Bismuth(III) Chloride-Catalyzed Highly Efficient Transesterification of β-Keto Esters

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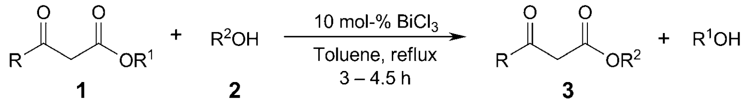
Bismuth(III) chloride was found to be an efficient catalyst for the transesterification of a variety of β-keto esters with a wide range of alcohols to afford transesterified products in good to high yields in short reaction times (see *Table*).

Introduction. – Bismuth(III) halides are inexpensive, relatively nontoxic, fairly water-insensitive, and environmentally benign reagents, which have been used as mild *Lewis* acid catalysts for an array of synthetic transformations [1][2]. Bismuth has the electron configuration $[Xe]4f^{14}5d^{10}6s^{2}6p^{3}$. Due to the weak shielding of the 4f electrons (lanthanide contraction), bismuth(III) compounds exhibit *Lewis* acidity. Earlier, we have shown the catalytic activity of $BiCl_3$ [3] in synthetic methodology. As a part of our research program, we were in need of benzyl esters, which can be cleaved by hydrogenolysis. The hydrolysis of alkyl such as methyl or ethyl esters requires base, which may pose some unavoidable side reactions like ring opening or decomposition of the material in lactones and macrolides or in the presence of base-sensitive functional groups. Therefore, we developed a method using $BiCl_3$ as a catalyst by which alkyl esters are converted to the benzyl esters in very high yields in pure form. We studied the generality of the catalyst action, and the results are presented here.

Results and Discussion. – The transesterification reaction of ethyl acetoacetate (=ethyl 3-oxobutanoate) with benzyl alcohol was studied in the presence of a catalytic amount of $BiCl_3$ as a model reaction. The reaction smoothly proceeded in refluxing toluene in a *Dean–Stark* apparatus to give transesterified product in 90% yield in 2 h. Under similar conditions, β-keto esters such as methyl, ethyl, and cycloalkyl acetoacetates underwent smooth transesterification with alcohols like butanol and allyl, propargyl, and homoallyl alcohol (= prop-2-en-1-ol, prop-2-yn-1-ol, and but-3-en-1-ol) giving good yields of transesterification products. Similarly, ethyl benzoylacetate (=ethyl 3-oxo-3-phenylpropanoate) (*Table*, *Entries 6* and *10*) underwent a clean transesterification with benzyl and homopropargyl alcohol, respectively. The transesterification reaction ran equally well with enantiomerically pure (+)- or (−)-menthol (=(1*S*,2*R*,5*S*)- and (1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexanol) (*Entries 3* and *9*) giving the products in good yields. It is important to note that with $BiCl_3$ as catalyst, methyl (cyclopropylcarbonyl)acetate (*Entry 2*) cleanly reacted with benzyl alcohol giving 75% yield of transesterified product. In all the cases, the reactions were completed within 3 – 4.5 h. The present protocol is general since a variety of structurally different β-keto esters underwent transesterification with various alcohols. In all the cases, 10 mol-% of the catalyst was used to drive the reaction to completion. These transesterified esters can be utilized in organic synthesis and in industry.

Table. *$BiCl_3$-Catalyzed Transesterification of β-Ketoesters*



Entry	R	R^1	R^2	Time [h]	Yield of **3**a)b) [%]
1	Me	Me	Bu	3	85
2	cyclopropyl	Me	$PhCH_2$	4	75
3	^{t}Bu	Et	(+)-menthyl	4.5	71
4	^{i}Pr	Et	$PhCH_2$	3	72
5	^{t}Bu	Et	$PhCH_2$	3.5	78
6	Ph	Et	$HC{\equiv}CCH_2$	3	81
7	^{i}Pr	Et	$H_2C{=}CHCH_2CH_2$	3	79
8	^{i}Pr	Et	$PhCH_2CH_2CH_2$	2.5	84
9	^{i}Pr	Et	(–)-menthyl	4.5	73
10	Ph	Et	$PhCH_2$	3	85
11	2-oxocyclopentyl	Et	$PhCH_2$	4	82
12	2-oxocyclopentyl	Et	$H_2C{=}CHCH_2$	4.5	85

a) All products were characterized by spectroscopic data. b) Yield after chromatography.

In summary, we established $BiCl_3$ as a novel catalyst for the rapid and efficient transesterification of β-keto esters with a variety of alcohols.

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Experimental Part

Transesterification: General Procedure. A mixture of β-keto ester **1** (1 equiv.), alcohol **2** (2 equiv.), and the catalyst $BiCl_3$ (10 mol-% of β-keto ester) in toluene (*ca.* 20 ml) was refluxed in a *Dean–Stark* apparatus to remove the alcohol formed (TLC monitoring). After the consumption of **1**, the catalyst was filtered and the filtrate concentrated. The residue was purified by chromatography (silica gel, hexane/AcOEt in different proportions): β-keto ester **3**. Isolated yields are indicated in the *Table*. All products were analyzed by NMR, IR, and GC/MS, and the spectra were consistent with the structure of the desired products.

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