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# Ultrasound assisted synthesis of $\delta$ -chloroesters from tetrahydrofuran and acyl chlorides in the presence of catalytic zinc dust

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## Abstract

Sonication of acyl chlorides and dry tetrahydrofuran (THF) in the presence of catalytic amounts of zinc dust at 35 kHz gives  $\delta$ -chloroesters in high yields.

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**Keywords:**  $\delta$ -chloroesters; Tetrahydrofuran (THF); Acyl chlorides; Zinc dust; Ultrasound

## 1. Introduction

The application of power ultrasound to chemical syntheses and its use in research and in industries are well known. Chemical ultrasonics began in 1927 when the acceleration of a conventional reaction was reported by Richards and Loomis [1]. Since then, a number of chemical reactions have been observed in an ultrasound field [2–7]. Sonic condition not only accelerates chemical reactions, it reduces the number of steps which are required using normal conditions, cruder reagents can be used and reactions can be initiated without any additives. The chemical effects of ultrasound are due to the phenomenon of acoustic cavitation [8]. The primary chemical reactions result from a transient state of high temperatures and pressures [9]. Under sonic conditions, the yields are high and the reactions occur in shorter reaction durations.

On the other hand, metal-assisted reactions are very popular in organic syntheses due to their catalytic nat-

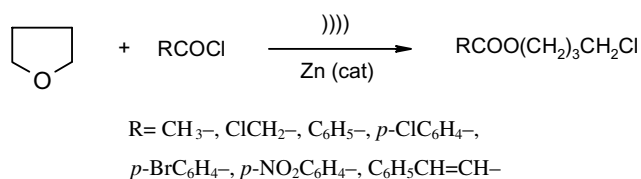
ure, selectivity and simple work-up. A number of reactions with metals under different reaction conditions for the reduction of different functional groups are documented in the literature. Boudjouk and Han have reported the preparation of 1,2-diketones from acid chlorides and lithium under sonic conditions [10].

In continuation of our work on the use of inexpensive, readily available metals and metal salts for organic functional group transformations [11–21], we expected that acid chlorides may be converted to 1,2-diketones by zinc metal in aprotic solvents. A set of four solvents—hexane, toluene, benzene and THF were selected to study the reaction of acyl halides with zinc dust under sonic conditions. While studying these reactions in dry THF, we found that acid chlorides react readily with THF in the presence of catalytic amounts of zinc metal to give  $\delta$ -chloroesters by the opening of the ether linkage.

Simple ethers such as dialkyl, aryl alkyl, diaryl, aryl allyl and dibenzoyl ethers have been shown earlier to give a mixture of the ester and the respective halide in moderate to good yields in presence of transition metal salts such as Mo, W, Pd and Co [22–26]. These methods,

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Scheme 1.

however, take a long time for completion of the reaction, take place at high temperatures, and give a mixture of products.

On the other hand, THF has been found to react with acyl chlorides in the presence of 25 mole% Zn metal in diethyl ether as solvent to give  $\delta$ -chloroesters. This reaction takes 3–18 h for completion [27]. As the reactions are studied in Et<sub>2</sub>O there exists an ambiguity in the reaction with the possibility of Et<sub>2</sub>O reacting with acyl chlorides in the presence of Zn metal to give the respective alkyl chloride and the ester in the reaction mixture, along with the corresponding  $\delta$ -chloroester.

We now wish to report the results of our study of the reactions of different acyl chlorides with THF in presence of catalytic amounts of zinc dust in the absence of any additional solvent under normal conditions as well as under the influence of ultrasound in a sonic bath operating at 35 kHz to give  $\delta$ -chloroesters in high yields as shown in Scheme 1.

## 2. Results and discussion

In order to standardize the reaction, different amounts of zinc dust were used to get  $\delta$ -chloroesters

from THF and benzoyl chloride; the results are summarized in Table 1. From the table, it is clear that the reaction can be carried out in presence of catalytic amounts of zinc dust (1 mmol) and that it is not possible without zinc dust (entry 5).

Under normal (silent) condition, benzoyl chloride, THF (taken in excess which also serves as solvent) and zinc dust (catalytic) were stirred at 25 °C. The reaction was monitored by TLC (5% EtOAc: pentane) and went to completion in 2 h to give 4-chlorobutyl benzoate in 90% yield.

In order to extend the reaction of THF with different acyl halides in the presence of catalyst zinc dust to get  $\delta$ -chloroesters, the study of reaction of THF with alkyl, aryl and allyl substituted acyl chlorides was taken up. The reactions were carried out under silent conditions as well as under the influence of ultrasound. These results are summarized in Table 2.

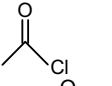
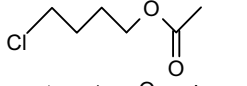
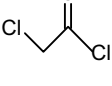
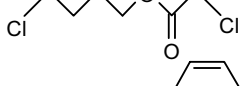
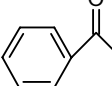
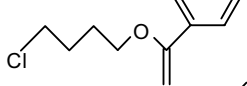
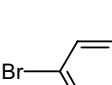
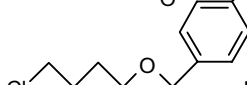
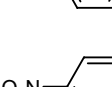
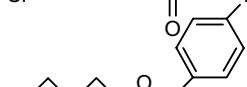
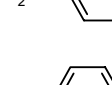
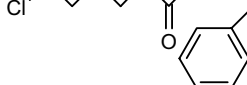
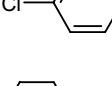
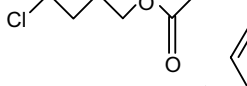
From Table 2 it is clear that the reaction takes about 1–24 h for completion under normal (silent) conditions. As the reaction takes a long time for completion [except the reaction with acetyl chloride (entry 1)], the reaction was carried out in a sonic bath working at 35 kHz. A noteworthy feature of this reaction is that the rate of the reaction gets accelerates and the reaction goes to completion within 5–50 min under the influence of ultrasound and different  $\delta$ -chloroesters are obtained in high yields.

It is also clear that, THF ring can be readily opened up by different acyl chlorides in the presence of catalytic amounts of zinc dust under sonic condition. While the yields of the products vary between 76% and 86% and the reaction takes up to 24 h for completion under silent condition, yields of the respective products under the

Table 1  
Reaction of THF and benzoyl chloride in presence of different amounts of zinc dust under normal conditions

Entry	Amount of Zn (mmol)	Product	Time (h)	Yield (%)
1	20		2	85
2	10		2	85
3	5		2	87
4	1		2	90
5	Nil	No reaction	24	–

Table 2  
Reaction of acyl chlorides with THF in presence of zinc dust<sup>a</sup>

Entry	Acid chloride	Product	Normal condition		Sonic condition	
			Time (h)	Yield (%)	Time (min)	Yield (%)
1			0.1	86	5	94
2			1	85	15	93
3			2	90	30	94
4			12	80	50	96
5			3	78	30	92
6			1	86	15	95
7			24	84	50	95

<sup>a</sup> Products are identified by the IR and <sup>1</sup>H NMR spectral analysis.

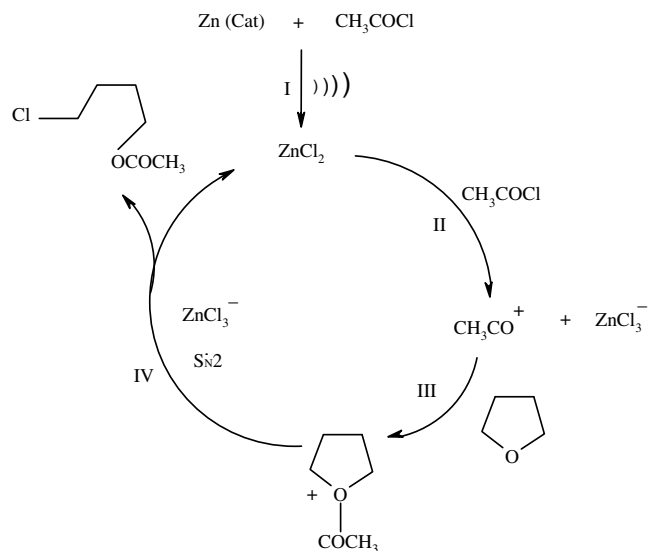
influence of ultrasound are between 92% and 96%. The reaction is general, as different acyl chlorides including aroyl chlorides having electron-releasing or electron-withdrawing groups react satisfactorily to give  $\delta$ -chloroesters within 50 min.

### 3. Mechanism

The reaction of acyl chlorides with THF in the presence of catalytic amounts of zinc dust under the influence of ultrasound is expected to proceed as shown in Scheme 2. In the first step of the reaction, catalytic amounts of  $ZnCl_2$  is expected to form by the reaction between zinc and acyl chloride. This  $ZnCl_2$  may react with another molecule of acyl chloride to give acyl cation and  $ZnCl_3^-$  in the step II. In step III, acyl cation so formed may react with THF to give an oxonium ion intermediate and in the step IV,  $ZnCl_3^-$  may interact with this oxonium ion intermediate to give the ring opening product  $\delta$ -chloroester.

In fact, we have found that, catalytic amount of  $ZnCl_2$  is sufficient to initiate the reaction under sonic condition, and this catalytic cycle continues till the completion of the reaction. As the reaction involves the for-

mation of a primary carbocation in the IV step of the reaction to regenerate  $ZnCl_2$ , the reaction is expected to proceed by  $S_N2$  mechanism to give the product.



Scheme 2.

Table 3  
Spectral data (IR and  $^1\text{H}$  NMR) of  $\delta$ -chloroesters

Entry	Product	IR [ $\nu$ ( $\text{cm}^{-1}$ )]	$^1\text{H}$ NMR ( $\text{CDCl}_3$ ) [ $\delta$ (ppm)]
1	$\text{CH}_3\text{CO}_2(\text{CH}_2)_4\text{Cl}$	1745, 762	1.66–1.80 [m, 4H ( $\text{CH}_2\text{CH}_2$ )], 1.97 [s, 3H ( $\text{CH}_3\text{CO}$ )], 3.49 [t, 2H ( $\text{CH}_2\text{Cl}$ ), $J = 6$ Hz], 4.01 [t, 2H ( $\text{CH}_2\text{O}$ ), $J = 6$ Hz]
2	$\text{ClCH}_2\text{CO}_2(\text{CH}_2)_4\text{Cl}$	1750, 762	1.6–1.9 [m, 4H ( $\text{CH}_2\text{CH}_2$ )], 2.05 [s, 2H ( $\text{CH}_2(\text{Cl})\text{CO}$ )], 3.5 [t, 2H ( $\text{CH}_2(\text{Cl})\text{CH}_2$ )], $J = 6$ Hz], 4.05 [s, 2H ( $\text{CH}_2\text{O}$ )], 1.93 [m, 4H ( $\text{CH}_2\text{CH}_2$ )], 3.59 [qua, 2H ( $\text{CH}_2\text{Cl}$ ), $J = 4.1$ Hz], 4.35 [t, 2H ( $\text{CH}_2\text{O}$ ), $J = 4.1$ Hz], 7.41–7.44–8.02–8.04 [m, 5H ( $\text{C}_6\text{H}_5$ )]
3	$\text{C}_6\text{H}_5\text{CO}_2(\text{CH}_2)_4\text{Cl}$	1729, 721	1.9 [m, 4H ( $\text{CH}_2\text{CH}_2$ )], 3.55 [m, 2H ( $\text{CH}_2\text{Cl}$ )], 4.35 [m, 2H ( $\text{CH}_2\text{O}$ )], 7.55–7.6–7.85–7.91 [dd, 4H ( $\text{C}_6\text{H}_4$ ), $J = 8.2$ Hz]
4	$\text{BrC}_6\text{H}_4\text{CO}_2(\text{CH}_2)_4\text{Cl}$	1734, 765	1.9 [m, 4H ( $\text{CH}_2\text{CH}_2$ )], 3.59 [m, 2H ( $\text{CH}_2\text{Cl}$ )], 4.34 [m, 2H ( $\text{CH}_2\text{O}$ )], 8.14–8.16, 8.22–8.25 [dd, 4H ( $\text{C}_6\text{H}_4$ ), $J = 8$ Hz]
5	$\text{NO}_2\text{C}_6\text{H}_4\text{CO}_2(\text{CH}_2)_4\text{Cl}$	1741, 727	1.95 [m, 4H ( $\text{CH}_2\text{CH}_2$ )], 3.60 [m, 2H ( $\text{CH}_2\text{Cl}$ )], 4.36 [m, 2H ( $\text{CH}_2\text{O}$ )], 7.57–7.6, 7.88–7.92 [dd, 4H ( $\text{C}_6\text{H}_4$ ), $J = 10$ Hz]
6	$\text{ClC}_6\text{H}_4\text{CO}_2(\text{CH}_2)_4\text{Cl}$	1709, 746	1.9 [m, 4H ( $\text{CH}_2\text{CH}_2$ )], 3.61 [m, 2H ( $\text{CH}_2\text{Cl}$ )], 4.36 [m, 2H ( $\text{CH}_2\text{O}$ )], 6.45 [d, 1H ( $\text{CH}(\text{OCO})=\text{CH}$ )], $J = 4$ Hz], 7.48 [d, 1H ( $\text{CH}(\text{C}_6\text{H}_5)=\text{CH}$ )], $J = 4$ Hz], 7.8 [m, 5H ( $\text{C}_6\text{H}_5$ )]
7	$\text{C}_6\text{H}_5\text{CH}=\text{CHCO}_2(\text{CH}_2)_4\text{Cl}$	1770, 768	

## 4. Experimental

### 4.1. Material and instruments

Different acyl chlorides were prepared by standard procedures [28] and purified before use. All reagents were obtained from Rankem. All the reactions were studied using Julabo, USR-3 German made sonic bath working at 35 kHz (constant frequency) maintained at 25 °C by constant circulation of water, without mechanical stirring. A Nicolet 400D FT-IR spectrophotometer was used for IR spectral analysis. NMR spectra were recorded on a 400 MHz Bruker instrument. The chemical shift values ( $\delta$  ppm) reported are relative to TMS in  $\text{CDCl}_3$  as solvent. Yields refer to the isolated yields of the products and are based on 10 mmol of starting acyl chloride.

### 4.2. General experimental procedure for the preparation of $\text{CH}_3\text{COO}(\text{CH}_2)_4\text{Cl}$

#### 4.2.1. Under sonic condition

Benzoyl chloride (1.41 g, 10 mmol), THF (10 mL) and zinc dust (0.065 g, 1 mmol) were sonicated in a bath at 35 kHz, while maintaining the temperature of the bath at 25 °C. The reaction went to completion in 30 min (TLC 5% EtOAc: pentane), the contents were extracted with ether ( $3 \times 10$  mL), and the combined ethereal extract was washed with saturated  $\text{NaHCO}_3$  solution, water, and then dried over anhydrous  $\text{Na}_2\text{SO}_4$ . The solvent was then removed under vacuum and the crude was subjected to silica gel chromatography using 5% EtOAc: pentane to get 4-chlorobutyl benzoate (2.00 g, 94% yield).

#### 4.2.2. Under normal condition

A mixture of benzoyl chloride (1.41 g, 10 mmol), THF (10 mL) and zinc dust (0.065 g, 1 mmol) was stirred at 25 °C. The reaction was monitored by TLC (5% EtOAc: pentane) and was complete in 2 h. After completion of the reaction, the contents were taken into ether (30 mL), and the ethereal solution was washed with saturated  $\text{NaHCO}_3$  solution and water, and then dried over anhydrous  $\text{Na}_2\text{SO}_4$ . The solvent was removed under vacuum and the crude was subjected to silica gel chromatography using 5% EtOAc: pentane to get 4-chlorobutyl benzoate (1.91 g, 90%). The IR and  $^1\text{H}$  NMR spectral data of the  $\delta$ -chloroesters prepared by this procedure are presented in Table 3.

## 5. Conclusion

In conclusion, we have developed a simple and economically viable method for the preparation of  $\delta$ -chloroesters using catalytic amounts of inexpensive, readily

available, abundant zinc metal, THF and acyl chlorides under sonic condition. These  $\delta$ -chloroesters are important in organic syntheses and find application in the syntheses of natural products where a four-carbon chain is required to be added. From the point of view of work-up and time for completion, the present reaction is superior as compared to existing methods.

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