25**, 1932 (1892)). ^p Sapn. equiv. calcd., 172; found, 175. Semicarbazone, m.p. 107-108°, isolated in 93.3% yield (Blaise and Koehler, *Bull. soc. chim.*, [4] **7**, 222 (1910)). ^q Lease and McElvain, *THIS JOURNAL*, **55**, 806 (1933)). ^r Sapn. equiv. calcd., 186; found, 186. Semicarbazone, m.p. 88-88.6° after one recrystallization from ethanol (see ref. in note *n*).

been reported with dimethylcadmium.^{5,6} With benzoyl chloride,⁷ about the same yields are obtained with each of these reagents. However, dibutylcadmium gave higher yields of the corresponding keto ester with β -carbomethoxypropionyl chloride⁸ than did methyl aluminum dichloride.

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Experimental

Acyl Chlorides.—Butyryl chloride (b.p. 99-101° (740 mm.)) was prepared from butyric acid.⁹ Benzoyl chloride was Mallinckrodt analytical reagent. A 453-g. sample of adipic acid was treated with 980 g. of thionyl chloride on a steam-bath for five hours. After discarding the first 20 ml. of distillate, 528 g. (93%) of adipyl chloride, b.p. 110° (5 mm.) was obtained.

ω -Carbomethoxypropionyl chloride, β -carbomethoxypropionyl chloride and δ -carbomethoxyvaleryl chloride were prepared from the acid esters,^{10,11,12} and β -carbomethoxypropionyl chloride was prepared by a similar procedure with special attention being given to the purification of the acid ester.

***p*-Cyanobenzoyl Chloride.**—*p*-Cyanobenzoic acid was prepared from *p*-toluonitrile by oxidation with chromium trioxide in a mixture of acetic and sulfuric acids.¹³ The recrystallized product, m.p. 218.5-219.3° (cor.),¹⁴ was

(5) J. Cason, *THIS JOURNAL*, **68**, 2078 (1928).

(6) J. Cason and F. S. Prout, *ibid.*, **66**, 46 (1944).

(7) H. Gilman and J. F. Nelson, *Rec. trav. chim.*, **55**, 518 (1936).

(8) E. Clotofski and W. Junge, *Ber.*, **74B**, 299 (1941).

(9) *Org. Syn.*, Coll. Vol. I, p. 147.

(10) "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., p. 276.

(11) *Org. Syntheses*, **26**, 21 (1945).

(12) *Ibid.*, **25**, 19 (1945).

(13) B. F. Aycock, *et al.*, *THIS JOURNAL*, in press.

(14) E. P. Valby and H. J. Lucas, *ibid.*, **81**, 2718 (1929).

treated with seven molar equivalents of thionyl chloride at reflux temperature for four hours. Excess thionyl chloride was then stripped off to a final temperature of 100° (1 mm.). The resulting *p*-cyanobenzoyl chloride,¹⁵ m.p. 68-70.5°, was used as a benzene solution.

9-Phenanthroyl chloride was prepared from 9-phenanthryl bromide.^{16,17,18}

Alkyl Aluminum Halides. Methyl Aluminum Sesquichloride and Methyl Aluminum Dichloride.—The reaction of methyl chloride with aluminum was carried out in equipment which consisted of a heavy Pyrex pressure bottle attached by means of a stopper and clamp to a steel pressure line leading to a methyl chloride cylinder. The line was fitted with a needle valve, a vent valve, and a closed U tube manometer type of pressure gage. In a 1 l. pressure bottle were placed 155 g. of aluminum turnings prepared under nitrogen, and 1 g. of aluminum chloride. Aluminum used in these reactions was ALCOA aluminum alloy 108 which contains 4% each of copper and silicon. The reaction bottle was then evacuated and the system closed. Following this, methyl chloride (Ansul) at a pressure of 2.5-3 atmospheres was admitted to the bottle from a cylinder held at 0°. Reaction did not start immediately so the bottle was heated with steam for a few minutes. When the reaction began, steam was removed and cooling was provided in the form of two air jets. The reaction was moderated by controlling the rate of methyl chloride addition with a needle valve. After five hours, when the remaining aluminum was submerged in sesquihalide, the bottle was shaken occasionally in order to hasten completion of the reaction. After seven hours, when reaction was substantially complete, the methyl chloride pressure was released and the bottle was detached from its stopper and clamp, which were replaced with a two-hole stopper carrying a decantation tube and nitrogen inlet. The clear amber methyl aluminum sesquichloride (349 g.) was then decanted under nitrogen pressure into a distillation flask, leaving behind a finely divided black sediment of

(15) J. N. Ashley, H. J. Barber, A. J. Ewins, G. Newbery and A. D. H. Self, *J. Chem. Soc.*, 103 (1942).

(16) *Org. Syn.*, **28**, 19, 34 (1948).

(17) W. E. Bachmann, *THIS JOURNAL*, **56**, 1367 (1934).

(18) E. Mosettig and J. Van de Kamp, *ibid.*, **56**, 2995 (1933).

copper and silicon. (When it was desired to use sesquichloride directly for reactions, this product would be decanted into benzene to make a 20-40% solution.) The decanted sesquichloride was treated with 256 g. of anhydrous aluminum chloride at 100° with swirling until the solution became homogeneous. The product was then allowed to cool to 80° and was diluted with benzene to give a 37% solution of methyl aluminum dichloride.

Ethyl Aluminum Dichloride.—A 250-ml. four-necked flask was provided with a Hershberg stirrer, nitrogen and ethyl chloride inlets, and a condenser having a balloon trap at the exit. In this flask were placed 39.7 g. of aluminum turnings prepared under nitrogen and 0.7 ml. of methyl aluminum sesquiodide catalyst. The flask was heated to 70° with stirring and ethyl chloride (Gebauer) was added slowly from a cylinder at a rate sufficient to maintain a pressure slightly in excess of atmospheric. The reaction was completed in 16 hours. At the end of this time 148.8 g. of ethyl aluminum sesquichloride was decanted and combined with 157.3 g. of the same material produced in another run. The combined products were treated with 165 g. of aluminum chloride at 150° until the mixture became a clear solution. The product, ethyl aluminum dichloride, was diluted to a 51.3% solution with benzene.

Butyl Aluminum Sesquiodide.—Using the same equipment as in the preparation of ethyl aluminum dichloride, 33.1 g. of aluminum turnings prepared under nitrogen was placed in the reaction flask which was then swept with nitrogen. Following this, 0.5 ml. of methyl aluminum sesquiodide catalyst was added. The reaction mixture was then heated at 75° with stirring while 221 g. (1.2 moles) of *n*-butyl iodide was run in from a separatory funnel over a two-hour period. The mixture was then stirred at 75° for an additional seven hours and allowed to stand at room temperature for three days. At the end of this time the product was heated in a vacuum distillation apparatus. No butyl iodide was recovered, but 10.6 g. of *n*-octane was collected, n_D^{20} 1.3990, b.p. 122-125°. Benzene was added to the residue in the distillation flask and an aliquot of the resulting solution was treated with alcohol; the butane collected indicated a total of 0.677 mole of available butyl to be present in the benzene solution.

Most alkyl aluminum halides are spontaneously inflammable and react violently with water. These properties require that they be handled under an atmosphere of dry nitrogen at all times, and in such a manner as to avoid the possibility of accidental contact with moisture. Reactions should be carried out in a hood, and pressure reactions should be run behind a shield.

Once prepared, alkyl aluminum halides are best handled in solution, as this decreases the danger of fire and makes handling considerably easier. Benzene appears to be the most useful reaction medium as it has a high solvent power for alkyl aluminum halides, acid chlorides, and the addition complexes formed from these compounds. Solutions of alkyl aluminum halides are most conveniently transferred by displacing them through tubing with nitrogen pressure or by injection with a syringe.

General Reaction of Ester Acid Chlorides with Alkyl Aluminum Chlorides.—To a mixture of 0.5 mole of the ester acid chloride in 1-4 times its volume of benzene was slowly added 1.1 mole of methyl aluminum dichloride as a 35% solution in benzene. The addition was carried out under nitrogen at 10-15° with stirring, after which the solution was allowed to stand at room temperature for two hours. The reaction mixture was then run slowly from the bottom of the reaction flask into 500 g. of ice or water held below

30° with stirring under nitrogen. The product was isolated from the resultant mixture by distilling the benzene layer.

When a simple acyl chloride is treated, only 0.6 mole of methyl aluminum dichloride is required. Inasmuch as the ester group forms a complex with methyl aluminum chlorides, it is necessary to use an additional equivalent of the organo-metallic to effect the desired reaction with a carbalkoxy acyl chloride (see Table II.) Table II shows the results of a series of runs in which the ratio of methyl aluminum sesquichloride or methyl aluminum dichloride to δ -carbethoxyvaleryl chloride was varied. Since a mole of sesquichloride contains one mole of dimethyl aluminum chloride and one mole of methyl aluminum dichloride, the reactant ratios are indicated as total available moles of methyl aluminum compound.

TABLE II
REACTIONS OF METHYL ALUMINUM SESQUICHLORIDE AND METHYL ALUMINUM DICHLORIDE WITH δ -CARBETHOXY-VALERYL CHLORIDE

	Moles of methyl aluminum compound per mole of δ -carbethoxy-valeryl chloride	Yield of ethyl ϵ -ketoenanthate, %
Sesquichloride	0.82	11
	1.5	52
	1.7	57
	2.3	90
Dichloride	1.2	23
	2.2	95

It is necessary that the methyl aluminum chloride be added to the acid chloride in order to prevent decomposition and darkening which occur with some compounds when there is a large excess of methyl aluminum chloride. It is also necessary to keep reaction temperatures at 10-15° for ester acid chlorides in order to prevent decomposition with the evolution of gas. The reactions with simple acid chlorides were run at higher temperatures (40-80°). Hydrolysis of these reaction mixtures must be carried out by adding the mixture to water. The reverse procedure results in vigorous decomposition, and formation of tars.

***p*-Cyanobenzoyl Chloride and Methyl Aluminum Dichloride.**—To a solution of 12.2 g. (0.0736 mole) of *p*-cyanobenzoyl chloride in 150 ml. of benzene was added 27.1 g. (0.24 mole) of methyl aluminum dichloride as a 39% solution in benzene. The addition was carried out with stirring at 45° over a 12-minute period, after which the solution was allowed to stand at 50° for 30 minutes. Hydrolysis was then carried out below 35°. The benzene layer was distilled to give 2.45 g. of product boiling below 210° (15 mm.) and 11.9 g. of residue (*p*-cyanobenzophenone, 78% yield). The identity of the distillate was not determined. The residue was recrystallized twice from a benzene-petroleum ether mixture and once from 60% ethanol, to give 9.3 g. of *p*-cyanobenzophenone, m.p. 113.5-114.5°. It gave an oxime, m.p. 171.5-174.5°, and was hydrolyzed to *p*-benzoylbenzoic acid m.p. 198.7-200.2°. The use of milder reaction conditions lowered the yields of *p*-cyanobenzophenone, but did not produce any *p*-cyanoacetophenone.

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