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Scandium Trifluoromethanesulfonate-Catalyzed Mild, Efficient, and Selective Cleavage of Acetates Bearing a Coordinative Group

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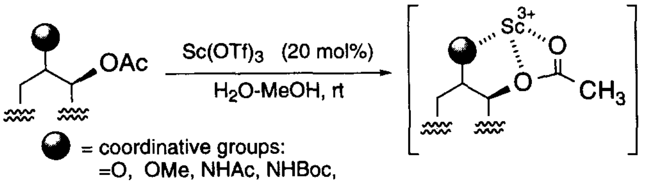
Abstract: Scandium trifluoromethanesulfonate is a useful Lewis acid catalyst for cleavage of acetates containing coordinative groups adjacent to the acetyl carbonyl. The reaction proceeds under weak acidic conditions at room temperature. Racemizable α-keto acyloxy compounds are deacetylated without racemization. Selective mono-deacetylation at the 10-position of paclitaxel has been achieved.

Keywords: *chelation; esters; hydrolysis; scandium and compounds*

An acyl group is a frequently used protective group of alcohols. Thus, the development of a mild and efficient method for the cleavage of acetates as a deprotection procedure is a significant aspect of experimental organic chemistry [1]. The most commonly adopted method for deacetylation is a basic hydrolysis because of its efficiency and irreversible nature. However, this procedure has the disadvantage of potential occurrence of such undesired side reactions as elimination and racemization [2]. During our study concerning the development of a new route to enantiomerically pure 1-amino-2-indanol, we found that a rare earth(III) trifluoromethanesulfonate, especially scandium trifluoromethanesulfonate ($Sc(OTf)_3$) works as an efficient deacetylation catalyst [3]. In studying details of the reaction, we found that the carbonyl group adjacent to an acetyl group played a significant role in the efficient deacetylation. Herein we report $Sc(OTf)_3$-catalyzed mild, efficient and selective cleavage of acetates bearing a coordinative group (Scheme 1).



Scheme 1.

Notes:

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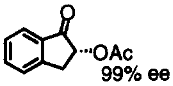
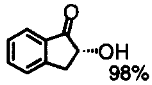
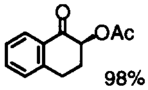
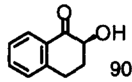
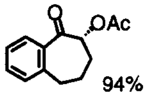
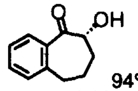
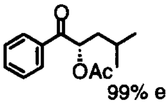
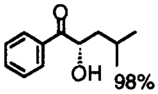
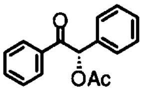
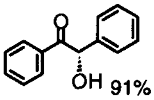
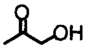
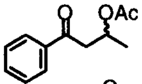
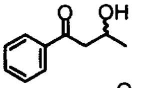
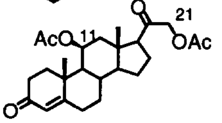
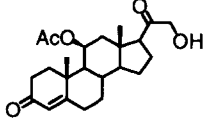
The effectiveness of $Sc(OTf)_3$ as a deacetylation catalyst arises, we consider, from the coordination of the catalyst [4-5] to a substrate molecule and the activation of an acetate [6-12]. Therefore, acetates bearing a coordinative group which can chelate to $Sc(OTf)_3$ are favorable substrates for the $Sc(OTf)_3$-catalyzed deacetylation [3]. This reaction proceeds in aqueous MeOH (pH 3) at room temperature; the catalyst is recovered after the reaction and is reusable.

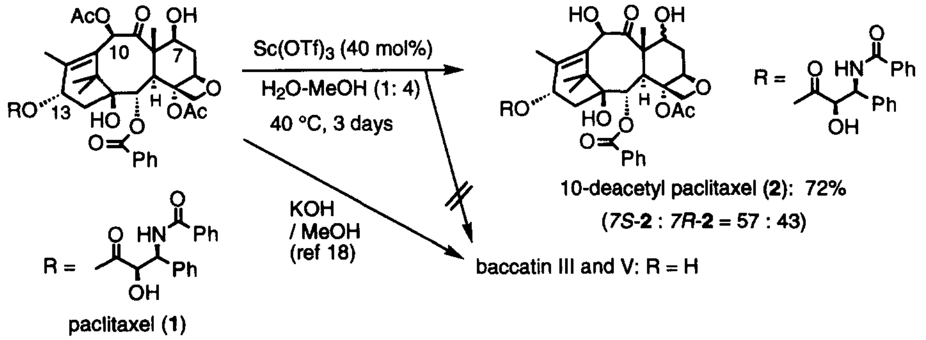
First, we examined the cleavage of acetates bearing a carbonyl group as a coordinative group as shown in Table 1. Cyclic or acyclic β-keto acetates were smoothly deacetylated to the corresponding β-keto alcohols in good yields (entries 1-6). In contrast, a γ-keto acetate required prolonged reaction time; the yield was low because elimination occurred as a side reaction (entry 7).

Table 1. $Sc(OTf)_3$-Catalyzed Cleavage of Acetates Bearing a Carbonyl Group[a]

Entry	Substrate	Product	Time, h	Yield,[b] %
1[c]	 99% ee	 98% ee (75% yield, 8% ee)[d]	40	93
2	 98% ee	 90% ee (23% yield, 26% ee)[d]	40	82
3	 94% ee	 94% ee (34% yield, 1% ee)[d]	40	84
4	 99% ee	 98% ee (53% yield, 33% ee)[d]	66	72
5	 99% ee	 91% ee (39% yield, 1% ee)[d]	73	90
6			40	77[e]
7			112	39
8			50	94

a: conditions; $Sc(OTf)_3$ 20 mol%, H_2O : MeOH = 1 : 4, 30 °C
b: isolated yield unless specified
c: ref. 3
d: the yield and ee in parentheses are results of the hydrolysis using LiOH (1.5 mol amt.)
e: HPLC yield

A salient feature of this reaction is the absence of, or the slight racemization during the deacetylation of such extremely racemizable acetates as α-acetoxy carbonyl ketones (entries 1-5). The advantage of this method in the application for the deacetylation of a racemizable compound is obvious by comparison with the results of the controlled experiments using lithium hydroxide [13-16]. Yields and % ee's are given in parentheses. Another feature of this procedure is the selective cleavage of an ester moiety close to a coordinative group. When a diacetate was used as a substrate (entry 8), the acetate at C-21 was selectively deacetylated to give the mono-acetate in 94% yield.



Scheme 2.

We extended the use of this procedure for the selective deacetylation of paclitaxel (**1**) (Scheme 2) [17].[3] Among four ester groups and one amido group of paclitaxel, the acetyl group at C-10 adjacent to the carbonyl group at C-9 was selectively removed to give 10-deacetyl paclitaxel (**2**) in 72% yield. Miller and Kingston reported that basic hydrolysis of **1** caused predominant removal of the C-13 side chain ester group to give baccatin III and V with concomitant epimerization at C-7 [18,19]. In contrast, formation of baccatin III and V was not observed when $Sc(OTf)_3$ was used as a catalyst. These experimental results clearly demonstrate the unique selectivity of the $Sc(OTf)_3$-promoted deacetylation.

We next examined cleavage of acetates bearing a coordinative group other than a carbonyl group. The results are summarized in Table 2. A methoxy group also served as a good coordinative group for $Sc(OTf)_3$ (entry 1). Amido and carbamate groups were also available as the coordinative group (entries 2 and 3). It is noteworthy that an acid-sensitive Boc group could survive under the reaction conditions in spite of the acidic nature of $Sc(OTf)_3$ [20,21]. Cleavage of an α-methoxy calboxylic acid ester and an α-keto carboxylic acid ester turned out sluggish, but gave the corresponding acids in moderate yields (entries 4 and 5). Throughout these experiments, neither cleavage nor elimination reaction of the coordinative group was observed.

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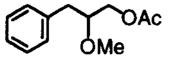
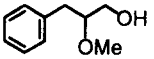
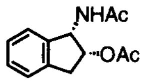
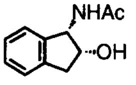
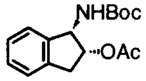
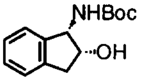
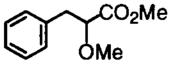
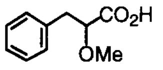
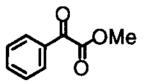
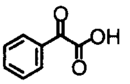
[3] Acetylaion of 10-deacetylbaccatin III using lanthanoid trifluoromethanesulfonate is reported (ref 17)

Table 2. $Sc(OTf)_3$-Catalyzed Cleavage of Acetates Bearing a Coordinative Group[a]

Entry	Substrate	Product	Time, h	Yield,[b] %
1			18	99
2			26	81
3			76	73
4			72	18[c]
5			96	47[c]

a: conditions: $Sc(OTf)_3$ 20 mol%, H_2O : MeOH = 1 : 4, 30 °C
b: isolated yield unless specified
c: HPLC yield

In summary, we have demonstrated that $Sc(OTf)_3$ is a useful Lewis acid catalyst for the cleavage of acetates bearing a coordinative group close to the acetyl group. Acetate is selectively cleaved when an acetamido or Boc group co-exists. The catalyst is recovered after the reaction and is reused. Since the racemization rarely occurs, we consider this procedure will find wide use in the deacetylation of racemizable substrates.

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