A mild and efficient synthesis of chloroesters by the cleavage of cyclic and acyclic ethers using $Bi(NO_3)_3 \cdot 5H_2O$ as a catalyst under solvent-free conditions

V. Suresh, N. Suryakiran, and Y. Venkateswarlu

Abstract: A facile, efficient synthesis of chloroesters is described. The reaction of cyclic and acyclic ethers with acid chlorides in the presence of catalytic amounts of $Bi(NO_3)_3$ ·5H₂O under solvent-free conditions yielded the corresponding chloroesters. Also, the catalyst can be recovered conveniently and reused efficiently for at least six times.

Key words: Bismuth(III) nitrate pentahydrate, cyclic and acyclic ethers, chloroesters.

Résumé : On décrit une méthode simple et efficace de synthèse des chloroesters. La réaction d'éthers cycliques et acycliques avec des chlorures d'acides, en présence de quantités catalytiques de $Bi(NO_3)_2$ ·5H₂O et dans des conditions sans solvant, fournit les chloroesters correspondants. De plus, il est possible de récupérer facilement le catalyseur et de le réutiliser d'une façon efficace au moins six fois.

Mots-clés: pentahydrate du nitrate de bismuth(III), éthers cycliques et acycliques, chloroesters.

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Introduction

The cleavage of cyclic and acyclic ethers with acid chlorides, leading to the synthesis of the corresponding chloroesters, is a versatile organic transformation, as they are important and key constituents in organic synthesis, particularly in the synthesis of natural products (1). Transformation of cyclic ethers into haloesters is a direct and straightforward method for producing bifunctional synthetic intermediates and also an important method for the removal of ethereal protecting groups (2). In organic synthesis, hydroxyl groups are protected as aliphatic, benzylic, and allylic ethers (3), which can subsequently be cleaved for further transformations (4-7). The cleavage of ethers with acyl chlorides has been reported using Lewis acids, such as SmI₂ (8), ZnCl₂ (9), FeCl₃ (10), I₂ (11), MoCl₅ (12), PdCl₂(PPh₃)₂ (13), CoCl₂ (3), and very recently InBr₃ (14). However, using strongly acidic conditions frequently leads to the formation of undesirable side products, which in turn decrease the purity and yields of the desired products. Most of the reported methods have one or other limitations, such as long reaction time, unavailability of the catalyst, difficulties in handling, and tedious workup procedures with unsatisfactory yields. Thus, a mild, efficient catalyst for the cleavage of cyclic and acyclic ethers with acid chlorides is highly desirable. In view of the merits in catalytic processes, we are interested in the development of

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Scheme 1.

$$\begin{bmatrix} 1 \\ 0 \end{bmatrix}^{n} + \begin{bmatrix} 0 \\ H_{3}C \end{bmatrix} \begin{bmatrix} Bi(NO_{3})_{3} \cdot 5H_{2}O \\ CI \end{bmatrix} \xrightarrow{H_{3}C} \begin{bmatrix} 0 \\ H_{3}C \end{bmatrix}^{n} CI \\ RT, 5-75 \text{ min} \end{bmatrix} \xrightarrow{H_{3}C} \begin{bmatrix} 0 \\ 0 \end{bmatrix}^{n} CI$$

inexpensive, mild, and non-polluting reagent for the acidchloride-directed cleavage of cyclic and acyclic ethers.

Organic reactions using mild and water-tolerant catalysts received much attention in recent years, as they can be handled conveniently, and the products can be easily recovered from the reaction mixture, thus making the experimental procedure simple and eco-friendly. Among Lewis acid catalysts, the bismuth(III) nitrate pentahydrate is relatively nontoxic, inexpensive, stable in atmospheric conditions, and used in various organic transformations (15). Also, to the best of our knowledge, there is no report on the use of Bi(NO₃)₃·5H₂O for the cleavage of cyclic and acyclic ethers with acid chlorides. Recently, we reported Bi(NO₃)₃·5H₂O as a mild and efficient Lewis acid catalyst for N-tert-butoxycarbonylation of amines (16). In continuation of our work on catalytic application of metal nitrate salts in the multi-step synthesis of natural products in our laboratory, we have observed that $Bi(NO_3)_3 \cdot 5H_2O$ can be utilized efficiently for the cleavage of cyclic and acyclic ethers with different acid chlorides into the corresponding chloroesters under solventfree conditions.

Results and discussion

In this report (Scheme 1), we describe an efficient and facile method for the synthesis of chloroesters. This method

Scheme 2. Plausible mechanism.



Table 1. Comparison of various catalysts on the reaction of tetrahydrofuran with acetyl chloride at room temperature under solvent-free conditions.

Entry	Catalyst [mol%]	Time (min)	Yield (%)
1	Bi(NO ₃) ₃ •5H ₂ O [50]	10	96
2	Bi(NO ₃) ₃ •5H ₂ O [10]	10	95
3	Bi(NO ₃) ₃ •5H ₂ O [5]	10	95
4	CAN [5]	90	85
5	$Zr(NO_3)_2 \cdot xH_2O$ [5]	40	80
6	La(NO ₃) ₃ •6H ₂ O [5]	30	90
7	Bi(OTf) ₃ [5]	60	90
8	BiCl ₃ [5]	120	90
9	$ZnCl_2$ [5]	60	95
10	I ₂ [5]	120	91
11	Zn [5]	180	87
12	Graphite [5]	360	90
13	$InBr_3$ [5]	180	89
14	HNO ₃	60	50

does not need expensive reagents or special care to exclude the moisture from the reaction medium. All the reactions proceeded efficiently and smoothly at room temperature, and the products were obtained in excellent yields (Table 1). Furthermore, the reaction conditions are very mild. Bismuth(III) nitrate pentahydrate is highly oxophilic and forms labile bond with carbonyl oxygen to initiate the formation of C-O bond with cyclic and acyclic ethers (Scheme 2). We first examined the reaction of tetrahydrofuran 1 with acetyl chloride 2 under solvent-free conditions to give the corresponding chloroesters 3 in 95% yield (Table 2, entry 2). To compare the catalytic activity of the bismuth(III) nitrate pentahydrate, we carried out the reaction in different Lewis acid catalysts, such as Bi(OTf)₃, BiCl₃, La(NO₃)₃·6H₂O, CAN, ZrO(NO₃)₂·xH₂O, and other reported catalysts. However, bismuth(III) nitrate pentahydrate was found to be the most effective in terms of reaction time as well as yields of the product (Table 1). This success of the reaction encouraged us to carry out the reaction on various cyclic and acyclic ethers with different acid chlorides in the presence of 5mol% of Bi(NO₃)₃·5H₂O. The ring cleavage of tetrahydropyran is considerably slower than that of tetrahydrofuran at room temperature with low yields (55%). Using slightly elevated temperature (50 °C), the reaction is completed in 1 h with 90% yield (Table 2, entries 7-9). In the case of asymmetrical ethers, the cleavage took place selectively at the unsubstituted side of ether (Table 2, entries 10 and 13). However, in the presence of cyclic and acyclic

ethers in the same substrate, formation of products (chloroesters) was observed only with acyclic part of the substrate (Table 2, entries 17 and 18).

Further, we have studied the reusability of the catalyst without any modification of the reaction conditions. After completion of the reaction, ethyl acetate (10 mL) was added; the catalyst was recovered by filtration and reused without loss of its activity for six runs (Table 3). The organic layer was concentrated under reduced pressure to get the crude product. From the foregoing results, it is evident that $Bi(NO_3)_3$ ·5H₂O is an efficient and reusable catalyst for the synthesis of chloroesters under solvent-free conditions.

Conclusion

In conclusion, we described an efficient and facile synthesis of chloroesters in the presence of catalytic amount of $Bi(NO_3)_3 \cdot 5H_2O$ under solvent-free conditions. The advantages of the method are reduced reaction time, inexpensive catalyst, and simple experimental and work up procedure with high yields of products. This makes it a useful addition to the existing methodologies.

Experimental

Typical experimental procedure for preparation of chloroesters

To a mixture of cyclic/acyclic ether (10 mmol) and acid chloride (10 mmol), was added Bi(NO₃)₃·5H₂O (5 mol%) at 0–5 °C followed by stirring at room temperature for an appropriate time (Table 2). After completion of the reaction as monitored by TLC, ethyl acetate (10 mL) was added, and the catalyst was recovered by filtration. The solvent ethyl acetate was washed with water, brine, dried over anhyd. so-dium sulphate, and removed under reduced pressure to give a crude product, which was purified on a silica-gel column to yield the pure products. The products were characterized by spectral and analytical data or by comparison with authentic samples.

Table 2. Entry 4

¹H NMR (CDCl₃, 300 MHz) δ : 1.99 (m, 4H), 3.6 (m, 2H), 4.4 (m, 2H), 7.28 (dd, J = 7.4 and 1.5Hz, 1H), 7.5 (d, J =1.5 Hz, 1H), 7.8 (d, J = 7.4 Hz, 1H). EI-MS: 281 (M⁺). Anal. calcd. for C₁₁H₁₁Cl₃O₂: C, 47.14; H, 3.92; Cl, 38.03. Found: C, 46.92; H, 3.94; Cl, 37.77.

Entry 5

¹H NMR (CDCl₃, 200 MHz) δ : 1.97 (m, 4H), 3.60 (m, 2H), 4.40 (m, 2H), 7.31 (m, 1H), 8.13 (dd, J = 8.1 and

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Entry	Ether	Acid chloride	Product ^a	Temp., Time (min)	Yield (%) ^b
1	\Box	н₃с└сі	H ₃ C ^O O ^{CI}	RT, 10	96
2	\bigcirc	CI	CI CI	RT, 10	96
3	\bigcirc	CI CI	CI CI	RT, 15	90
4	\bigcup_{O}			RT, 15	87
5	\Box	CI CI		RT, 15	92
6	\bigcup_{o}	H ₃ C~O O CI	H ³ C ~ O O O O O CI	RT, 10	98
7	\bigcirc	о н₅с ⊂сі	H _a c ^O o~~~Cl	50 °C, 60	90
8	\bigcirc	CI	C CI	50 °C, 75	90
9	\bigcirc			50 °C, 60	90
10	O CAC	CI		RT, 10	85
11	Color	р н₃с⊄сі	(9:1)	RT, 15	70
12	cı 🗸	CI CI	(9:1) CI OCOPh + CI OCOPh	RT, 5	90
13	CI	о н _а с ^с сі		RT, 5	85
14	н°с∽о∕он°	CI	(9:1)	RT, 30	85
15	Ph ^O Ph		CI ↓ Or Ph	RT, 10	90
16	^{Ph} ∽0∼ ^{Ph}	, ↓ CI		RT, 10	91
17	Concerne Con	CI CI		RT, 25	85
18	$\Omega_{\rm o}$			RT, 30	80

Table 2. Bi(NO₃)₃·5H₂O-catalyzed cleavage of cyclic and acyclic ethers by acid chlorides under solvent-free conditions.

Table 3. Synthesis of chloroesters using $Bi(NO_3)_3 \cdot 5H_2O$ as an efficient and reusable catalyst.

Entry	Substrates	Time (min)	Yield (%)
1	CI + O H₃C CI	10	96
2	2nd run	10	95
3	3rd run	10	96
4	4th run	10	96
5	5th run	10	95
6	6th run	10	95

1.5 Hz, 1H,), 8.51 (dd, J = 8.1 and 1.5 Hz, 1H). EI-MS: 248 (M⁺). Anal. calcd. for C₁₀H₁₁Cl₂NO₂: C, 48.38; H, 4.43; Cl, 28.62; N, 5.64. Found: C, 48.41; H, 4.47; Cl, 28.58; N, 5.65.

Entry 6

¹H NMR (CDCl₃, 200 MHz) δ : 1.39 (t, J = 6.90 Hz, 3H), 1.90 (m, 4H), 3.58 (m, 2H), 4.31 (m, 4H). EI-MS: 208 (M⁺). Anal. calcd. for C₈H₁₃ClO₄: C, 46.15; H, 6.49; Cl, 17.06. Found: C, 46.05; H, 6.28; Cl, 16.99.

Entry 10a

¹H NMR (CDCl₃, 200 MHz) δ : 1.66 (m, 2H), 1.79 (m, 2H), 2.00 (s, 3H), 3.41 (m, 2H), 4.29 (d, 2H, J = 3.5 Hz), 4.79 (m, 1H), 7.47 (m, 2H), 7.73 (m, 1H), 7.6 (m, 1H). EI-MS: 275 (M⁺). Anal. calcd. for C₁₃H₁₆Cl₂O₂: C, 56.72; H, 5.81; Cl, 25.81. Found: C, 56.74; H, 5.86; Cl, 25.77.

Entry 10b

¹H NMR (CDCl₃, 200 MHz) δ : 1.72 (m, 4H), 2.02, (s, 3H), 2.15 (m, 2H), 4.00 (m, 2H), 6.67 (m, 1H), 7.50 (m, 2H), 7.61 (m, 1H), 7.87 (m, 1H). EI-MS: 275 (M⁺). Anal. calcd. for C₁₃H₁₆Cl₂O₂: C, 56.72; H, 5.81; Cl, 25.81. Found: C, 56.75; H, 5.84; Cl, 25.75.

Entry 17

¹H NMR (CDCl₃, 300 MHz) δ : 3.03 (t, J = 6.79 Hz, 2H), 4.49 (t, J = 7.5 Hz, 2H), 7.23 (m, 8H), 7.7 (d, 1H, J = 1.5 Hz). EI-MS: 260 (M⁺). Anal. calcd. for C₁₅H₁₃ClO₂: C, 69.23; H, 4.99; Cl, 13.65. Found: C, 69.10; H, 5.03; Cl, 13.60.

Entry 18

¹H NMR (CDCl₃, 300 MHz) δ: 1.97 (m, 1H), 2.64 (m, 2H), 4.41 (t, J = 6.79 Hz, 2H,), 7.3 (m, 1H), 7.47 (s, 1H), 7.81 (d, 2H, J = 7.5 Hz). EI-MS: 243 (M⁺). Anal. calcd. for C₁₁H₈Cl₂O₂: C, 54.32; H, 3.29; Cl, 29.21. Found: C, 54.35; H, 3.32; Cl, 29.17.

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