

Reaction of Organic Halogen Compounds with Metals (Part II)

A Formation of Organic Chlorine Zinc Complex in Various Solvents.

by

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有機할로겐化合物과 金屬과의 反應 (第2報)

有機亞鉛 클로린복합물 생성에 關한 各種 溶媒效果

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要 約

토루엔, 디메틸폴로움아마이드, 디메틸설포옥사이드, 테트라하이드로퓨란, 아세토나이트라일 및 디옥센 등 溶媒存在下에서 모노클로로醋酸과 亞鉛을 反應시켜 본 結果, 溶媒效果를 나타 내었다.

反應試藥의 反應度가 溶媒의 極性 및 親水性에 따라 增加하였다. 같은 溶媒系를 使用하여 에틸모노클로로醋酸을 反應시켜 본 結果, 溶媒效果를 나타냈으나 酸의 境遇보다 그 差가 크지 못하였다.

酸, 에스타, 亞鉛 및 카보닐化合物(벤즈알데하이드 및 4-헵타논)의 反應에 있어서는 알데하이드의 境遇에 있어서는 Reformatsky 反應生成물을 주었으나, 4-헵타논의 反應度는 없었다.

反應生成物의 收率は 試藥添加方法에 따라 變化되었다. 最高收率は 酸의 境遇 하이드로옥시酸(38.5%), 0.8g의 salt(아세토나이트라일 溶媒)이며, 에스타의 境遇에는 에틸신나메이트(19.3%), 폴리머(21.6%)이었다.

카보닐化合物의 境遇에 있어서는 反應溫度에 따라 試藥의 反應度의 變化가 있었다.

研究結果를 溶媒效果에 關聯시켜 論議하였으며, 研究方法에 關하여 記述하였다.

Abstract

Reaction of monochloroacetic acid with zinc in presence of toluene, dimethylformamide, dimethyl sulfoxide, tetrahydrofuran, acetonitrile, and dioxane solvents showed the solvent effect in order of dimethylformamide, dioxane, dimethyl sulfoxide, toluene, acetonitrile, and tetrahydrofuran. The increasing reactivity of the reagents was observed in order of the polarity and hydrophilicity of the solvent.

The same reaction of ethyl monochloroacetate in the same series of solvents showed also the solvent effect, but the difference was not large as compared to that of the acid. The reaction of the acid, ester, zinc, and carbonyl precursors such as benzaldehyde and 4-heptanone gave the Reformatsky reaction product in the case of the aldehyde, but the reactivity with 4-heptanone was slight. The yield of the product was varied by the method of addition of reagents. The best yield observed in case of the acid reaction was 38.5% of the hydroxy acid and 0.8 g of the salt in presence of acetonitrile and in case of the ester reaction 19.3% of ethyl cinnamate and 21.6% of polymer. The variation of the reactivity of reagents due to the reaction temperature was observed in case of carbonyl reaction. The result was discussed in terms of the solvent effect and the procedures were described.

Introduction

In continuation of the previous series of this research¹⁾ the variation of the reactivity of organic halogen compounds with zinc in presence of various polar solvents with hydrophilic property was investigated.

For the solvent acetonitrile²⁾, tetrahydrofuran²⁾, dimethyl sulfoxide³⁾, and dioxane²⁾, which were known to be a polar solvent with relative hydrophilic property, were chosen. In each reaction the inert solvent toluene, was used as the reaction standard.

The reaction of chloro acid and ester with carbonyl compounds such as benzaldehyde and 4-heptanone in presence of the zinc under various solvents was also studied in order to effect a modification of the Reformatsky procedure for the chlorine compounds.

The solvent effect for the formation of organozinc complex and the mode of the reactivity of the complex with carbonyl compounds under the solvent system were reported.

Experimental

Starting materials.—The materials used in this investigation were obtained from commercial sources. Acetonitrile, dioxane, tetrahydrofuran, and monochloroacetic acid (Fisher certified), dimethylformamide, dimethyl sulfoxide, and zinc powder (Wako Chemicals), and toluene (U. S. P.) were obtained from the commercial source as indicated. The materials were used without further purification. Ethyl monochloroacetate was prepared by Fisher esterification of the acid.

Identification of products.—The reaction products obtained from the present investigation were all known compounds. Therefore, the identification was made by physical and qualitative examination and spectrophotocchemical examination, wherever necessary.

Reaction of monochloroacetic acid with zinc under various solvents.

—Into a 100 ml., round bottomed, three necked flask equipped with a stirrer, condenser, and thermometer were placed 0.15 mole of metallic zinc powder, and 50~100cc. of the solvent and the mixture was refluxed under vigorous stirring. Through an addition funnel 0.1 mole of the halogen compounds was added in a several portions to the boiling mixture. The reaction mixture was then refluxed under vigorous stirring during the course of 4 hours. The reaction mixture was filtered and the unreacted zinc was treated by washing it with a large quantity of boiling water. The zinc recovered was dried and weighed. The filtrate from the filtration of the reaction mixture was distilled, and the residue from the distillations was distilled under reduced pressure in case of liquid products after acidification and extraction with ether, or was crystallized in case of solid product. The products obtained was a trace quantity of the acetic acid, and decomposition product. No appreciable quantity of the dimerized product was obtained. The results which were primarily concerned to the determination of the reactivity of the compounds with metals in the solvents are summarized in the Table 1 and 3.

Standard procedures of the reaction of organic fluoroacid with zinc in various solvents.

—The same procedures described in the previous experiment (see above reaction) were adopted. The reaction mixture was filtered and the inorganic mass filtered was triturated with water, dried, and weighed. The filtrate contained the equivalent quantity of the salt. The results were summarized in Table 2.

Reaction of monochloroacetic acid, benzaldehyde, and zinc in various solvents.—The apparatus and procedure for the previous reaction described above

Table 1 Relative reactivity of the reaction of monochloroacetic acid with excess zinc in various solvents. ***

Solvent	Amount	Temp.	Time	Unreacted zinc*	Equivalent reactivity** of zinc	Remark
	cc	°C	hrs	g	%	
Dioxane	50	105	4	3.3	97.0	
Dimethyl sulfoxide	50	150	4	3.4	95.4	
Tetrahydrofuran	50	64~6	4	6.3	50.8	
Acetonitrile	70	82	4	5.7	58.4	
N, N-dimethylformamide	70	150	4	3.0	101.0****	
Toluene	80	110	4	4.3	18.2	

* The unreacted zinc obtained from the reaction was sometimes contaminated with zinc chloride and oxide. It was therefore washed many times with a large quantity of the distilled water, dried, and weighed.

** The equivalent reactivity of the zinc was calculated on basis of the acid used.

*** 0.1 mole of the acid and 0.15 mole of zinc were reacted.

**** The yield indicated that the acid reacted with excess zinc.

Table 2 The reactivity of heptafluoro-butyric acid with zinc in various solvents. *

Reagents	Amount	Metal	Amount	Solvent	Amount	Temp.	Time	Unreacted zinc	Equivalent reactivity of zinc
	g		g		cc	°C	hrs	g	%
C ₃ F ₇ COOH	10.7	Zn	4.8	Toluene	50	110	4	4.4	9.09
"	10.7	Zn	4.8	Dioxane	50	105	4	4.6	9.04
"	10.7	Zn	4.8	Acetonitrile	50	82	4	4.4	9.08

* 0.05 mole of the acid and 0.075 mole of the zinc were reacted. It was aimed to reproduce the reaction conditions of the Table 1.

Table 3 Relative reactivity of the reaction of ethyl monochloroacetate with zinc in various solvents. **

Reagent	Amount	Metal	Amount	Solvent	Amount	Temp.	Time	Unreacted zinc	Equivalent* reactivity of zinc
CH ₂ ClCOO-	g		g		cc	°C	hrs	g	%
C ₂ H ₅	5.1	Zn	2.7	Toluene	50	110	4	2.5	6.0
"	6.1	Zn	3.3	Aceto- nitrile	50	82	4	3.0	10.0
"	6.1	Zn	3.3	Dioxane	50	105	4	3.0	10.0

* The zinc obtained from the reaction was covered with a white solid, zinc oxide, and hydroxide, which was difficult to remove without decomposing the zinc. Therefore the unreacted zinc was treated with hot acetonitrile, dried, and weighed.

** A 0.1 mole scale reaction run.

were adopted in this reaction except few modifications. Into the flask were placed 9.5 g. (0.15 mole) of zinc in 50 cc. of various solvents. The reaction mixture was stirred vigorously under reflux. Through the addition funnel 9.5 g. (0.1 mole) of the acid dissolved in the solvent were added in one portion to the boiling mixture. After vigorous reaction was ceased (15 minutes) 11.0 g. (0.1 mole) of benzaldehyde was added to the reaction mixture during the course of 10 minutes and the reaction mixture was refluxed for 4 hours. The reaction mixture was cooled and the inorganic solid mass was filtered, and

the filtrate was distilled under reduced pressure to give a brownish syrupy residue. The residue was acidified with 20% solution of sulfuric acid and the aqueous solution was extracted twice with ether. The ether solution was dried over anhydrous calcium chloride and distilled. From the ether distillation a brownish viscous tar was obtained. The tarry material was difficult to be distilled because of decomposition. It was therefore washed with 5% sodium hydroxide solution and the insoluble residue was triturated with alcohol to give the hydroxy acid, which was not crystallized (a racemic mixture). From the alkaline

washing the acid salt was obtained. (I.R. for the acid, characteristic frequency 3490, 1690, 1280, 1240, 700 cm^{-1}). The results were summarized in the Table 4.

Reaction of monochloroacetic acid, 4-heptanone, and zinc in various solvents.—The same procedure for the reaction of benzaldehyde was adopted in this reaction run. 9.5 g. (0.1 mole) of the acid, 10.0 g. of zinc (0.15 mole), and 11.4 g. (0.1 mole) of 4-heptanone were reacted. From the separation procedure described above no appreciable quantity of the product was obtained except the acetic acid and recovered heptanone. The results were summarized in Table 4.

Reaction of ethyl monochloroacetate and zinc in various solvents.—The same procedures for the aldehyde reaction run of the acid was adopted in this reaction run. 12.0 g (0.1 mole) of the ester, 6.5 g. (0.1 mole) of zinc in 50~100 cc. of the solvent were reacted as previously. From the reaction mixture unreacted zinc was recovered, which was purified by washing it with a large quantity of water, dried, and weighed. There were no other products except the recovery of the unreacted ester. Because of the separation scheme adopted the amount of the recovery of the ester was not measured. The results were summarized in Table 3.

Reaction of ethyl monochloroacetate, benzaldehyde, and zinc in various solvents.—The procedures and separating scheme for the reaction of aldehyde and acid were adopted for the present reaction run. 12.5 g. of the ester (0.1 mole), 6.5 g. (0.1 mole) of zinc, and 11.0 g. (0.1 mole) of benzaldehyde were reacted in 100 cc. of the solvent as previously. From the reaction the crude zinc was recovered, which was washed with boiling water, dried, and weighed.

By triturating the filtrate of the reaction mixture, benzaldehyde, ethyl cinnamate boiling 148~52°C/12mm. (I.R. 3050, 1740, 1650, 1320, 1206, 990, 870, 760, 710 cm^{-1}), and a polymerized tar, which was composed of ethyl cinnamate unit identified by infrared spectrophotometry, were obtained. The results were summarized in Table 5.

Reaction of ethyl monochloroacetate, zinc, and 4-heptanone in the various solvents.—The same procedures and separation scheme as that of the benzaldehyde reaction were adopted. From the reaction mixture the crude zinc was recovered, which

was purified by washing it with a large quantity of water, dried, and weighed. There were no other significant quantity of the products except the recovered ester and 4-heptanone. The results were summarized in Table 5.

Reversed addition procedure.—The reactions of the acid, benzaldehyde, and zinc and of the ester, benzaldehyde, and zinc were repeated by reversing the addition method of reagents. The zinc, aldehyde, and the solvent were mixed in the reaction flask and the mixture was refluxed under vigorous stirring. From an addition funnel the acid or ester dissolved in the solvent was added dropwise and the reaction mixture was refluxed for 4 hours under stirring. The same method of separation was conducted as described in the usual reaction. The results were summarized in the Table 4 and 5.

Slow addition procedure.—The reactions of the acid, or ester, benzaldehyde, and zinc were repeated by modifying the method of addition of the reagents. To the boiling mixture of the zinc, acid or ester, and solvent the benzaldehyde was added dropwise during the course of 10~25 minutes. The reaction time, temperature, and product separation were the same as that of the usual reaction run. The results were summarized in the Table 4 and 5.

Results and Discussion.

The reactions of monochloroacetic acid with zinc under various solvent systems showed an enhanced reactivity of the zinc in a polar and hydrophilic solvent in the order of dimethyl formamide, dioxan, dimethyl sulfoxide, toluene, acetonitrile, and tetrahydrofuran, regardless the difference in the reaction temperature as summarized in the Table 1.

The solvents adopted in the present investigation, which was a continuation of the previous series of the research¹⁾, were of a polar character with hydrophilic property. These solvents are known to have a dissolution and solvating effect for the reaction intermediate in the reaction of lithium aluminum hydride reduction²⁾, chlorination³⁾, organo metallics reaction^{2,3)}, Grignard reactions, and various nucleophilic displacement reaction at a saturated carbon compounds. Therefore the observed enhancement of the reactivity was considered as the dissolution effect of the organo zinc chloro-complex(I) formed during the reaction.

Table 4 A modified Reformatsky reaction of monochloroacetic acid in presence of benzaldehyde and 4-heptanone under various solvents. **

	Solvent	Temp.	Time	Unreacted zinc	Equivalent reactivity of zinc	Product	Remark
		°C	hrs	g	%	%	
Benzaldehyde	Toluene	110	4	Paste with zinc		(acid 5.3) (salt 0.18 g)	
	Acetonitrile	82	4	3.8	89.2	(acid 30.0) (salt 1.03 g)	
	Dioxane	105	4	2.0	117.7*	(acid 15.7) (salt 0.85 g)	
	Tetrahydrofuran	64~6	4	5.7	58.4	(acid trace) (salt trace)	
	Acetonitrile	82	4	4.5	78.4	(acid 38.5) (salt 0.85 g)	reversed addition
	Acetonitrile	82	4	3.6	92.3	(acid 25.9) (salt 0.92 g)	slow addition
4-Heptanone	Acetonitrile	82	4	5.7	58.4	none	
	Dioxane	105	4	3.2	97.0	4-heptanone recovered	
	Tetrahydrofuran	64~6	4	5.51	63.1	"	"

* The value indicated that the acid reacted with excess zinc.

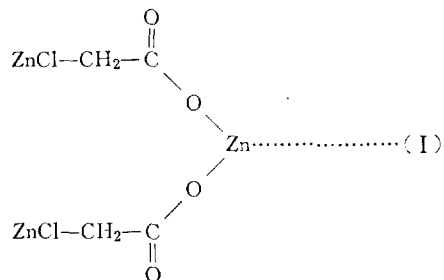
** 0.1 mole of the acid, 0.15 mole of zinc, and 0.1 mole of the carbonyl compounds were used.

Table 5 A modified Reformatsky reaction of ethyl monochloroacetate in presence of benzaldehyde and 4-heptanone under various solvents. *

	Solvent	Temp.	Time	Unreacted zinc	Equivalent reactivity of zinc	Product	Remark
		°C	hrs	g	%	%	
Benzaldehyde	Toluene	110	4	2.4	62.6	(ester 3.8) (polymer 13.9)	
	Acetonitrile	82	4	2.2	65.5	(ester 19.3) (polymer 21.6)	
	Dioxane	105	4	2.5	61.1	(ester 17.6) (polymer 9.3)	
	Acetonitrile	82	4	3.7	43.1	(ester 10.5) (polymer 21.8)	reversed addition
	Acetonitrile	82	4	4.1	37.0	(ester 6.2) (polymer 12.3)	slow addition
	Acetonitrile	82	4	4.1	37.0	(ester 6.2) (polymer 12.3)	slow addition
4-Heptanone	Toluene	110	4	6.3	3.1	trace	
	Acetonitrile	82	4	5.8	10.7	"	
	Dioxane	105	4	5.0	23.0	"	

* 0.1 mole of the ester, 0.1 mole of zinc, and 0.1 mole of carbonyl compounds were used.

However, there were a discrepancy in the enhancement of the reactivity in the case of acetonitrile and

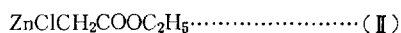


tetrahydrofuran. As compared to the toluene solvent system the acetonitrile and tetrahydrofuran system are more polar character and hence the increasing of the reactivity will duly be expected, if the dissolution effect by the solvent is a major driving force of the reaction. The reaction temperature was the refluxing temperature of the solvent and therefore the difference in reaction temperature was 28°C for acetonitrile and 46°C for tetrahydrofuran as compared to that of toluene (110°C). These marked differences in reaction temper-

ature, the low reaction temperature, might be effected in the formation of the complex.....(I), regardless the increased polarity and hydrophilicity of the solvent itself. These facts were further verified by observing the reaction of heptafluoro-butyric acid, which is a stronger acid than the monochloroacetic acid, with the zinc in the same solvent systems. As summarized in Table 2, the extent of the formation of the zinc salt of the acid in the solvents was not much differed each other, even though the hydrophilic solvent is able to increase the solubility of the acid salt. The formation of the salt depends mainly on the reaction temperature regardless the character of the solvent adopted.

The reaction of ethyl monochloroacetate with zinc under various solvent systems showed an enhanced formation of the zinc complex(II) even for the low boiling acetonitrile as compared to the toluene system, even though the difference was not large. (Table 3)

When the reaction was completed, there observed an insoluble complex formation on the surface of zinc in case of toluene whereas clear solution was obtained in case of the acetonitrile and dioxane system. Since the complex(II) does not involve the carboxylic acid



function, the difference of the solvent effect by acetonitrile in the formation of complex(I) and (II) might be due to the presence of the acid function in the complex(I), which is mainly temperature dependent. For the formation of complex(II), acetonitrile, which has a low refluxing temperature, showed a solvent effect although the effect was not large.

In the reactions described in Table 1, 2 and 3 the product separation was attempted in every cases, but there observed no significant formation of dimerized product except the acid salt and acetic acid or ethyl acetate, which corresponds to the decomposition product of the complex during the acidification of the reaction mixture.

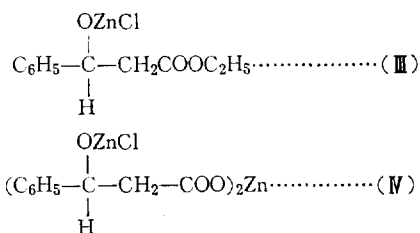
Even though a formation of dimerized product was observed in case of ethyl bromoacetate⁵⁾, the present system was not reactive enough to form the dimer because of the less reactivity of chlorine complex(I) and (II).

The study on the solvent effect observed in the formation of (I) and (II) described hereto was further extended to the study on the modification of the Re-

formatsky procedures. As described previously⁵⁾ Reformatsky reaction of chloro ester and acid was not extensively studied, because of the inertness of the chloro ester. In addition to this, the reaction procedure in a inert solvent suffers from an induction period, side product formation, and solubility of the solvent⁵⁾. As described in the previous series of this research an adoption of a polar and hydrophilic solvent, such as dimethyl formamide, enhanced the reactivity of the chloro ester and acid, which did not require an induction period and shorten the reaction time. It was also possible to effect a simultaneous addition of zinc and reagent without preforming the organo zinc complex solution. In the present solvent system the formation of chlorine complex (I) and (II) was not efficient as compared to the dimethyl formamide system as described in Table 1 and 3. Therefore it was not possible to prepare a high concentration of a solution of complex (I) and (II). The reactivity of the chloro ester was only 6.0 % in toluene and 10% in acetonitrile and dioxane. In case of the acid a syrupy paste of complex salt was observed for the toluene system, which covered the surface of the zinc during the reaction. This is due to the less reactivity of chloro compounds. However, when the chloro acid or ester and zinc were reacted in one portion at the refluxing temperature of the solvent, and the carbonyl compounds were added immediately to the boiling mixture, a vigorous reaction was introduced and the consumption of zinc was increased remarkably as compared to that of the reaction of chloro acid or ester and zinc alone, which was an indication of proceeding the Reformatsky reaction in the reaction system. As described in the Table 4 and 5, 4-heptanone was not able to be reacted with chloro acid or ester. The amount of consumption of zinc during the reaction was not changed as compared to that of the reaction conducted without 4-heptanone. (Table 1, 3) There were no significant amount of the Reformatsky reaction product in this case. Benzaldehyde was reacted remarkably under this condition to form the Reformatsky reaction product. (Table 4, 5)

The reactivity of the benzaldehyde reactions was in order of the solvent effect as observed in Table 1 and 3, but there were little discrepancy in the case of toluene and acetonitrile. In case of toluene the amount of consumption of zinc after the reaction of chloro ester

was corresponded to that of the acetonitrile and dioxane, which is an indication of the equivalent reactivity of benzaldehyde in all solvents, but the amount of product was less than that of acetonitrile and dioxane. This is probably due to the reaction temperature of chloro ester and benzaldehyde⁶⁾. The high refluxing temperature for the toluene system (110°C)⁶⁾ was able to promote the reaction regardless of the solvent effect, but the formed intermediate of the type (III) could not be further dissolved in the solvent system and hence resulted a decomposition which cut down the amount of the product. In case of the reaction of the chloro acid the reaction run conducted in the toluene system yielded a syrupy paste during the reaction, which was a decomposition mass.



The amount of products was also small as compared to that of the acetonitrile and dioxane system.

These observations lead the author to a conception of a solvent effect for the intermediate (III) and (IV). The better solvating solvent, a polar and hydrophilic solvent, could enhance the simultaneous addition reaction to form a considerable quantity of the reaction product, because of a rapid formation of the complex in the solution and dissolution of the intermediate (III) and (IV) in the solvent.

The total yield of the reaction product of the chloro ester and acid was, however, relatively small with a considerable formation of the side product, polymer, because of a rapid addition and vigorous reaction path. However, this procedure may still be useful for the

special reaction of the aldehyde, where the corresponding bromo acid or ester is not available or difficult to be obtained even though the yield of the product is relatively small.

In conclusion the observed solvent effect of the present system was apparent for the case of the formation of organo zinc complex (I), (II), (III), and (IV). Even in the case of the reaction, where the reaction path is governed by the reaction temperature, the solvent effect is sometimes more important factor than the temperature itself. The existing conception of the polar and hydrophilic character of the solvent described hereto may not be sufficient enough to account the solvent effect observed in the formation of organo zinc chloro complex. Therefore a further investigation along this line is anticipated in the future by means of more elaborate reaction technique.

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Literature

- 1) Y.S. Kim: *This Journal* **7**, 216 (1963)
- 2) R. Adams et al: *Organic Reactions*, Vol. VI (John Wiley and Sons, Inc., New York, 1957), p. 486
- 3) Glen A. Russel et al: *J. Am. Chem. Soc.* **80**, 4987 (1958); *J. Org. Chem.* **28**, 1933 (1963)
- 4) G.R. Leader and J.F. Gormley: *J. Am. Chem. Soc.* **73**, 5731 (1951)
- 5) R. Adams et al: *Organic Reactions*, Vol. I (John Wiley and Sons, Inc., New York, 1957), p. 4
- 6) Natelson and Galifried: *J. Am. Chem. Soc.* **61**, 970 (1939)