SHORT PAPER

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A convenient and chemoselective acetylation and formylation of alcohols and phenols using acetic acid and ethyl formate in the presence of Bi(III) salts†

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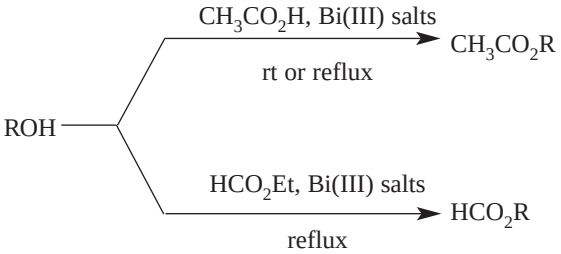
A variety of alcohols are acetylated and formylated efficiently with acetic acid and ethyl formate in the presence of catalytic amounts of Bi(III) salts such as $BiCl_3$, $Bi(TFA)_3$ and $Bi(OTf)_3$. $BiCl_3$ and $Bi(OTf)_3$ are also effective catalysts for acetylation of phenols. All of these catalysts are ineffective in formylation of phenols. Selective acetylation and formylation of alcohols in the presence of phenols is an additional advantage of this procedure.

Keywords: alcohols, phenols, bismuth salts

The acylation of alcohols is one of the most important transformations in organic chemistry since esters are useful as solvents and in making artificial flavours and essences. Many methods have already been reported for the acetylation of alcohols with acetic acid, acetyl chloride and acetic anhydride in the literature.[1-14] Formylation is also a very important process in organic chemistry and a wide variety of methods have been proposed for this purpose previously.[3,4,15-26] Due to the instability of the anhydride and the acid chloride of formic acid, formylation of alcohols by ethyl formate is an important synthetic reaction. However, some of the reported methods for the acetylation and formylation of alcohols suffer from one or more of the following disadvantages such as high temperature[2] and drastic reaction conditions,[15] the formation of undesirable or toxic byproducts,[14,23-25] expensive reagents,[4,10,13,24] hygroscopicity[25] and thermal instability of the reagents,[26] long reaction times,[5,6,14] low yields of the desired products[2,7,14] and bulk requirement of the solid bed.[8] Therefore, introduction of new methods and catalysts for the acetylation and formylation of alcohols is still in demand.

In connection with our on going work on catalysis by Bi(III) salts,[27] we now report a convenient method for the acetylation and formylation of alcohols catalysed by $BiCl_3$, $Bi(TFA)_3$ and $Bi(OTf)_3$ as non-toxic, stable and easily available catalysts (Scheme 1). $Bi(TFA)_3$ is prepared by the reaction of bismuth trichloride with silver trifluoroacetate and $Bi(OTf)_3$ is prepared by the reaction of trifluoromethanesulfonic acid with bismuth trifluoroacetate.[28]



Scheme 1

The treatment of a series of primary, secondary and tertiary alcohols with acetic acid in the presence of catalytic amounts of $BiCl_3$, $Bi(TFA)_3$ and $Bi(OTf)_3$ at room temperature or under reflux conditions afforded the corresponding acetates in excellent yields (Table 1, entries 1–16). Under the same reaction conditions, phenols, naphthols and dihydroxyl compounds are converted into the corresponding acetates and diacetates efficiently when the reaction is catalysed by $BiCl_3$ and $Bi(OTf)_3$. In the presence of $Bi(TFA)_3$, naphthols are acetylated in only 10–20% yields but phenols and dihydroxyl compounds remained unchanged in the reaction mixture (Table 1, entries 17–25).

In order to explore further the synthetic utility of this procedure, formylation of alcohols and phenols were also investigated. As shown in Table 2, a series of primary and secondary alcohols were treated with ethyl formate in the presence of Bi(III) salts under reflux conditions to afford the corresponding formates in excellent yields (Table 2, entries 1–14). Tertiary alcohols such as t-butyl alcohol remained unchanged but triphenylmethanol was formylated in 85–90 yields (Table 2, entries 15 and 16). However, these catalysts are not effective for the formylation of phenols (Table 2, entries 17–20). The experimental results show that $Bi(OTf)_3$ is more reactive than $BiCl_3$ and $Bi(TFA)_3$ in these reactions. To stress the selectivity of the described method, competitive acetylation and formylation of alcohols and phenols were also studied in the presence of these catalysts. As shown in Table 3, alcohols are acetylated and formylated selectively in the presence of phenols. Such a selectivity is of practical importance in esterification reactions.

In conclusion, we have described an efficient and selective method for acetylation and formylation of alcohols and phenols using $BiCl_3$, $Bi(TFA)_3$ and $Bi(OTf)_3$. In addition, high yields of the products, low reaction times, easy workup, stability and non-toxicity of the catalysts make this method a useful addition to the present methodologies.

Experimental

IR spectra were run on a Philips PU9716 spectrophotometer. ^{1}HNMR spectra was recorded in $CDCl_3$ solvent on a Bruker AM 80 MHz spectrometer using TMS as an internal standard. GC analysis was performed with a Shimadzu 16A gas chromatograph with a flame ionisation detector using a column of 15% Carbowax 20M Chromosorb-W 60–80 mesh. $Bi(TFA)_3$ and $Bi(OTf)_3$ were prepared according to the described procedures.[28]

Acetylation; general procedure: To a solution of substrate (1 mmol) in acetic acid (3 ml) were added the catalysts [0.1-0.2 mmol of $BiCl_3$, 0.3 mmol of $Bi(TFA)_3$ and 0.05 mmol of $Bi(OTf)_3$]. The reaction mixture was stirred at room temperature or under reflux conditions for the appropriate time according to Table 1. The progress of the reaction was monitored by GLC or TLC. Acetic acid was removed under reduced pressure and ether (20 ml) was added. The reaction mixture was washed with 5% aqueous solution of $NaHCO_3$, then with water and dried with $MgSO_4$. Evaporation of the solvent followed by

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† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

Table 1 Acetylation of alcohols and phenols with acetic acid in the presence of Bi(III) salts

Run	Substrate	Product[a]	Yield/%[b] (time/min)		
			$BiCl_3$	$Bi(TFA)_3$	$Bi(OTf)_3$
1	Benzyl alcohol	Benzyl acetate	95(60)	97(50)	99(15)[d]
2	2-Methoxybenzyl alcohol	2-Methoxybenzyl acetate	99(70)	96(60)	98(40)[d]
3	3-Methoxybenzyl alcohol	3-Methoxybenzyl acetate	95(75)	90(70)	98(20)[d]
4	2-Nitrobenzyl alcohol	2-Nitrobenzyl acetate	93(75)	91(60)	98(60)[d]
5	3-Nitrobenzyl alcohol	3-Nitrobenzyl acetate	98(70)	95(60)	98(45)[d]
6	4-Nitrobenzyl alcohol	4-Nitrobenzyl acetate	99(75)	98(70)	99(60)[d]
7	4-Chlorobenzyl alcohol	4-Chlorobenzyl acetate	98(60)	97(150)	99(35)[d]
8	4-Bromobenzyl alcohol	4-Bromobenzyl acetate	95(70)	96(180)	97(30)[d]
9	Benzoin	Benzoin acetate	95(65)	97(60)	99(60)[d]
10	Cinnamyl alcohol	Cinnamyl acetate	93(75)	85(135)	95(45)[d]
11	2-Phenylethanol	2-Phenylethyl acetate	95(60)	97(30)	97(30)[d]
12	1-Heptanol	1-Heptyl acetate	95(60)	97(60)	99(30)[d]
13	1-Octanol	1-Octyl acetate	90(60)	96(30)	98(30)[d]
14	(-)-Menthol	(-)-Menthyl acetate	90(65)	94(60)	98(30)[d]
15	Triphenylmethanol	Triphenylmethyl acetate	73(120)	70(180)	82(60)
16	t-Butyl alcohol	t-Butyl acetate	80(100)	75(120)	84(85)
17	Phenol	Phenyl acetate	97(80)	0(100)	98(60)
18	2-Nitrophenol	2-Nitrophenyl acetate	70(120)	0(120)	75(120)
19	4-Nitrophenol	4-Nitrophenyl acetate	98(90)	0(120)	98(65)
20	4-Methoxyphenol	4-Methoxyphenyl acetat 95(60)	96(75)	0(120)	98(45)
21	α-Naphthol	α-Naphthyl acetate	97(90)	20(120)	92(65)
22	β-Naphthol	β-Naphthyl acetate	98(100)	10(150)	95(75)
23	Catechol	Benzene-1,2-diyl diacetate	90(75)[c]	0(120)	92(120)
24	Resorcinol	Benzene-1,3-diyl diacetate	95(60)[c]	0(120)	96(75)
25	Hydroquinone	Benzene-1,4-diyl diacetate	98(60)[c]	0(120)	99(60)

[a]All products were identified by comparison of their physical and spectral data with those of authentic samples. [b]Isolated yields. [c]Reaction was performed in the presence of 0.2 mmol of $BiCl_3$.[d]Reaction was performed at room temperature.

Table 2 Formylation of alcohols and phenols in refluxing ethyl formate in the presence of Bi(III) salts

Run	Substrate	Product[a]	Yield/%[b] (time/min)		
			$BiCl_3$	$Bi(TFA)_3$	$Bi(OTf)_3$
1	Benzyl alcohol	Benzyl formate	95(90)	90(120)	96(30)
2	2-Methoxybenzyl alcohol	2-Methoxybenzyl formate	90(100)	91(60)	98(40)
3	3-Methoxybenzyl alcohol	3-Methoxybenzyl formate	90(120)	95(120)	99(40)
4	2-Nitrobenzyl alcohol	2-Nitrobenzyl formate	90(120)[c]	75(120)	92(60)[d]
5	3-Nitrobenzyl alcohol	3-Nitrobenzyl formate	90(90)[c]	80(120)	95(60)[d]
6	4-Nitrobenzyl alcohol	4-Nitrobenzyl formate	85(135)[c]	90(140)	93(60)[d]
7	4-Chlorobenzyl alcohol	4-Chlorobenzyl formate	98(90)	92(120)	98(30)
8	4-Bromobenzyl alcohol	4-Bromobenzyl formate	96(120)	80(120)	96(30)
9	Benzoin	Benzoin formate	90(135)[c]	96(120)	97(60)
10	Cinnamyl alcohol	Cinnamyl formate	95(120)	85(135)	96(65)
11	2-Phenylethanol	2-Phenylethyl formate	95(120)	98(60)	99(30)
12	1-Heptanol	1-Heptyl formate	93(90)[c]	96(80)	97(20)
13	1-Octanol	1-Octyl formate	95(90)[c]	98(80)	99(20)
14	(-)-Menthol	(-)-Menthyl formate	95(60)[c]	75(75)	87(60)[d]
15	Triphenylmethanol	Triphenylmethyl formate	90(120)[c]	85(80)	88(60)[e]
16	t-Butyl alcohol	t-Butyl formate	0(60)[c]	0(60)	0(60)[e]
17	Phenol	Phenyl formate	0(180)[c]	0(180)	0(120)[e]
18	2-Nitrophenol	2-Nitrophenyl formate	0(180)[c]	0(180)	0(120)[e]
19	α-Naphthol	α-Naphthyl formate	0(120)[c]	0(120)	0(120)[e]
20	Catechol	Benzene-1,2-diyl diformate	0(120)[c]	0(120)	0(120)[e]

[a]All products were identified by comparison of their physical and spectral data with those of authentic samples. [b]Isolated yields. [c]Reaction was performed in the presence of 0.2 mmol of $BiCl_3$.[d,e]Reaction was performed in the presence of 0.02 and 0.03 mmol of $Bi(OTf)_3$ respectively.

silica-gel chromatography provided the pure acetate (Table 1), 2-nitrobenzyl acetate (run 4): m.p. 37 °C (lit[29] m.p. 35–36 °C); IR (KBr): ν_{max} 3085, 2960, 2850, 1745, 1615, 1574, 1525, 1435, 1380, 1340, 1225, 1035, 855, 785, 725 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$): δ (ppm) 2.1 (3H, s), 5.42 (2H, s), 7.28–8.3 (4H, m).

Formylation; general procedure: A solution of substrate (1 mmol) in ethyl formate (3 ml) was treated with the catalyst [0.15–0.2 mmol of $BiCl_3$, 0.3 mmol of $Bi(TFA)_3$ and 0.01-0.03 mmol of $Bi(OTf)_3$]. The reaction mixture was stirred under reflux conditions for the appropriate time according to Table 2. The progress of the reaction mixture was monitored by GLC or TLC. The solvent was evaporated and ether (20 ml) was added. The reaction mixture was washed with water and dried with $MgSO_4$. Evaporation of the solvent followed by silica-gel chromatography gave the pure formate (Table 2), 4-chlorobenzyl formate (run 7): n_D^{20}=1.5293 (lit[3] n_D^{20}=1.5299); IR (neat): ν_{max} 3060, 2940, 2880, 1720, 1600, 1575, 1490, 1455, 1405, 1365, 1250, 1160, 1075, 860, 775, 715 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$): δ (ppm) 5.13 (2H, s), 7.25 (4H, s), 8.08 (1H, s).

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Table 3 Competitive acetylation and formylation of alcohols and phenols in refluxing acetic acid and ethyl formate in the presence of Bi(III) salts

Run	Substrate	Product[a]	Yield/%[b] (time/min)		
			$BiCl_3$	$Bi(TFA)_3$	$Bi(OTf)_3$
1	Benzyl alcohol	Benzyl acetate	90(60)	100(75)	100(20)
	Phenol	Phenyl acetate	10	0	0
2	4-Nitrobenzyl alcohol	4-Nitrobenzyl acetate	95(75)	100(75)	90(60)
	Phenol	Phenyl acetate	3	0	10
3	4-Chlorobenzyl alcohol	4-Chlorobenzyl acetate	90(60)	95(150)	95(35)
	Phenol	Phenyl acetate	5	0	5
4	Benzyl alcohol	Benzyl formate	90(90)	95(120)	100(45)
	Phenol	Phenyl formate	0	0	0
5	4-Nitrobenzyl alcohol	4-Nitrobenzyl formate	80(120)	92(180)	95(60)
	Phenol	Phenyl formate	0	0	0
6	4-Chlorobenzyl alcohol	4-Chlorobenzyl formate	93(90)	95(120)	93(40)
	Phenol	Phenyl formate	0	0	0

[a]GLC yield.

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