

Condensation of Carboxylic Acids

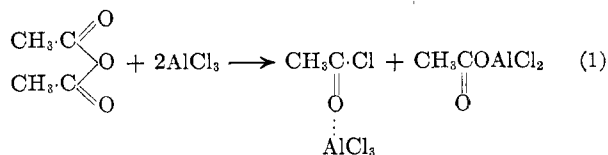
P. H. GROGGINS, R. H. NAGEL, AND A. J. STIRTON

THIS investigation deals with the preparation of alkyl aryl and diaryl ketones by condensing monocarboxylic acids—for example, acetic, propionic, and benzoic acids—according to the Friedel and Crafts reaction. Mono- and dicarboxylic acids have been previously condensed with aromatic compounds containing a hydroxyl group. Nencki and his co-workers (7), as well as other investigators, have prepared acyl resorcinols by condensing fatty acids with resorcinol in the presence of small quantities of zinc chloride. A number of investigators (3, 4, 5, 8) have condensed *o*-phthalic acids with aromatic compounds, and more recently Adams and Noller (1) have recognized that there might be a side reaction involving carboxylic acids when the aliphatic acid anhydrides were condensed.

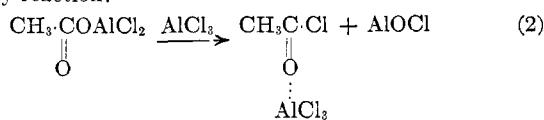
The condensation of aliphatic or aromatic monocarboxylic acids with aromatic hydrocarbons or their halogen derivatives for the preparation of alkyl aryl and diaryl ketones constitutes a new field of research.¹ A preliminary study of such condensations, as well as the probable mechanism of the reaction is reported here.

In the preceding paper (page 1313) it was shown that, in the condensation of acetic anhydride with toluene according to the Friedel and Crafts reaction, yields in excess of 100 per cent were obtained, when calculated on the basis of only one of the acetyl groups being available for reaction. These high yields were attributed to secondary reactions (Equations 2 and 3) involving the aluminum chloride salt of acetic acid, thus:

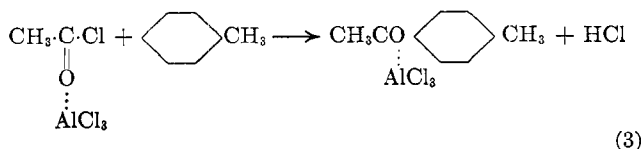
Primary reaction (2):



Secondary reaction:



In the presence of toluene, for example, the acid chloride addition complex reacts to form the alkaryl alkyl ketone:

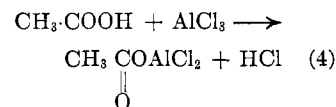


A method is presented for the preparation of alkyl aryl and diaryl ketones using carboxylic acids instead of the more expensive anhydrides or acid chlorides. The resultant yields compare favorably with those previously obtained by condensing either acid chlorides or acid anhydrides when the latter is considered as having two acyl groups available for reaction, but the products are not quite as pure.

Evidence is obtained for the hypothesis that in the condensation of carboxylic acids the synthesis proceeds through the intermediate formation of an acid chloride derivative.

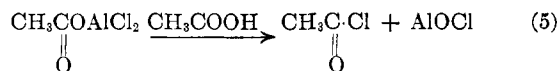
The research on which this preliminary report is based indicates that the reaction involving the employment of carboxylic acids is of wide application and may effect substantial economies in the manufacture of some alkyl aryl ketones.

Evidence in support of the hypothesis that the aluminum chloride salt of acetic and homologous acids could react according to this mechanism was obtained by the following procedure: When molar proportions of acetic acid and anhydrous aluminum chloride were warmed to 40° to 60° C., the principal reaction appeared to be the formation of the aluminum chloride salt of acetic acid:



The subsequent behavior of this salt was governed by the following considerations: If the reaction was carried out in the

presence of an excess of acetic acid, the reaction according to Equation 5 took place and acetyl chloride was distilled off:



When 0.5 mole (30 grams) of acetic acid and 0.2 mole (26 grams) of aluminum chloride were caused to react, the conversion of acetic acid to acetyl chloride was approximately 20 per cent of theory. In the presence of more than a molar equivalent of aluminum chloride, practically no acetyl chloride distilled over, presumably because it was fixed as the nonvolatile, conducting aluminum chloride complex (Equation 2). In the presence of toluene and 2.5 moles of aluminum chloride, acetic acid reacts substantially according to Equations 4, 2, and 3 to produce 4-methylacetophenone with yields of approximately 80 per cent of theory (Table II).

The procedure employed in this investigation has been described in the preceding paper. Here, also, the influence of halogen carriers and halogen compounds was ascertained.

TABLE I. PREPARATION OF ACETOPHENONE FROM ACETIC ACID AND BENZENE

(Benzene, 5 moles = 390 grams; glacial acetic acid,^a 1 mole = 60 grams; temperature, 86° C.; theoretical yield, 120 grams)

EXPT. No.	ADDED SUBSTANCE Compound	GRAMS	ANHYDROUS AlCl ₃ Moles	TIME Hours	YIELD		M. P. ° C.
					Grams	% of theory	
1	Control	0	3	5.5	77	64.1	15.6
2	KClO ₃	10	3	5.5	70	58.3	14.0
3	Fe powder	5	3	5.5	79	65.7	15.4
4	SOCl ₂	5	3	5.5	90	75.0	15.2
5	SOCl ₂	10	3	5.5	82	67.7	15.2
6	{ Al powder } { SOCl ₂ } 2 } 10 }		3	5.5	84	69.5	16.0
7	PCl ₃	5	3	5.5	94	78.0	15.8
8	Control	0	2.5	10	80.5	67.0	16.0

^a The acetic acid used in these and subsequent experiments boiled over a range of 114° to 116° C. as compared with 118.1° for pure material.

^b Melting point of acetophenone = 19.6° C.

In the preparation of acetophenone from technical glacial acetic acid and benzene, the data shown in Table I were obtained. The results indicate that the incorporation of small proportions of thionyl chloride and phosphorous trichloride,

¹ Groggins and Nagel, U. S. Patent 1,966,797 (1934), assigned to the Secretary of Agriculture, from whom license to use may be obtained.

which are known to be useful agents for the conversion of carboxylic acids to the corresponding acid chlorides, is beneficial.

Table II gives the data obtained in the preparation of 4-methylacetophenone from acetic acid and toluene. The results confirm previous observations that halogen carriers possess no marked advantage when toluene is condensed to form alkaryl alkyl ketones and indicate that a molar ratio of approximately 2.5 parts of anhydrous aluminum chloride to carboxylic acid gives the best results.

TABLE II. PREPARATION OF 4-METHYLACETOPHENONE^a FROM ACETIC ACID AND TOLUENE

(Toluene, 5 moles = 460 grams; glacial acetic acid, 1 mole = 60 grams; temperature, 108° C.; time, 7 hours; theoretical yield, 134 grams)

EXPT. No.	ADDED SUBSTANCE		ANHYDROUS AlCl ₃		YIELD ^b	
	Compound	Grams	Moles	Grams	% of theory	
1	Control	0	2.0	82	61.2	
2	Al powder	2	2.0	90	67.2	
3	Fe powder	5	2.0	89	66.4	
4	Control	0	2.5	107	80.0	
5	Al powder	2	2.5	105.5	78.7	
6	SOCl ₂	5	2.5	96	71.7	
7	{ Al powder SOCl ₂ }	{ 2 5 }	2.5	98	73.1	
8	Fe powder	5	2.5	114	85.1	
9	Al powder	2	3.0	91	67.9	
10	Fe powder	5	3.0	98	73.1	

^a Melting point of 4-methylacetophenone = -23° C.

^b This product, unlike that derived from acetic anhydride, showed no definite freezing point when cooled by solid carbon dioxide, but on purification the boiling point, index of refraction, and melting point of the semi-carbazone were identical with those of 4-methylacetophenone.

The data in Table III show that aryl ketones, such as 4-chlorobenzophenone, can also be made by this process. Here benzoic acid was employed instead of the customary anhydride or acid chloride, the control yield being about 73 per cent of theory. The addition of aluminum powder or thionyl chloride did not appreciably affect the results.

TABLE III. PREPARATION OF 4-CHLOROBENZOPHENONE FROM BENZOIC ACID AND CHLOROBENZENE

(Chlorobenzene, 5 moles = 562 grams; benzoic acid, 1 mole = 122 grams; anhydrous aluminum chloride, 3 moles = 400 grams; temperature, 108° C.; time, 6 hours; theoretical yield, 216.5 grams)

EXPT. No.	ADDED SUBSTANCE		YIELD		M. P. ^a ° C.
	Compound	Grams	Grams	% of theory	
1	Control	0	160	73.8	60.5 ^b
2	Al powder	2	157	72.5	61
3	{ Al powder SOCl ₂ }	{ 2 10 }	142	65.5	61
4	{ Al powder Red phosphorus }	{ 2 5 }	126	58.1	56
5	PCl ₅	5	152	70.3	60
6	{ Fe powder SOCl ₂ }	{ 5 5 }	159	73.4	63
7	SOCl ₂	5	153.5	70.8	62

^a Melting point of 4-chlorobenzophenone = 78° C.

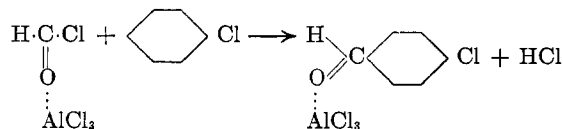
^b After two recrystallizations from diluted ethanol the product melted at 78.4° C. Presumably traces of 2-chlorobenzophenone were removed (*β*).

When propionic acid is condensed with toluene, the yield of the propionphenone is of the same order as the yields obtained in the preparation of acetophenones. Similar results were also obtained by condensing acetic acid with diphenyl.

The preceding experiments suggested the use of formic acid as the carboxylic acid component. Here, however, the similar formation of an acid chloride intermediate product, formyl chloride, would result in the synthesis of aldehydes and not ketones:



If the aluminum chloride salt were formed and converted to the acid chloride complex, as in the previously described syntheses, the following reaction might be realized:



Thus far, presumably either because of the pronounced differences in the chemistry of formic acid in comparison with its higher homologs, or because of the failure to provide proper equilibrium conditions, only a 1 to 2 per cent yield of *p*-chlorobenzaldehyde has been obtained by this procedure. The reaction appeared to pass through the aldehyde stage and then continue until a resinous mass was formed.

It is clear that numerous syntheses are made possible, if not practicable, by the procedure presented in this paper. A new field of investigation is opened up which, however, is circumscribed by the degree of reactivity of certain classes of compounds. Thus, when naphthalene is employed as the aryl component, there is a marked tendency to form dinaphthyl at the temperatures required for the conversion of the carboxylic acid to the acid chloride derivative. In the condensation of anthraquinone- β -carboxylic acid with suitable benzenoid compounds, it was found that the reaction did not proceed unless it was first converted *in situ* to the acid chloride derivative.

From the data already available (Tables I to III), it is clear that yields of 70 to 80 per cent of theory can be obtained. These results compare favorably with those obtained from the anhydride when 1 mole of the latter is considered equivalent to 2 moles of the carboxylic acid as an acylating agent. It is apparent that there are a number of economical and operating advantages in using carboxylic acids, but it should be recognized that 2 moles of acid necessitate approximately 5 moles of aluminum chloride, whereas approximately 3.3 moles are required when 1 mole of anhydride is employed.

ACKNOWLEDGMENT

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NOTABLE EXPANSION OF GERMAN RAYON INDUSTRY FORECAST. An enormous expansion in Germany's rayon production may eventuate as a result of the looked-for shortage of textile raw materials, according to a report made public by the Commerce Department. It is estimated that rayon production in Germany will approximate 88,000,000 pounds during the current year, compared with an annual average output of between 62,000,000 and 66,000,000 pounds in the last four years. The German rayon industry is operating at full capacity, but notwithstanding, Ger-

many has been compelled to rely to an increasing extent on foreign supplies.

It is proposed to provide for an increase of the production capacity of the German rayon industry up to 154,000,000 pounds annually. The extent to which Germany is apparently determined to insure its independence of foreign textile raw materials may be gaged by the fact that it is planned to increase the production of all artificial fibers to 220,000,000 pounds annually.