Highly Powerful and Practical Acylation of Alcohols with Acid Anhydride Catalyzed by $Bi(OTf)_3$

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$Bi(OTf)_3$-catalyzed acylation of alcohols with acid anhydride was evaluated in comparison with other acylation methods. The $Bi(OTf)_3$/acid anhydride protocol was so powerful that sterically demanding or tertiary alcohols could be acylated smoothly. Less reactive acylation reagents such as benzoic and pivalic anhydride are also activated by this catalysis. In these cases, a new technology was developed in order to overcome difficulty in separation of the acylated product from the remaining acylating reagent: methanolysis of the unreacted anhydride into easily separable methyl ester realized quite easy separation of the desired acylation product. The $Bi(OTf)_3$/acid anhydride protocol was applicable to a wide spectrum of alcohols bearing various functionalities. Acid-labile THP- or TBS-protected alcohol, furfuryl alcohol, and geraniol could be acylated as well as base-labile alcohols. Even acylation of functionalized tertiary alcohols was effected at room temperature.

Introduction

The acylation of alcohols is one of the important and routinely utilized transformations in organic synthesis.[1] Especially in the synthesis of complicated natural products and glycosylation of sugars, acyl groups play a pivotal role as protecting groups of hydroxyls. Despite a number of precedents, new efficient methodologies for acylation are still in strong demand. Acid anhydrides have been the most commonly used reagents in the presence of an acid or base catalyst[2] and the utility of this protocol was boosted by the discovery of the (dimethylamino)pyridine (DMAP) catalyst.[3a] Following the evolution of DMAP, other basic catalysts have been investigated. Bu_3P is a highly active promoter,[3b] and recently it has been shown that the optically active phosphine is efficient for kinetic resolution of racemic secondary alcohols.[3c] The aminophosphine superbase is another basic catalyst which is able to accerelate acetylation of alcohols with Ac_2O with high efficiency.[3d] Although these phosphorus catalysts are useful with regard to high catalytic activities, the procedure is tedious because all the manipulation should be performed under the anhydrous and degassed conditions due to the instability of the phosphorus catalysts in air. In parallel with the progress of basic catalysts, acidic promoters have also been investigated so far. Particularly, metal triflates were developed intensively, and a variety of efficient catalysts such as scandium triflate,[3e] silyl triflate,[3f] and indium triflate[3g] were found to be effective as well. These acidic catalysts, however, suffer from some drawbacks despite their great usefulness. $Sc(OTf)_3$ is highly active so that even tertiary alcohol could be acylated smoothly. However, the acylation with this catalyst must be carried out under anhydrous conditions and occasionally at low temperatures to suppress elimination. Although Me_3SiOTf is one of the most powerful activators of acid anhydrides, the silyl triflates are labile toward moisture, and therefore the silyl triflate-catalyzed acylation must be carried out under strictly anhydrous conditions. It has been shown that this triflate can be used as an acylation catalyst for various functionalized alcohols, but its acidity is too strong for acid-sensitive alcohols to survive intact.[3f] We have been involved in the development of organotin acylation catalysts for a long time.[3h,3i,4] Organotin catalysts are so mild that various selective acylation reactions are feasible, and they are practical in use because most of them are stable in the air. On the other hand, their acidity is not strong enough to perform acylation of sterically hindered alcohols. We have prepared several types of organotin triflates with the hope of increasing Lewis acidity due to the strong electron-attractive power of triflate. This was indeed the case, but organotin triflates were not acidic enough for acylation of tertiary alcohols. In this context, we were intrigued by employing bismuth triflate $Bi(OTf)_3$[5] since it had proved to be easy

(1) Green, W.; Wuts, P. G. M. In *Protective Group in Organic Synthesis*, 3rd ed.; John Wiley & Sons: New York, 1999; p 150.

(2) Larock, R. C. *Comprehensive Organic Transformations*; VCH Publishers: New York, 1989; p 980.

(3) For references on the acylation of alcohol with Ac_2O: (a) DMAP: Steglich, W.; Hofle, G. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 981. (b) Bu_3P: Vedejs, E.; Bennet, N. S.; Conn, L. M.; Diver, S. T.; Gingras, M.; Lin, S.; Oliver, P. M.; Peterson M. J. *J. Org. Chem.* **1993**, *58*, 7286. (c) Nonracemic tertiary phosphine: Vedejs, E.; MacKay, J. A. *Org. Lett.* **2001**, *3*, 535. (d) Aminophosphine superbase: D'Sa, B. A.; Verkade, J. G. *J. Org. Chem.* **1996**, *61*, 2963. (e) $Sc(OTf)_3$: Ishihara, K.; Kubota, M.; Kurihara, H.; Yamamoto, H. *J. Org. Chem.* **1996**, *61*, 4560. (f) Me_3SiOTf: Procopiou, P. A.; Baugh S. P. D.; Flack S. S.; Inglis, G. G. A. *J. Org. Chem.* **1998**, *63*, 2342. (g) $In(OTf)_3$: Chauhan, K. K.; Frost, C.; Love G. I.; Waite, D. *Synlett* **1999**, 1743. (h) Distannoxane: Orita, A.; Sakamoto, K.; Hamada, Y.; Mitsutome, A.; Otera, J. *Tetrahedron* **1999**, *55*, 2899. (i) Cationic organotin dimer: Sakamoto, K.; Hamada, Y.; Akashi, H.; Orita, A.; Otera, J. *Organometallics* **1999**, *18*, 3555.

(4) Orita, A.; Mitsutome, A.; Otera, J. *J. Org. Chem.* **1998**, *63*, 2420.

(5) Both $Sc(OTf)_3$ and Sc_2O_3, which is a starting material for the triflate, can be purchased from Aldrich. The price of Sc_2O_3 is $159.9 for 5 g (72.5 mmol). Bi_2O_3, the starting compound for $Bi(OTf)_3$, is also commercially available, and its price is cheaper: $187.1 for 250 g (1.07 mol). $Bi(OTf)_3$ is accessible alternatively by the reaction of Ph_3Bi ($ 57.3, 25 g, 56.8 mmol) and TfOH. In this study, $Bi(OTf)_3$ was prepared as a tetrahydrate according to this procedure. Labrouillere, M.; Le Roux, C.; Gaspard, H.; Laporterie, A.; Dubac, J. *Tetrahedron Lett.* **1999**, *40*, 285 and references therein.

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Table 1. $Bi(OTf)_3$-Catalyzed Acetylation of Alcohol[a]

entry	alcohol	catalyst/mol %	time/h	yield %[b]
1	$PhCH_2CH_2OH$ (**1**)	0.01	10 min	98
2		0.005	2.5	99
3		0.001	1.5	19
4		0.001	24	70
5		0.001	48	95
6[c]		0.5	4	92
7	$PhCH(OH)CH_3$ (**2**)	0.005	2	95
8	$C_6H_{13}CH(OH)CH_3$ (**3**)	0.005	17	98
9		0.005	3	98

[a] Reaction conditions: alcohol (10 mmol), Ac_2O (10 equiv), 25 °C. [b] GC yield. [c] Ac_2O (1.5 equiv), CH_2Cl_2 (wet, 10 mL). [d] At 40 °C.

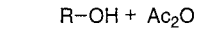
to handle due to its stability in air and sufficiently acidic to catalyze Friedel−Crafts,[6] Diels−Alder[7] and ene reactions.[8] Despite such an extensive elaboration of bismuth-catalyzed C−C bond forming reactions, acylation by the use of $Bi(OTf)_3$ has never been investigated. Here we disclose the high usefulness of $Bi(OTf)_3$-catalyzed acylation in comparison with other catalysts.[9]

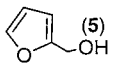
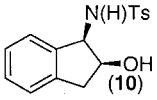
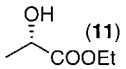
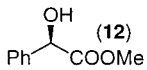
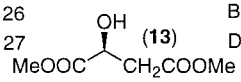
Results and Discussion

First, we investigated the catalytic activity of $Bi(OTf)_3$ for acetylation of unfunctionalized alcohols such as 2-phenethyl alcohol (**1**), 1-phenethyl alcohol (**2**), and 2-octanol (**3**) with acetic anhydride (Table 1). Treatment of primary alcohol **1** with 10 equiv of acetic anhydride in the presence of 0.01 mol % of $Bi(OTf)_3$ at 25 °C gave 2-phenethyl acetate quantitatively in 10 min (entry 1). With 0.005 mol % of $Bi(OTf)_3$, acetylation necessitated a longer reaction time, but proceeded quantitatively in 2.5 h (entry 2). Remarkably a low catalyst loading such as 0.001 mol % is sufficient although a longer reaction time is needed for satisfactory yield (entries 3−5). This $Bi(OTf)_3$−Ac_2O protocol could be carried out in the presence of organic solvent as well. For example, **1** was acetylated in CH_2Cl_2 with 1.5 equiv of Ac_2O using 0.5 mol % of $Bi(OTf)_3$, where CH_2Cl_2 could be used without dehydration (entry 6). Secondary alcohol **2** was also converted smoothly to the desired acetate in the presence of 0.005 mol % of $Bi(OTf)_3$ (entry 7). Although 2-octanol (**3**) is less reactive than **2**, either longer reaction times or higher reaction temperatures realized acetylation in quantitative yields (entries 8 and 9).

With these preliminary results in hand, we scrutinized the efficiency and versatility of $Bi(OTf)_3$-catalyzed acetylation at 25 °C using functionalized primary and secondary alcohols. In Table 2, the optimized reaction conditions and the yields are shown together with the results catalyzed by other promoters for comparison. Acid-sensitive geraniol (**4**) in Ac_2O was transformed to geranyl acetate in 81% yield by loading 0.01 mol % of $Bi(OTf)_3$ (entry 1). The reaction of **4** was improved by addition of donor solvent such as acetonitrile though somewhat longer reaction times were needed (entries 2 and 3). On

Table 2. Acetylation of Functionalized Primary and Secondary Alcohol[a]



		conditions			
entry	alcohol	cat/mol%	solv/mL	time/h	yield/%[b]
1	Geraniol (**4**)	$Bi(OTf)_3$/0.01	none	3.5	81
2		$Bi(OTf)_3$/1.0	MeCN/1	8.5	95
3		$Bi(OTf)_3$/0.1	MeCN/1	24	90
4		$Sc(OTf)_3$/0.1	MeCN/1	24	64[c]
5		Bu_3P/10	CH_2Cl_2/5	14	96
6	 (**5**)	$Bi(OTf)_3$/0.05	none	5.5	80
7		$Bi(OTf)_3$/0.05	THF/0.5	4	93
8		$Sc(OTf)_3$/0.05	MeCN/0.5	5	67
9[d,e]		Me_3SiOTf/2.0	CH_2Cl_2/2.5	4	49
10		Bu_3P/10	CH_2Cl_2/5	12	97
11	$(C_7H_{15})_2CHOH$ (**6**)	$Bi(OTf)_3$/0.5	none	3	87
12		$Bi(OTf)_3$/0.5	THF/5	3	95
13[e,f]	Menthol (**7**)	$Bi(OTf)_3$/1.0	none	1.5	97
14	Borneol (**8**)	$Bi(OTf)_3$/0.5	THF/3	7	99
15		$Bi(OTf)_3$/0.5	toluene[g]/1	3	95
16	$Cl_3CCH(OH)_2$ (**9**)	$Bi(OTf)_3$/0.5	toluene[g]/1	16	96
17	 (**10**)	$Bi(OTf)_3$/1.0	none	5	98[h]
18		none	pyridine/1.5	11	98
19	 (**11**)	$Bi(OTf)_3$/0.5	THF/5	2	91
20		$Bi(OTf)_3$/0.1	CH_2Cl_2[g]/5	5	92
21		$Sc(OTf)_3$/0.5	MeCN/5	3	96
22		DMAP/10	pyridine/3	24	100
23	 (**12**)	$Bi(OTf)_3$/0.5	THF/1	2	93
24		Bu_3P/10	CH_2Cl_2/1	9	98
25		DMAP/10	pyridine/3	22	94
26	 (**13**)	$Bi(OTf)_3$/0.5	THF/1	5	93
27		DMAP/10	pyridine/3	24	92

[a] Reaction conditions: alcohol (1.0 mmol), Ac_2O (10 equiv), 25 °C. [b] GC yield. [c] The alcohol (32%) remained untouched. [d] Ac_2O (1.5 equiv). [e] At 0 °C. [f] Ac_2O (5.0 equiv). [g] The wet solvent was used. [h] Isolated yield.

the other hand, $Sc(OTf)_3$ was not so efficient as $Bi(OTf)_3$: the treatment of **4** with $Sc(OTf)_3$−Ac_2O in 24 h gave a mixture which consisted of 64% of geranyl acetate and 32% of **4** remaining unreacted (entry 4). Bu_3P gave geranyl acetate in an excellent yield, yet 10 mol % catalyst loading was required (entry 5). In $Bi(OTf)_3$-promoted acetylation of acid-labile furfuryl alcohol (**5**), it was disclosed again that the addition of donor solvent such as THF resulted in a remarkable improvement of the yield (entries 6 and 7). With other metal triflates such as $Sc(OTf)_3$ and Me_3SiOTf, the yields were only moderate because of decomposition of the products induced by strong Lewis acids (entries 8 and 9). Although Bu_3P could work, the reaction proceeded only sluggishly taking 12 h for completion with higher catalyst concentration (entry 10). When the $Bi(OTf)_3$ protocol was applied to secondary alcohols such as 8-pentadecanol (**6**), menthol (**7**) and borneol (**8**), the desired acetates were obtained in good yields (entries 11−15), where no olefin was detected by TLC monitoring indicative of being free from elimination. Notably, in acetylation of **8**, toluene could be utilized without dehydration (entry 15), and 2,2,2-trichloroethane-1,1-diol (chloral hydrate) (**9**) also could be trans-

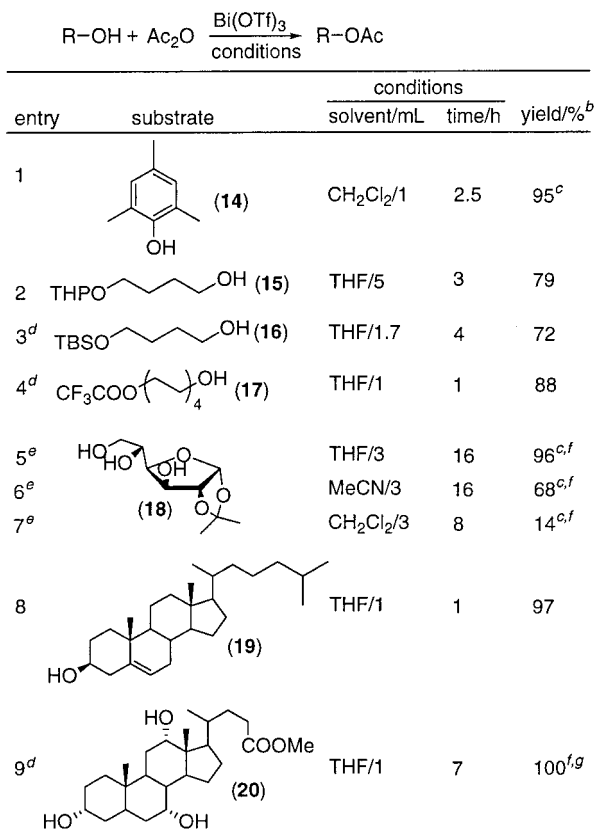
(6) (a) Desmurs, J. R.; Labrouillere, M.; Le Roux, C.; Gaspard, H.; Laporterie, A.; Dubac, J. *Tetrahedron Lett.* **1997**, *38*, 8871. (b) Répichet, S.; Le Roux, C.; Dubac, J.; Desmurs, J. R. *Eur. J. Org. Chem.* **1998**, 2743.

(7) Garrigues, B.; Gonzaga, F.; Robert, H.; Dubac, J. *J. Org. Chem.* **1997**, *62*, 4880.

(8) Laurent-Robert, H.; Le Roux, C.; Dubac, J. *Synlett* **1998**, 1138.

(9) For preliminary report on our study, see: Orita, A.; Tanahashi, C.; Kakuda, A.; Otera, J. *Angew. Chem., Int. Ed.* **2000**, *39*, 2877. After completion of the present work, Bi(III)-catalyzed acylation of simple alcohols appeared: Mohammadpoor-Baltork, I.; Aliyan, H.; Khosropour, R. *Tetrahedron* **2001**, *57*, 5851.

Table 3. Acetylation of Functionalized Alcohol[a]



entry	substrate	conditions: solvent/mL	time/h	yield/%[b]
1	(**14**)	CH_2Cl_2/1	2.5	95[c]
2	THPO, OH (**15**)	THF/5	3	79
3[d]	TBSO, OH (**16**)	THF/1.7	4	72
4[d]	CF_3COO, OH (**17**)	THF/1	1	88
5[e]	(**18**)	THF/3	16	96[c,f]
6[e]		MeCN/3	16	68[c,f]
7[e]		CH_2Cl_2/3	8	14[c,f]
8	(**19**)	THF/1	1	97
9[d]	COOMe (**20**)	THF/1	7	100[f,g]

[a] Reaction conditions: alcohol (1.0 mmol), Ac_2O (10 mmol), and $Bi(OTf)_3$ (1.0 mol %) at 25 °C. [b] Isolated yield. [c] GC yield. [d] $Bi(OTf)_3$ (0.5 mol %) was used. [e] Ac_2O (9.0 mmol) was used. [f] Triacetate. [g] $Bi(OTf)_3$ (5.0 mol %) was used.

formed to acylal in a wet toluene (entry 16). The $Bi(OTf)_3$-catalyzed acetylation of β-amino alcohol **10** proceeded to completion without epimerization in 5 h at 25 °C (entry 17). In contrast, basic catalysis promoted by pyridine required a longer reaction time (11 h) (entry 18). When three types of alcohols possessing an ester function **11**, **12**, and **13** were examined, each alcohol underwent smooth acetylation in the presence of $Bi(OTf)_3$ to afford the desired acetate without racemization (entries 19, 20, 23, and 26). Acetylation of ethyl lactate (**11**) took place in wet CH_2Cl_2 as well as in dry THF (entries 19 and 20). Although both $Sc(OTf)_3$ and DMAP served as well, $Sc(OTf)_3$ must be used in dry MeCN and DMAP required 24 h for the reaction to complete (entries 21 and 22). Thus, from the practical point of view, a combination of $Bi(OTf)_3$−Ac_2O seems to be a highly convenient acetylating method because the bismuth catalyst is highly reactive and resistant against moisture, and dry solvents are not always necessary. Upon acetylation of **12** and **13**, basic catalysts such as Bu_3P and DMAP were promising but prolonged reaction periods were crucial for complete acetylation (entries 24, 25, and 27).

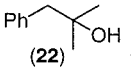
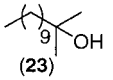
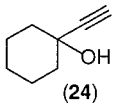
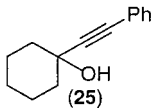
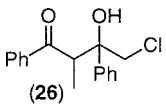
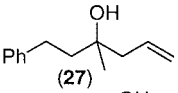
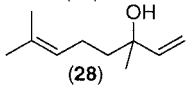
To explore generality and scope further, the $Bi(OTf)_3$-catalyzed acylation was examined using other functionally and sterically diverse alcohols as depicted in Table 3. When 2,4,6-trimethylphenol (**14**) was subjected to the present protocol, smooth transformation took place as reported in the acetylation of phenol derivative assisted by $Sc(OTf)_3$[3e] or Me_3SiOTf[3f] (entry 1). With 2,6-dimethylphenol, however, a complex mixture of products was formed indicating that acetylation on the benzene ring had occurred due to strong $Bi(OTf)_3$ Lewis acidity. Exposure of primary alcohols bearing functions such as THP **15**, TBS **16**, and trifluoroacetyl group **17** to Ac_2O in the presence of $Bi(OTf)_3$ at 25 °C afforded the desired acetates in the yields of 79, 72, and 88% (entries 2, 3, and 4). It is noteworthy that such acid-sensitive functional groups as THP and TBS can survive even though the yields are somewhat moderate (entries 2 and 3). Acetal-protected sugar **18** was also smoothly acetylated in THF to provide the corresponding triacetate in 96% yield, with the acetal function being untouched (entry 5). It was reported that Me_3SiOTf is not applicable to acetylation of sugar having acetal function.[3f] In $Bi(OTf)_3$-catalyzed acetylation of **18**, the addition of donor solvent was crucial, and the usages of solvents possessing less donating ability gave rise to decomposition of the products (entries 6 and 7). Treatment of steroidal compounds such as cholesterol (**19**) and methly cholate (**20**) yielded mono- and triacetate, respectively, in quantitative yields (entries 8 and 9). Remarkably, in the case of cholate **20**, $Bi(OTf)_3$-catalyzed acetylation of the sterically demanding 12α-hydroxy group proceeded quite smoothly in contrast to the prolonged heating in pyridine−Ac_2O.[10]

Acetylation of tertiary alcohols is considered as one of the most difficult transformations due to a large steric hindrance around the tertiary hydroxy group. Actually, somewhat vigorous reaction conditions were necessary for DMAP-catalyzed acetylation of tertiary alcohols. By contrast, $Bi(OTf)_3$ protocol has proven to be a powerful tool to acetylate various types of tertiary alcohols under milder conditions as presented in Table 4. 1-Adamantanol (**21**) was the first choice of tertiary alcohol. With $Bi(OTf)_3$, the 0.01 mol % catalyst loading allowed rapid acetylation of **21** (entry1). With other metal triflates such as $Sc(OTf)_3$ and Me_3SiOTf, the reaction went smoothly only in dry solvents (entries 2 and 4), and, otherwise, the yields of acetates was unsatisfactory (entry 3). DMAP was not capable of completing acetylation in 24 h (entry 5). 2-Methyl-1-phenylpropan-2-ol (**22**) in acetic anhydride was converted to the acetate in the presence of not only $Bi(OTf)_3$ but also $Sc(OTf)_3$ or $ZnCl_2$ (entries 6, 7, and 8), though acetylation of **22** by DMAP proceeded only sluggishly to give an unsatisfactory result (entry 9). In acid-catalyzed acetylation of 2-methyldodecan-2-ol (**23**) at 25 °C, the $Bi(OTf)_3$ protocol afforded the best result although the formation of tridecene could not be avoided completely (entries 10−13). Acetylation of **23** utilizing basic catalysts such as Bu_3P and DMAP was also not so efficient for practical use (entries 14 and 15). The $Bi(OTf)_3$ could be applied to propargylic alcohols. When 1-ethynylcyclohexan-1-ol (**24**) and 1-(2-phenylethynyl)cyclohexan-1-ol (**25**) were subjected to the $Bi(OTf)_3$-catalyzed acetylation, the desired acetates were obtained in 94% and 81% yields, respectively, even at 25 °C (entries 16 and 21). It has been reported that under catalysis of $Sc(OTf)_3$ and Me_3SiOTf, acetylation of tertiary propargyl alcohols should be carried out below 0 °C.[3e,f] In fact, acetylation of **24** and **25** executed with $Sc(OTf)_3$ and Me_3SiOTf at 25 °C produced a large amount of elimination products resulting in lower yields (entries 17, 18, and 22). With Bu_3P, acetylation proceeded only sluggishly to furnish a mixture of the desired acetate and starting alcohol (entries 19 and 23). The DMAP-catalyzed acetylation of propargyl alcohols also proceeded slowly, and

(10) Hofle, G.; Steglich, W. *Synthesis* **1972**, 619.

Table 4. Acetylation of Tertiary Alcohol[a]

R−OH + Ac_2O $\xrightarrow[\text{conditions}]{\text{catalyst}}$ R−OAc

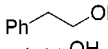
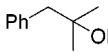
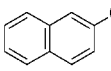
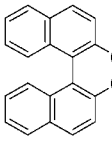
		conditions			
entry	alcohol	cat/mol%	cosolv/mL	time/h	yield/%[b]
1	1-Adamantanol	$Bi(OTf)_3$/0.01	none	6	98
2[c]	(**21**)	$Sc(OTf)_3$/0.5	MeCN/1	8.5	99
3[c]		$Sc(OTf)_3$/0.5	MeCN[d]/1	8.5	87
4[e]		Me_3SiOTf/2.0	CH_2Cl_2/3	3.5	94
5		DMAP/10	pyridine/3	24	75[f]
6		$Bi(OTf)_3$/0.5	THF/1	2	98
7	(**22**)	$Sc(OTf)_3$/0.5	MeCN/5	3	92
8		$ZnCl_2$/10	CH_2Cl_2/5	20	92
9		DMAP/10	pyridine/3	24	60[g]
10		$Bi(OTf)_3$/0.5	THF/5	8	75[h]
11[i]	(**23**)	$Sc(OTf)_3$/1.0	MeCN/3	1	68[h]
12		$ZnCl_2$/10	CH_2Cl_2/5	20	62[h]
13		Me_3SiOTf/10	CH_2Cl_2/3	2	62[h]
14		Bu_3P/10	CH_2Cl_2/3	23	1[h,j]
15		DMAP/100	pyridine/3	16	35
16		$Bi(OTf)_3$/0.5	MeCN[d]/2	4	94
17		$Sc(OTf)_3$/0.5	MeCN/2	4	88
18		Me_3SiOTf/10	CH_2Cl_2/3	2	62
19	(**24**)	Bu_3P/10	CH_2Cl_2/3	19	24[k]
20		DMAP/150	pyridine/3	17	72
21		$Bi(OTf)_3$/0.5	THF/2	2	81
22		$Sc(OTf)_3$/0.05	MeCN/5	5	67
23		Bu_3P/10	CH_2Cl_2/2.5	16	55[l]
24	(**25**)	DMAP/10	pyridine/3	18	85
25		$Bi(OTf)_3$/3.0	MeCN/3	1	96[h]
26		$Sc(OTf)_3$/0.5	MeCN/0.5	5	87[h]
27	(**26**)	Bu_3P/10	CH_2Cl_2/1	20	2[h,m]
28		DMAP/10	pyridine/3	17	0[n]
29		$Bi(OTf)_3$/0.5	THF/1	5	91
30		$Sc(OTf)_3$/1.0	MeCN/1	4.5	88
31	(**27**)	DMAP/150	pyridine/3	12	48
32		$Bi(OTf)_3$/0.5	THF/3	12	80
	(**28**)				

[a] Reaction conditions: alcohol (1.0 mmol), acetic anhydride (10 equiv), 25 °C. [b] GC yield. [c] At 0 °C. [d] The wet solvent was used. [e] Ac_2O (1.5 equiv). [f] The alcohol (11%) remained intact. [g] The alcohol (33%) remained intact. [h] Isolated yield. [i] Ac_2O (3.0 equiv). [j] The alcohol (67%) remained intact. [k] The alcohol (55%) remained intact. [l] The alcohol (25%) remained intact. [m] The alcohol (93%) remained intact. [n] Alcohol was consumed.

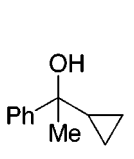
in these cases, 1.5 equiv of DMAP or prolonged reaction period were crucial for reaching a practical level of yield (entries 20 and 24). It also should be noted that the present protocol allowed a tertiary alcohol **26** having a β-chlorine to be acetylated even at 25 °C without significant elimination (entry 25). On the other hand, $Sc(OTf)_3$ was not so potent as $Bi(OTf)_3$ (entry 26), and Bu_3P showed no catalysis with 93% of the starting alcohol **26** recovered (entry 27). This aldol substrate **26** is sensitive toward base as well as acids: for instance, the conventional DMAP/Ac_2O acetylation protocol was not found to be applicable (entry 28). In the case of homoallyl tertiary alcohol **27**, the yields with bismuth and scandium triflates were comparable (entries 29 and 30), but even 1.5 equiv of DMAP were not sufficient for clear acetylation of **27** (entry 31). Linalool (**28**) underwent acetylation at 25 °C to provide linalyl acetate quantitatively without any concomitant formation of a migration product, geranyl acetate (entry 32). However, it was reported that the attempted acetylation of linalool under catalysis of $Sc(OTf)_3$ at −20 °C gave rise to a mixture of the desired acetate (68%) and geranyl acetate (8%)[3e] and that Me_3SiOTf gave rise to a mixture of the desired acetate and the starting alcohol at −10 °C.[3f] On the other hand, catalysis by DMAP is ineffective, and even upon treatment of **28** with an excess amount of DMAP in Ac_2O/Et_3N, it takes 14 h at room temperature to go to completion (80% isolated yield). Despite such versatility of $Bi(OTf)_3$/Ac_2O acetylation method, neither cyclopropyl **29** nor diphenyl tertiary alcohol **30** was not employable inducing a complicated mixture of unidentified compounds.

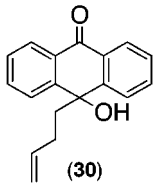
Table 5. Benzoylation of Alcohols by Use of $Bi(OTf)_3$ and $(PhCO)_2O$[a]

R−OH + $(PhCO)_2O$ $\xrightarrow[\text{conditions}]{Bi(OTf)_3}$ R−OCOPh

		conditions			
entry	alcohol	cat/mol%	anhydride/eq	time/h	yield/%[b]
1	 (**1**)	1.0	1.5	24	90
2	 (**31**)	1.0	1.5	22	99
3	 (**2**)	1.0	1.5	24	0[c]
4	 (**3**)	5.0	1.5	8	2[d]
5	 (**22**)	5.0	5.0	48	0[c]
6[e]	 (**32**)	1.0	1.5	1	98, 88[f]
7[e]	 (**33**)	1.0	3.0	1	90[f,g]
8[e]	 (**34**)	1.0	3.0	1	98[f,g]

[a] Reaction conditions: alcohol (1.0 mmol), CH_2Cl_2 (3 mL), 25 °C. [b] GC yield. [c] Alcohol was consumed. [d] The alcohol (83%) remained. [e] Reaction was carried out using wet CH_2Cl_2 in the air. [f] Isolated yield after benzoylation in wet CH_2Cl_2 followed by addition of MeOH (wet, 10 mL) and heating under reflux for 8 h. [g] Only dibenzoate was obtained.

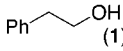
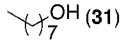
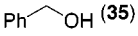
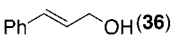
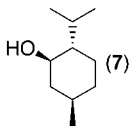
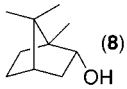
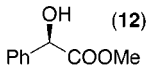
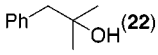

(**29**)


(**30**)

The $Bi(OTf)_3$/acid anhydride protocol was further extended to benzoylation at 25 °C (Table 5). The reaction of primary alcohols such as **1** and **31** with 1.5 equiv of $(PhCO)_2O$ in the presence of 1.0 mol % of $Bi(OTf)_3$ provided the desired benzoates in 90% and 99% yield, respectively, where CH_2Cl_2 could be used without purification (entries 1 and 2). With secondary benzyl alcohol **2** and tertiary alcohol **22**, the expected benzoates were not obtained but instead, complex mixtures involving elimination products were furnished (entries 3 and 5).

Table 6. Pivaloylation of Alcohols[a]

R−OH + *t*-BuCOX $\xrightarrow{\text{catalyst}}$ R−OCO*t*-Bu

		conditions				
entry	alcohol	cat/mol%	$(t\text{-BuCO})_2O$/eq	cosolv/mL	time/h	yield/%[b]
1	 (**1**)	$Bi(OTf)_3$/3.0	1.5	CH_2Cl_2/3	4	96
2		$Sc(OTf)_3$/3.0	1.5	MeCN/3	4	79[c]
3		TMSOTf/10.0	1.5	CH_2Cl_2/3	1	75
4		DMAP/150	1.5	pyridine/1	7	74
5	 (**31**)	$Bi(OTf)_3$/3.0	3.0	CH_2Cl_2/3	4	98
6	 (**3**)	$Bi(OTf)_3$/3.0	3.0	CH_2Cl_2/3	4	97
7		$Sc(OTf)_3$/3.0	3.0	MeCN/3	8	93[c]
8	 (**2**)	$Bi(OTf)_3$/3.0	1.5	THF/3	4	95[c]
9		$Sc(OTf)_3$/3.0	3.0	MeCN/3	4	84[c]
10	 (**35**)	$Bi(OTf)_3$/3.0	3.0	CH_2Cl_2/3	4	76
11		DMAP/150	3.0	pyridine/1	6	69
12	 (**36**)	$Bi(OTf)_3$/3.0	3.0	CH_2Cl_2/3	3	1
13		DMAP/150	3.0	pyridine/1	6	1
14	 (**7**)	$Bi(OTf)_3$/3.0	1.5	CH_2Cl_2/3	4	98
15		$Sc(OTf)_3$/3.0	3.0	MeCN/3	4	97[c]
16		$Bi(OTf)_3$/3.0	3.0[d]	CH_2Cl_2/3	4	93[e]
17		$Sc(OTf)_3$/3.0	3.0[d]	MeCN/3	4	97[e]
18		DMAP/10.0	3.0[d]	pyridine/3	4	97[e]
19	 (**8**)	$Bi(OTf)_3$/3.0	1.5	CH_2Cl_2/3	4	97
20		$Bi(OTf)_3$/3.0	2.0[d]	CH_2Cl_2/3	4	91[e]
21	 (**12**)	$Bi(OTf)_3$/3.0	1.5	CH_2Cl_2/3	4	95[e]
22		$Sc(OTf)_3$/3.0	1.5	MeCN/3	4	98[e]
23		Me_3SiOTf/10.0	1.5	CH_2Cl_2/3	5	96[e]
24		$MgBr_2$/200, NEt_3/300	2.0	CH_2Cl_2/3	6	97[e]
25		DMAP/10.0	1.5	pyridine/3	24	72[e]
26		$Bi(OTf)_3$/3.0	1.5[d]	CH_2Cl_2/3	4	97[e]
27	1-Adamantanol (**21**)	$Bi(OTf)_3$/3.0	1.5	CH_2Cl_2/3	4	93
28	 (**22**)	$Bi(OTf)_3$/3.0	3.0	CH_2Cl_2/3	5	0

[a] Pivaloylation was done at 25 °C according to the conditions described in the table. When anhydride was employed, after pivaloylation, methanol (10 mL) was added and the mixture was stirred at 50 °C for 7 h in order to consume the remaining anhydride. After usual aqueous workup, filtration through a thin pad of silica gel gave a pure compound. [b] Isolated yield. [c] GC yield without decomposition of anhydride by methanol. [d] Pivaloyl chloride was used instead of anhydride. [e] Isolated yield without decomposition of remaining pivalating reagent by methanol.

Benzoylation of **3** assisted by $Bi(OTf)_3$ was sluggish, and thus 83% of **3** was recovered after 8 h (entry 4). In remarkable contrast with aliphatic alcohols, phenol derivatives underwent quite smooth benzoylation in 1 h (entries 6−8). In these cases, although benzoylation itself took place cleanly, benzoic anhydride still remaining in the reaction mixture often prevented easy isolation of the product because of the similar R_f values of the product and anhydride. Benzoic anhydride is stable enough to survive upon usual aqueous workup. To overcome this problem, after completion of benzoylation, methanol was added to consume the remaining anhydride in the reaction mixture. Methyl benzoate generated therein could be more easily separated from the product. This in situ decomposition procedure[11] is applicable to a variety of aromatic alcohol such as β-naphthol (**32**), catechol (**33**), and binaphthol (**34**), the hydroxy groups of which are fairly sterically hindered, and, in all cases, the desired benzoates can be isolated easily by column chromatography on silica gel (entries 6−8). This benzoylation occurred for 2,4,6-trimethylphenol (**14**) despite of steric hindrance around hydroxyl group. However, the benzoate of **14** and methyl benzoate derived from the reaction of benzoic anhydride with methanol have considerably similar R_f values to prevent purification of the product again. We examined the $Bi(OTf)_3$-promoted benzoylation of acid-labile primary alcohols such as geraniol (**4**) and furfuryl alcohol (**5**), but all attempts failed only to afford a complex mixture of products. When benzoyl chloride was utilized as a benzoylating reagent, it was found that the chloride was not as effective as the anhydride because the hydrogen chloride generated upon the benzoylation might have promoted elimination of the benzoate formed.

Pivalate is one of the most stubborn protecting groups due to its steric hindrance. Such steric bulkiness causes difficulty in introduction of pivaloyl group on alcohols. In this context, we examined the activity of $Bi(OTf)_3$ for pivalation. The results along with those of some other representative methods for comparison are shown in Table 6. When 2-phenethyl alcohol (**1**) in dichloromethane was treated with 1.5 equiv of pivaloic anhydride in the

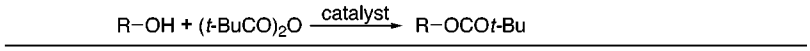
(11) Although the methanolysis technique for unreacted acylating reagent was reported by Procopiou (see ref 3f), this technique was effective in the $Bi(OTf)_3$ acylation protocol as well. However, when Me_3SiOTf/acylation−methanolysis protocol was applied to pivalation by ourselves, unfortunately, we failed to obtain reproducible results probably due to the sensitivity of Me_3SiOTf to moisture (vide infra).

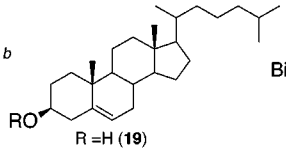
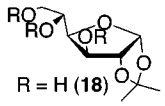
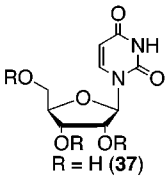
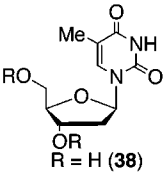
presence of 3.0 mol % of $Bi(OTf)_3$, the pivalation proceeded smoothly to completion in 4 h. As was the case for the benzoylation, it required tedious manipulation to separate the pivalate from the remaining pivaloic anhydride in the crude products on account of their close R_f values. Therefore, the consumption of the rest of pivaloic anhydride was tested through methanolysis. It follows that pivalation and subsequent addition of methanol realized smooth isolation, namely, filtration of crude products through a thin pad of silica gel with hexane afforded pure 2-phenethyl pivalate in 96% yield (entry 1). For the $Bi(OTf)_3$ protocol, CH_2Cl_2 and MeOH could be used without dehydration. With other catalysts, however, pivalation utilizing anhydride was sluggish in wet solvent only to give unsatisfactory results. The $Sc(OTf)_3$ and Me_3SiOTf catalysts showed remarkable acceleration of pivalation allowing the reaction to finish in a few hours, but upon decomposition of the remaining pivalating reagents, the product was observed to decompose slowly (entries 2 and 3).[11] Basic promoter DMAP was not so effective despite 150 mol % loading and a longer reaction time (entry 4). In the cases of octanols **31** and **3**, the $Bi(OTf)_3$ protocol furnished the desired pivalates in 98% and 97% yields, respectively (entries 5 and 6). With $Sc(OTf)_3$, however, the pivalate was decomposed upon treatment with methanol (entry 7). It was disclosed that pivalation of benzylic and cinnamyl alcohols (**2**, **35**, and **36**) was difficult due to instability of the alcohols and/or pivalates in our protocol. The pivalate of **2** underwent elimination in methanol at 50 °C, and therefore the pivalation/methanol-assisted consumption method described above was not suitable for **2** regardless of catalysts employed (entries 8 and 9). Transformation of benzyl alcohol **35** both by use of $Bi(OTf)_3$ and DMAP gave the desired pivalate in moderate yields (entries 10 and 11). The $Bi(OTf)_3$- or DMAP-assisted pivalation of cinnamyl alcohol **36** was not successful, as could be explained in terms of innate labile nature of **36** under both acidic and basic conditions (entries 12 and 13). The $Bi(OTf)_3$-assisted pivalation could be realized for sterically hindered or functionalized secondary alcohols. Menthol (**7**) was cleanly pivalated by catalysis of $Bi(OTf)_3$ even in wet CH_2Cl_2, to give a 98% yield of the pivalate (entry 14). Although the use of $Sc(OTf)_3$ and $(t\text{-BuCO})_2O$ effected pivalation of **7**, MeCN had to be dehydrated before use (entry 15). Notably, for pivalation of **7**, *t*-BuCOCl was also employable (entries 16−18). The $Bi(OTf)_3$-assisted reaction of **7** with *t*-BuCOCl could be performed in wet solvent without loss of catalytic efficiency (entry 16). In the pivalation using the chloride, the methanolysis of the crude products was no longer necessary because the R_f values of the pivalate esters and the chloride were different enough to separate them easily by means of chromatography. Borneol (**8**) did not show any problem on $Bi(OTf)_3$-catalyzed pivalation to provide good yields in both cases using the chloride and anhydride (entries 19 and 20). In the reaction of methyl mandelate (**12**) with pivalic anhydride, the methanol-decomposition step was unnecessary because the polar methoxy carbonyl function allowed easy separation of the pivalate from the anhydride by column chromatography on silica gel (entry 21). The pivalate of **12** obtained in entry 21 proved to keep the original optical purity by means of chiral HPLC analysis. Pivalation of alcohol **12** was also promoted by other Lewis acids such as $Sc(OTf)_3$, Me_3SiOTf, and $MgBr_2/Et_3N$ and Lewis base such as DMAP (entries 22−25). These Lewis acids necessitated anhydrous conditions while longer reaction time was demanded for DMAP. Pivaloyl chloride as well as anhydride was employable for pivalation catalyzed by $Bi(OTf)_3$ (entry 26). The pivalation of tertiary alcohols were dependent on the substrate. Thus, 1-adamantanol (**21**) underwent smooth pivalation (entry 27) whereas 2-methyl-1-phenylpropan-2-ol (**22**) suffered elimination under the standard reaction conditions described above (entry 28).

These results led us to apply $Bi(OTf)_3/(t\text{-BuCO})_2O$ protocol to functionally and sterically diverse alcohols such as steroids, sugars, and nucleosides as shown in Table 7. When cholesterol (**19**) was treated with 1.5 equiv of $(t\text{-BuCO})_2O$ in the presence of $Bi(OTf)_3$, pivalation proceeded quite smoothly. The subsequent reaction of the remaining $(t\text{-BuCO})_2O$ with MeOH and subjecting the crude mixture to column chromatography on silica gel provided cholesteryl pivalate in 97% isolated yield (entry 1).[11] Subjection of 1,2-*O*-isopropylidene-D-glucofuranose (**18**) to the $Bi(OTf)_3$ protocol provided the desired product, of which three hydroxyl groups had been pivalated even in wet CH_2Cl_2 (entry 2). Although $Sc(OTf)_3$ and DMAP were also employable to pivalate **18**, they had serious drawbacks, respectively. As described before, $Sc(OTf)_3$ was unable to consume pivalic anhydride efficiently without loss of the product upon treatment with MeOH, and thus Kuhgelrohr distillation before column chromatography was crucial to separate the product from pivalic anhydride (entry 3). The DMAP-catalyzed pivalation must be carried out at 50 °C, and further addition of 1 equiv of catalyst and a long reaction period were necessitated upon the decomposition step of pivalic anhydride (entry 4). Uridine (**37**) and thymidine (**38**) were transformed to the desired pivalates in the presence of $Bi(OTf)_3$, $Sc(OTf)_3$, or DMAP, and the subsequent column chromatography provided the corresponding pivalates in pure forms (entries 5−9). It should be mentioned again that only $Bi(OTf)_3$ was effective to catalyze pivalation in wet solvents.

In conclusion, a powerful and versatile acylation method by virtue of $Bi(OTf)_3$ catalysis has been developed. This method includes a lot of unique merits, namely, a cheap and easy-to-handle catalyst, operational simplicity and no need for absolutely dry reaction conditions. Workup and isolation of the product are quite easy: $Bi(OTf)_3$ is removable at ease by washing with water, and often a simple filtration through a thin pad of silica gel of the crude products furnished pure acylated products. Although a slight excess amount of acylating reagent should be used for complete conversion of the alcohol in question, it sometimes causes tedious separation of the acylation product from the remaining acylating reagent. To overcome such an obstacle, methanolysis technique has been applied. Addition of methanol after completion of acylation transforms the remaining acylating reagent to methyl ester which is separable from the desired acylation products. Although this technique is particularly useful for $Bi(OTf)_3$/anhydride protocol, addition of methanol induces decomposition of the acylated product in the cases of $Sc(OTf)_3$ and Me_3SiOTf. For the DMAP protocol, transformation of the remaining anhydride with methanol is too slow for practical use. Although the catalyst $Bi(OTf)_3$ is highly active for acylation, a variety of functions can survive. For acylation of acid-labile alcohols, addition of coordinating solvent

Table 7. Pivaloylation of Sugar and Nucleoside by Use of $(t\text{-BuCO})_2O$



		conditions				
entry	substrate	cat/mol%	$(t\text{-BuCO})_2O$/eq	cosolv/mL	time/h	yield/%[a]
1[b]	 R =H (**19**)	$Bi(OTf)_3$/3.0	1.5	CH_2Cl_2/3	5	97
2[b]	 R = H (**18**)	$Bi(OTf)_3$/3.0	4.5	CH_2Cl_2/3	7	91
3[c]		$Sc(OTf)_3$/3.0	4.5	MeCN/3	6	92
4[d]		DMAP/10	4.5	pyridine/3	32	97
5	 R = H (**37**)	$Bi(OTf)_3$/3.0	4.5	CH_2Cl_2/3	20	98
6		$Sc(OTf)_3$/3.0	9	MeCN/3	24	90
7	 R = H (**38**)	$Bi(OTf)_3$/3.0	3	CH_2Cl_2/3	24	98
8		TMSOTf/10	3	CH_2Cl_2/3	24	96
9		DMAP/10	4	pyridine/3	24	92

[a] Isolated yield. [b] Pivaloylation was done at 25 °C according to the conditions described in the table. After pivaloylation, methanol (10 mL) was added and the mixture was stirred at 50 °C for 16 h in order to consume anhydride remaining. [c] After pivalation, Kuhgelrohr distillation followed by column chromatography on silica gel gave the desired pivalate. [d] After pivalation, DMAP (1.0 equiv) and methanol (10 mL) were added, and the mixture was stirred at 50 °C for 16 h.

allows to subtly tune the Lewis acidity of $Bi(OTf)_3$ realizing smooth acetylation of functionalized tertiary alcohol as well. Even linalool, which is quite sensitive to acid, is acylated by $Bi(OTf)_3/Ac_2O$/THF protocol at room temperature.

Experimental Section

General. All reactions of acylation under anhydrous conditions were carried out under an atmosphere of nitrogen with freshly distilled solvents under anhydrous conditions, unless otherwise noted. Acylation in wet solvent was carried out in the air. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl. Other solvents such as CH_2Cl_2, MeCN, toluene, Et_3N, and pyridine were distilled from CaH_2. NMR spectra were recorded at 25 °C. Mass spectra were recorded in EI (electron ionization). Silica gel (Daiso gel IR-60) was used for column chromatography. $Bi(OTf)_3$ was prepared according to the literature method.[5] Other catalysts such as $Sc(OTf)_3$, TMSOTf, $ZnCl_2$, $MgBr_2$, DMAP, and Bu_3P were commercially available. Acylating reagents such as acetic, benzoic, and pivalic anhydride and benzoyl and pivaloyl chloride were commercially available and used without purification. Alcohols such as **1**−**9**, **11**−**14**, **18**, **19**, **21**, **22**, **24**, **28**, and **31**−**38** were commercially available. $(C_7H_{15})_2CHOH$ (**6**) was prepared by DIBALH reduction of 8-pentadecanone. Alcohols **15**, **16**, and **17** were prepared by treatment of the corresponding diol with dihydropyran, TBSCl, and trifluoroacetic anhydride, respectively.[1] Triol **20** was prepared from cholic acid and methyl iodide by CsF-catalyzed methylation in DMF.[12] 2-Methyl-2-dodecanol (**23**) was prepared from 2-dodecanone and methylmagnesium bromide. Propargyl alcohol (**25**) was synthesized by reaction of cyclohexanone with magnesiumphenyl acetylide prepared from phenylacetylene and methylmagnesium bromide. Homoallyl alcohol (**27**) was prepared from the reaction of phenylbutanone with allylmagnesium bromide. Other alcohols were prepared according to literature methods: **10**,[13] **26**,[14] **29**,[15] and **30**.[16] The following acetates are commercially available: **1**, **4**, **5**, **7**, **8**, **19**, and **28**. The following alcohols have been reported as acylated forms: acetate; **2**,[4] **3**,[4] **9**,[17] **11**,[18] **12**,[19] **13**,[20] **14**,[10] **15**,[4] **16**,[4] **20**,[10] **21**,[21] **22**,[22] **24**,[3e] and **25**:[23] benzoate; **1**,[24] **31**,[25] **32**,[26] **33**[3e] and **34**:[27] pivalate; **1**,[28] **2**,[29] **3**,[30] **7**,[17] **8**,[31] **19**,[32] **21**,[33] **31**,[25] **35**,[34] and **38**.[35]

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$Bi(OTf)_3$-Catalyzed Acetylation in Ac_2O (representative procedure). To a round-bottomed flask were added acetic anhydride (8.4 mL, 89 mmol), 2-phenethyl alcohol (1.22 g, 10.0 mmol), and an acetic anhydride solution (1.0 mL) of $Bi(OTf)_3$, which had been prepared from $Bi(OTf)_3$ (7.3 mg, 0.01 mmol, calculated as the tetrahydrate) and Ac_2O (10 mL), and the mixture was stirred at 25 °C for 10 min. After ethyl acetate and $NaHCO_3$aq had been added, organic and aqueous layers were separated. The aqueous layer was extracted with ethyl acetate three times, and the organic layers were combined and dried over $MgSO_4$. GC analysis of the crude mixture showed the formation of 2-phenethyl acetate in 98% yield.

$Bi(OTf)_3$-Catalyzed Acetylation in CH_2Cl_2 (representative procedure). A CH_2Cl_2 solution (10 mL, not purified and wet) of 2-phenethyl alcohol (1.22 g, 10.0 mmol) and Ac_2O (1.4 mL, 15.0 mmol) was stirred at 25 °C in the presence of $Bi(OTf)_3$ (36.4 mg, 0.5 mol %, calculated as the tetrahydrate) for 4 h. After ethyl acetate and $NaHCO_3$aq had been added, organic and aqueous layers were separated. The aqueous layer was extracted with ethyl acetate three times, and the organic layers were combined and dried over $MgSO_4$. GC analysis of the crude mixture showed the formation of 2-phenethyl acetate in 92% yield.

$Bi(OTf)_3$-Catalyzed Acetylation in THF (representative procedure). To a flame-dried round-bottomed flask were added THF (0.5 mL), furfuryl alcohol (98.1 mg, 1.0 mmol), Ac_2O (0.94 mL, 10.0 mmol), and $Bi(OTf)_3$ (0.36 mg, 0.05 mol %, calculated as the tetrahydrate). The mixture was stirred at 25 °C for 4 h. After ethyl acetate and $NaHCO_3$aq had been added, organic and aqueous layers were separated. The aqueous layer was extracted with ethyl acetate three times, and the organic layers were combined and dried over $MgSO_4$. GC analysis of the crude mixture showed the formation of furfuryl acetate in 93% yield.

$Sc(OTf)_3$-Catalyzed Acetylation in MeCN (representative procedure). To a flame-dried round-bottomed flask were added MeCN (0.5 mL) and furfuryl alcohol (98.1 mg, 1.0 mmol). In another dried flask was prepared an acetic anhydride solution (10 mL) of $Sc(OTf)_3$ (26.2 mg, 0.053 mmol), and 1 mL of this solution was diluted to 10 mL by acetic anhydride. The acetic anhydride solution (0.94 mL) of $Sc(OTf)_3$ (0.25 mg, 0.05 mol %) thus prepared was added to the former reaction vessel, and the mixture was stirred at 25 °C for 5 h. After ethyl acetate and $NaHCO_3$aq had been added, organic and aqueous layers were separated. The aqueous layer was extracted with ethyl acetate three times, and the organic layers were combined and dried over $MgSO_4$. GC analysis of the crude mixture showed the formation of furfuryl acetate in 67% yield.

Me_3SiOTf-Catalyzed Acetylation in CH_2Cl_2 (representative procedure). To a flame-dried round-bottomed flask were added CH_2Cl_2 (2.5 mL) and furfuryl alcohol (98.1 mg, 1.0 mmol). In another dried flask was prepared an acetic anhydride solution (10 mL) of Me_3SiOTf (0.26 mL, 1.4 mmol). The acetic anhydride solution (0.14 mL) of Me_3SiOTf (0.0036 mL, 2.0 mol %) was added to the former reaction vessel at 0 °C, and the mixture was stirred at the temperature for 4 h. After ethyl acetate and $NaHCO_3$aq had been added, organic and aqueous layers were separated. The aqueous layer was extracted with ethyl acetate three times, and the organic layers were combined and dried over $MgSO_4$. GC analysis of the crude mixture showed the formation of furfuryl acetate in 49% yield.

Bu_3P-Catalyzed Acetylation in CH_2Cl_2 (representative procedure). To a flame-dried round-bottomed flask were added CH_2Cl_2 (5.0 mL), furfuryl alcohol (98.1 mg, 1.0 mmol), and Ac_2O (0.94 mL, 10.0 mmol). Bu_3P (20.2 mg, 10.0 mol %) was added by a syringe at 25 °C, and the reaction mixture was stirred at the temperature for 12 h. After ethyl acetate and $NaHCO_3$aq had been added, organic and aqueous layers were separated. The aqueous layer was extracted with ethyl acetate three times, and the organic layers were combined and dried over $MgSO_4$. GC analysis of the crude mixture showed the formation of furfuryl acetate in 97% yield.

DMAP-Catalyzed Acetylation in Pyridine (representative procedure). To a flame-dried round-bottomed flask were added pyridine (3.0 mL), ethyl (*S*)-lactate (118.1 mg, 1.0 mmol), Ac_2O (0.94 mL, 10.0 mmol), and DMAP (12.2 mg, 10 mol %), and the reaction mixture was stirred at 25 °C for 24 h. After ethyl acetate and $NaHCO_3$aq had been added, organic and aqueous layers were separated. The aqueous layer was extracted with ethyl acetate three times, and the organic layers were combined and dried over $MgSO_4$. GC analysis of the crude mixture showed the formation of furfuryl acetate in quantitative yield.

$ZnCl_2$-Catalyzed Acetylation in CH_2Cl_2 (representative procedure). To a flame-dried round-bottomed flask were added CH_2Cl_2 (5.0 mL), 2-methyl-1-phenylpropan-2-ol (150.2 mg, 1.0 mmol), Ac_2O (0.94 mL, 10.0 mmol), and $ZnCl_2$ (13.6 mg, 10.0 mol %), and the reaction mixture was stirred at 25 °C for 20 h. After ethyl acetate and $NaHCO_3$aq had been added, organic and aqueous layers were separated. The aqueous layer was extracted with ethyl acetate three times, and the organic layers were combined and dried over $MgSO_4$. GC analysis of the crude mixture showed the formation of 2-acetoxy-2-methyl-1-phenylpropane in 92% yield.

Acetate of 10: ^{1}H NMR ($CDCl_3$) δ 1.91 (s, 3H), 2.45 (s, 3H), 2.90 (d, J = 17.3 Hz, 1H), 3.08 (dd, J = 17.3, 5.0 Hz, 1H), 4.97 (dd, J = 10.3, 5.0 Hz, 1H), 5.05−5.10 (m, 1H), 5.20−5.30 (br, 1H), 7.15−7.30 (m, 4H), 7.33 (d, J = 7.9 Hz, 2H), 7.81 (d, J = 7.9 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 20.9, 21.5, 37.4, 59.4, 74.8, 124.2, 125.0, 126.9, 127.4, 128.7, 129.9, 137.8, 138.6, 139.6, 143.9, 169.8; elemental analysis calcd (%) for $C_{18}H_{19}NO_4S$: C 62.59, H 5.54, N 4.06; found C 62.48, H 5.64, N 4.03.

Acetate of 17: ^{1}H NMR ($CDCl_3$) δ 1.30−1.47 (m, 8H), 1.55−1.69 (m, 2H), 1.70−1.80 (m, 2H), 2.03 (s, 3H), 4.05 (t, J = 6.8 Hz, 2H), 4.36 (t, J = 6.8 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 20.4, 25.2, 25.5, 27.8, 28.3, 28.7, 28.8, 64.1, 67.9, 114.4 ($^1J_{C-F}$ = 284 Hz), 157 ($^2J_{C-F}$ = 41 Hz), 170.7. HRMS (EI) Found: *m*/*z* 284.1228. Calcd for $C_{12}H_{19}O_4F_3$: 284.1235.

Acetate of 18: ^{1}H NMR ($CDCl_3$) δ 1.32 (s, 3H), 1.53 (s, 3H), 2.02 (s, 3H), 2.07 (s, 6H), 4.12 (dd, J = 5.5, 12.2 Hz, 1H), 4.42 (dd, J = 2.9, 9.3 Hz, 1H), 4.49 (d, J = 3.6 Hz, 1H), 4.57 (dd, J = 2.4, 12.2 Hz, 1H), 5.17−5.26 (m, 1H), 5.35 (d, J = 2.9 Hz, 1H), 5.93 (d, J = 3.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 20.7 (3C), 26.2, 26.7, 63.4, 67.5, 74.7, 76.7, 83.2, 105.1, 112.5, 169.2, 169.7, 170.6; elemental analysis calcd (%) for $C_{15}H_{22}O_9$: C 52.02, H 6.40; found C 51.81, H 6.69.

Acetate of 23: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, J = 7.0 Hz, 3H), 1.15−1.30 (m, 18H), 1.42 (s, 6H), 1.97 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 13.9, 22.1, 22.5, 23.7, 25.8, 29.2, 29.4, 29.5, 29.7, 29.8, 31.8, 40.6, 82.1, 170.0; elemental analysis calcd (%) for $C_{15}H_{30}O_2$: C 74.32, H 12.47; found C 74.09, H 12.71.

Acetate of 26: ^{1}H NMR ($CDCl_3$) δ 1.05 (d, J = 7.0 Hz, 3H), 1.80 (s, 3H), 4.54 (d, J = 11.7 Hz, 1H), 4.60 (q, J = 7.0 Hz, 1H), 4.83 (d, J = 11.7 Hz, 1H), 7.00−7.08 (m, 2H), 7.25−7.38 (m, 3H), 7.44−7.53 (m, 2H), 7.55−7.62 (m, 1H), 8.02 (d, J = 7.3 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 12.7, 21.1, 44.6, 46.8, 85.3, 125.5, 127.8, 128.0, 128.2, 128.5, 132.7, 137.1, 138.7, 168.6, 200.4; elemental analysis calcd (%) for $C_{19}H_{19}ClO_3$: C 68.98, H 5.79; found C 68.92, H 5.87.

Acetate of 27: ^{1}H NMR ($CDCl_3$) δ 1.48 (s, 3H), 1.98 (s, 3H), 1.97−2.07 (m, 1H), 2.10−2.23 (m, 1H), 2.53−2.75 (m, 4H), 5.11 (d, J = 11.5 Hz, 1H), 5.11 (d, J = 15.7 Hz, 1H), 5.71−5.86 (m, 1H), 7.15−7.20 (m, 3H), 7.25−7.31 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 22.1, 23.6, 29.9, 40.1, 42.7, 83.4, 118.3, 125.7, 128.3, 128.4, 133.0, 141.9, 170.2; elemental analysis calcd (%) for $C_{15}H_{20}O_2$: C 77.55, H 8.68; found C 77.26, H 8.70.

$Bi(OTf)_3$-Catalyzed Benzoylation of Phenethyl Alcohol (1) (representative procedure). To a flame-dried round-bottomed flask were added CH_2Cl_2 (3 mL), phenethyl alcohol (122.2 mg, 1.0 mmol), $(PhCO)_2O$ (339.3 mL, 1.5 mmol), and

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$Bi(OTf)_3$ (7.3 mg, 1.0 mol %, calculated as the tetrahydrate). The mixture was stirred at 25 °C for 24 h. After ethyl acetate and $NaHCO_3$aq had been added, organic and aqueous layers were separated. The aqueous layer was extracted with ethyl acetate three times, and the organic layers were combined and dried over $MgSO_4$. GC analysis of the crude mixture showed the formation of phenethyl benzoate in 90% yield.

$Bi(OTf)_3$-Catalyzed Benzoylation of 2-Naphthol (32) (representative procedure). A CH_2Cl_2 solution (3 mL, not purified and wet) of 2-naphthol (144.2 mg, 1.0 mmol) and $(PhCO)_2O$ (339.3 mg, 1.5 mmol) was stirred at 25 °C in the presence of $Bi(OTf)_3$ (7.3 mg, 1.0 mol %, calculated as the tetrahydrate) for 1 h. MeOH (10 mL, not purified and wet) was added, and the mixture was heated under reflux for 8 h. The mixture was evaporated, and to the crude products were added ethyl acetate (30 mL) and $NaHCO_3$aq. The organic and aqueous layers were separated, and the aqueous layer was extracted with ethyl acetate three times. The combined organic layers were dried over $MgSO_4$ and evaporated to give a mixture of products, which was subjected to column chromatography on silica gel (8:2 AcOEt/hexane) to give pure 2-naphthyl benzoate in 88% yield.

$Bi(OTf)_3$-Catalyzed Pivalation of Menthol (7) with (t-$BuCO)_2O$ (representative procedure). A CH_2Cl_2 solution (3 mL, not purified and wet) of menthol (156.3 mg, 1.0 mmol) and (t-$BuCO)_2O$ (279.5 mg, 1.5 mmol) was stirred at 25 °C in the presence of $Bi(OTf)_3$ (21.8 mg, 3.0 mol %, calculated as the tetrahydrate) for 4 h. MeOH (10 mL, unpurified and wet) was added, and the mixture was stirred at 50 °C for 7 h. The mixture was passed through a pad of silica gel with hexane, and the filtrate was evaporated. To the crude product was added ethyl acetate (30 mL), and this organic layer was washed with $NaHCO_3$ aq three times and dried ($MgSO_4$). Evaporation furnished the pure pivalate ester (98% yield, 235.6 mg).

$Bi(OTf)_3$-Catalyzed Pivalation of Menthol (7) with t-BuCOCl (representative procedure). A CH_2Cl_2 solution (3 mL, not purified and wet) of menthol (156.3 mg, 1.0 mmol) and t-BuCOCl (361.8 mg, 3.0 mmol) was stirred at 25 °C in the presence of $Bi(OTf)_3$ (21.8 mg, 3.0 mol %, calculated as the tetrahydrate) for 4 h. After ethyl acetate and $NaHCO_3$ aq had been added, organic and aqueous layers were separated. The aqueous layer was extracted with ethyl acetate three times, and the organic layers were combined and dried over $MgSO_4$. After filtration and evaporation, the obtained crude product was subjected to column chromatography on silica gel (hexane) to furnish the pure pivalate ester (93% yield, 223.6 mg).

$MgBr_2$/Et_3N-Catalyzed Pivalation of Methyl (R)-Mandelate (12) with (t-$BuCO)_2O$. A CH_2Cl_2 solution (3 mL) of methyl (R)-mandelate (166.2 mg, 1.0 mmol) and (t-$BuCO)_2O$ (372.6 mg, 2.0 mmol) was stirred at 25 °C in the presence of $MgBr_2$ (368.2 mg, 200 mol %) and Et_3N (303.6 mg, 300 mol %) for 6 h. After ethyl acetate and $NaHCO_3$ aq had been added, organic and aqueous layers were separated. The aqueous layer was extracted with ethyl acetate three times, and the organic layers were combined and dried over $MgSO_4$. After filtration and evaporation, the obtained crude product was subjected to column chromatography on silica gel (5:95 AcOEt/hexane) to furnish the pure pivalate ester (97% yield, 242.8 mg).

Pivalate of 12: ^{1}H NMR ($CDCl_3$) δ 1.29 (s, 9H), 3.70 (s, 3H), 5.89 (s, 1H), 7.36−7.41 (m, 3H), 7.45−7.50 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 27.0, 38.7, 52.5, 74.1, 127.3, 128.7, 129.0, 134.0, 169.4, 177.8; elemental analysis calcd (%) for $C_{14}H_{18}O_4$: C 67.18, H 7.25; found C 67.06, H 7.25.

Pivalate of 18: ^{1}H NMR ($CDCl_3$) δ 1.14 (s, 9H), 1.19 (s, 9H), 1.20 (s, 9H), 1.33 (s, 3H), 1.54 (s, 3H), 4.13 (dd, J = 4.0, 12.4 Hz, 1H), 4.39 (d, J = 3.7 Hz, 1H), 4.54 (dd, J = 2.9, 9.7 Hz, 1H), 4.60 (dd, J = 2.2, 12.4 Hz, 1H), 5.12−5.19 (m, 1H), 5.25 (d, J = 2.9 Hz, 1H), 5.90 (d, J = 3.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 26.2, 26.7, 26.8, 26.9, 27.0, 38.5, 38.7, 38.8, 62.2, 67.6, 74.5, 76.1, 83.1, 104.9, 112.4, 176.3, 176.7, 177.6. HRMS (EI) Found: m/z 528.3302. Calcd for $C_{28}H_{48}O_9$: 528.3298.

Pivalate of 37: ^{1}H NMR ($CDCl_3$) δ 1.20 (s, 9H), 1.25 (s, 9H), 1.26 (s, 9H), 4.26−4.35 (m, 2H), 4.43 (dd, J = 11.9, 2.9 Hz, 1H), 5.26−5.35 (m, 2H), 5.77 (dd, J = 8.2, 2.0 Hz, 1H), 6.11 (d, J = 5.7 Hz, 1H), 7.45 (d, J = 8.2 Hz, 1H), 8.88 (br, 1H); ^{13}C NMR ($CDCl_3$) δ 26.9, 27.0, 27.2, 38.8 (3C), 63.4, 70.3, 72.8, 80.8, 86.5, 103.3, 138.9, 150.0, 162.7, 177.1, 177.2, 177.8; elemental analysis calcd (%) for $C_{24}H_{36}N_2O_9$: C 58.05, H 7.31, N 5.64; found C 58.07, H 7.54, N 5.67.

Supporting Information Available: Copies of ^{13}C NMR spectra for tripivalates of **18** and **37**. This material is available free of charge via the Internet at http://pubs.acs.org.

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