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Simple and Efficient Method for the Synthesis of δ-Chloroesters from Tetrahydrofuran and Acyl Chlorides in the Presence of Catalytic Iodine

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Simple and Efficient Method for the Synthesis of δ-Chloroesters from Tetrahydrofuran and Acyl Chlorides in the Presence of Catalytic Iodine

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Abstract: Acyl chlorides and dry tetrahydrofuran (THF) in the presence of catalytic amounts of iodine at 25°C give δ-chloroesters in excellent yields.

Keywords: acyl chlorides, δ-chloroesters, iodine, tetrahydrofuran (THF)

INTRODUCTION

The preparation of δ-chloroesters are important in organic synthesis and find application in the syntheses of natural products where a four-carbon chain is required. These δ-chloroesters are also used as intermediates in the synthesis of valuable pharmaceuticals. It has been known for some time that tetrahydrofuran undergoes cleavage in the presence of Lewis acids such as $ZnCl_2$,[1] BCl_3,[2] and Bi(III)halides;[3] organolanthanide complexes;[4] and iodides.[5] However, quite a few of the reported methods have limitations mainly with respect to yield, cost, and availability of the reagents. Some of the systems require longer duration, stringent conditions, work at reflux temperature of the solvent or at higher temperatures, environmentally toxic catalysts, and cumbersome methodologies. Thus, the search for new catalysts and methods is still of practical

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importance. In this article, we describe our successful work on iodine as a catalyst for the cleavage of tetrahydrofuran in the presence of acyl chlorides at 25°C.

RESULTS AND DISCUSSION

An earlier report from our laboratory describes synthesis of δ-chloroesters from tetrahydrofuran and acyl chloride in the presence of zinc dust.[6] Because the reaction takes a long time for completion, the reaction has been studied under sonication. In continuation with our work, we are reporting a novel method of synthesis of δ-chloroesters from tetrahydrofuran using a catalytic amount of iodine and acid chlorides in the absence of any additional solvent at 25°C as shown in Scheme 1.

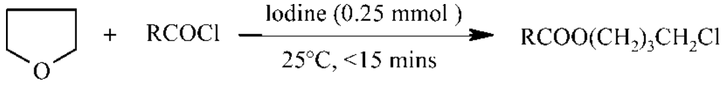
To standardize the reaction, different amounts of iodine were used to get δ-chloro esters from THF and benzoyl chloride; the results are summarized in Table 1. From the table, it is clear that the reaction can be carried out in the presence of catalytic amounts of iodine and that it is not possible without iodine (entries 7 and 8).

EXPERIMENTAL

Different acyl chlorides were prepared by standard procedures[7] and purified before use. All reagents were purchased from BDH and S. D. Fine chemicals, and all the chemicals and solvents were distilled before use. Reactions were monitored on thin-layer chromatography (TLC) by comparison with the authentic samples. 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 (δ ppm) reported are relative to TMS in $CDCl_3$ as solvent. Yields refer to the isolated yields of the products and are based on 10 mmol of starting acyl chloride.

General Procedure for the Preparation of $CH_3COO(CH_2)_4Cl$

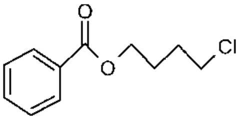
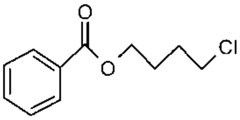
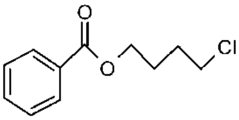
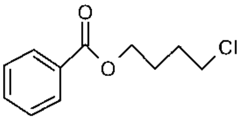
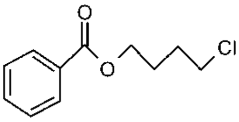
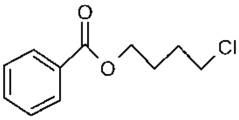
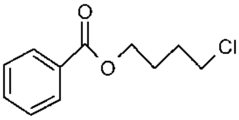
Acetyl chloride (0.78 g, 10 mmol) and tetrahydrofuran (10 ml) were taken in a 25-ml round-bottom flask. Iodine (0.063 g, 0.25 mmol) was added to



R = CH_3-, C_6H_5-, $ClCH_2$-, p-Cl C_6H_5-,
p-BrC_6H_4-, p-$NO_2C_6H_4$-, $C_6H_5CH{=}CH$-

Scheme 1.

Table 1. Reaction of THF and benzoyl chloride in the presence of different amounts of iodine at 25°C

Entry	Amount of iodine (mmol)	Product	Time	Yield (%)
1	10		30 min	78
2	7.5		30 min	80
3	5		30 min	80
4	2.5		30 min	82
5	1		30 min	85
6	0.1		30 min	90
7	0.05		5 min	94
8	Nil	No reaction	24 h	—

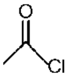
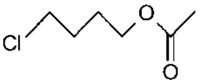
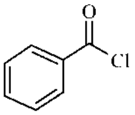
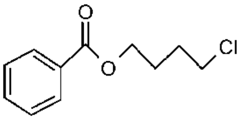
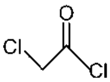
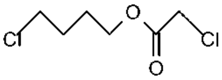
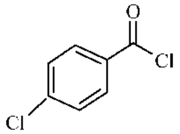
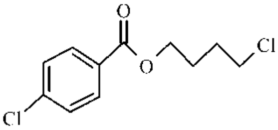
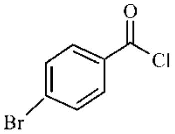
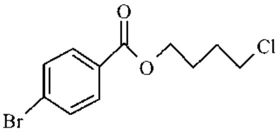
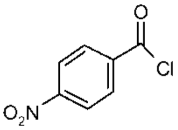
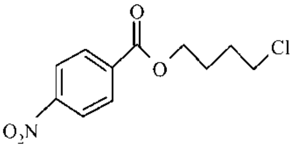
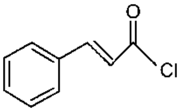
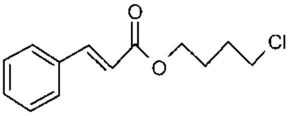
this and stirred at 25°C for 3 min. The progress of the reaction was monitored by TLC; after completion of the reaction, 25 ml of ether was added. The organic layer was washed with saturated $Na_2S_2O_3$ (10 mL) followed by water (3 × 10 ml), dried over anhydrous Na_2SO_4, concentrated in vacuo, and purified by column chromatography (5% ethyl acetate–petroleum ether) to afford pure 4-chlorobutyl acetate (1.44 g, 96%). The IR and ^{1}H NMR spectral data of the δ-chloroesters are presented in Table 2.

To extend the reaction of THF with different acyl halides in the presence of iodine to get δ-chloroesters, the reaction of THF with alkyl, aryl, and allyl substituted acyl chlorides was studied. The reactions were carried out under normal conditions, and the results are summarized in Table 3. From Table 3, it is clear that aroyl chlorides containing both electron- withdrawing and electron-donating groups react equally efficiently to give δ-chloroesters in excellent yields in less than 15 min.

Table 2. Spectral data (IR and ^{1}H NMR) of δ-chloroesters

Entry	Product	IR [υ (cm^{-1})]	^{1}H NMR (CDCl$_3$) [δ (ppm)]
1	$CH_3CO_2(CH_2)_4Cl$	1740, 762	1.60–1.80 [m, $4H(C\underline{H}_2C\underline{H}_2)$], 1.97 [s, $3H\ (C\underline{H}_3CO\text{-})$], 3.42 [t, $2H(C\underline{H}_2Cl)$, $J = 6$ Hz), 4.00 [t, $2H\ (C\underline{H}_2O\text{-})$, $J = 6$ Hz].
2	$C_6H_5CO_2(CH_2)_4Cl$	1724, 721	1.97 [m, $4H(C\underline{H}_2C\underline{H}_2)$], 3.60 [t, $2H\ (C\underline{H}_2Cl)$, $J = 4.1$ Hz], 4.35 [t, $2H(C\underline{H}_2O\text{-})$, $J = 4.1$ Hz], 7.41–8.04 [m, $5H(C_6\underline{H}_5)$].
3	$ClCH_2CO_2(CH_2)_4Cl$	1750, 762	1.6–1.9 [m, $4H(CH_2CH_2)$], 2.05 [s, $2H\{ClC\underline{H}_2COO\text{-}\}$], 3.5 [t, $2H\{CH_2C\underline{H}_2Cl\}$, $J = 6$ Hz], 4.05 [t, $2H(C\underline{H}_2O\text{-})$, $J = 6$ Hz].
4	$ClC_6H_4CO_2(CH_2)_4Cl$	1719, 740	1.95 [m, $4H(CH_2CH_2)$], 3.60 [m, $2H(CH_2Cl)$], 4.37 [m, $2H(CH_2O\text{-})$], 7.57–7.92 [dd, $4H(C_6H_4)$, $J = 10$ Hz].
5	$BrC_6H_4CO_2(CH_2)_4Cl$	1718, 756	1.91 [m, $4H(CH_2CH_2)$], 3.55 [m, $2H(CH_2Cl)$], 4.34 [m, $2H(CH_2O\text{-})$], 7.55–7.91 [dd, $4H(C_6H_4)$, $J = 8.2$ Hz].
6	$NO_2C_6H_4CO_2(CH_2)_4Cl$	1729, 726	1.90 [m, $4H(CH_2CH_2)$], 3.59 [m, $2H(CH_2Cl)$], 4.36 [m, $2H(CH_2O\text{-})$], 8.16–8.24 [dd, $4H(C_6H_4)$, $J = 8$ Hz].
7	$C_6H_5CH{=}CHCO_2(CH_2)_4Cl$	1770, 768	1.89 [m, $4H(C\underline{H}_2C\underline{H}_2)$], 3.61 [m, $2H(C\underline{H}_2Cl)$], 4.36 [m, $2H(C\underline{H}_2O\text{-})$], 6.45 [d, $1H\{CH(OCO\text{-}) = C\underline{H}\text{-}\}$, $J = 16$ Hz], 7.7 [d, $1H\{C\underline{H}(C_6H_5) = CH\}$, $J = 16$ Hz], 7.38–7.56 [m, $5H(C_6\underline{H}_5)$].

Table 3. Reaction of acyl chlorides with THF in presence of iodine at 25°C[a]

Entry	Acid chloride	Product	Time	Yield (%)
1			3	96
2			5	94
3			5	90
4			5	92
5			10	90
6			10	89
7			15	92

[a] Products are identified by the IR and ^{1}H NMR spectral analysis.

CONCLUSION

In conclusion, we have presented novel, rapid, efficient, economically viable protocol for the preparation of δ-chloroesters from THF and acyl chlorides using catalytic amounts of nontoxic, readily available, and inexpensive iodine.

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