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Transesterification of various alcohols with vinyl acetate under mild conditions catalyzed by diethylzinc using *N*-substituted diethanolamine as a ligand

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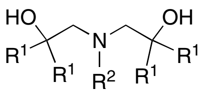
Abstract—Commercially available, inexpensive *N*-phenyldiethanolamine (**6**) is an efficient ligand for zinc-catalyzed transesterification. The use of **6**/Et_2Zn for reactions between various alcohols and vinyl acetate at room temperature produced the desired products in good yields.

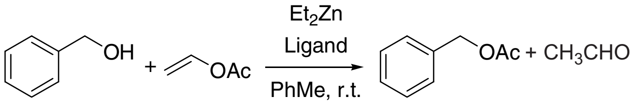
Transesterification is a convenient method for the preparation of versatile esters from inexpensive alcohols and esters.[1] Acidic[2] or basic[3] catalysts are commonly used to promote this reaction in heating, but they exhibit low chemselectivity, and labile functional groups can be damaged. They may also lead to the formation of side products. Although organometallic catalysts such as $Cp^*_2Sm(thf)_2$,[4] distannoxanes,[5] and iminophosphoranes[6] are better than simple acids, they still require long reaction times to complete the reaction, and from an environmental point of view, these catalysts cannot be recommended. *N*-heterocyclic carbenes[7] are reported to be quite effective, but they are difficult to prepare. We report here an efficient method of transesterification using a zinc catalyst with **1**–**6** as ligands under mild conditions.



1 : R^1 = H, R^2 = H
2 : R^1 = H, R^2 = Me
3 : R^1 = H, R^2 = Et
4 : R^1 = H, R^2 = Bn
5 : R^1 = Ph, R^2 = Bn
6 : R^1 = H, R^2 = Ph

We investigated the effect of using **1**–**6** as ligands for the zinc-catalyzed transesterification of benzyl alcohol with vinyl acetate in toluene as a solvent at room temperature (Table 1). Without a ligand and Et_2Zn, the reaction did not occur (entry 1). Using Et_2Zn as a catalyst, the reaction occurred, but we obtained benzyl acetate in low yield (entry 2). Additions of **1**–**3** led to lower yields

Table 1. Effect of ligand on the transesterification of benzyl alcohol with vinyl acetate[a]



Entry	Ligand	Ligand:Et_2Zn (mol %)	Yield (%)[b]
1	—	—	0
2	—	—:10	30
3	**1**	5:10	4
4	**2**	5:10	8
5	**3**	5:10	16
6	**4**	5:10	46
7	**5**	5:10	52
8	**6**	5:10	99

[a] Reaction conditions: BnOH (1 mmol), vinyl acetate (5 mmol), PhMe (2 mL), rt, 1 h.
[b] Determined by ^1H NMR.

Keywords: Zinc; Transesterification; Ester; Vinyl acetate.

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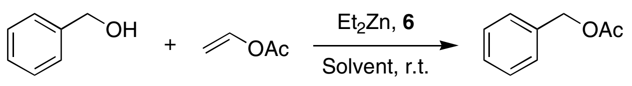
compared to the case without ligands (entries 3–5). *N*-Benzyldiethanolamine (**4**) and its derivative **5** led to moderate yields (entries 6 and 7). When *N*-phenyldiethanolamine (**6**) was employed, the reaction yielded the desired product quantitatively in 1 h (entry 8). In this case, the aldol product from acetaldehyde was not detected by ^{1}H NMR analysis of crude product.

In the presence of **6** as a ligand, the effect of the solvent was examined. As shown in Table 2, toluene and hexane led to high yields (entries 1 and 2). By contrast, polar solvents such as THF, acetonitrile, ethyl acetate, and chloroform were less effective (entries 3–6). Thus, nonpolar solvents are more suitable for this reaction.

Under optimized reaction conditions, transesterifications of vinyl acetate with benzylic alcohols bearing a variety of functional groups were carried out at room temperature, and the results are summarized in Table 3. All substrates yielded good conversions. 4-Methoxybenzyl alcohol and 4-chlorobenzyl alcohol were smoothly converted into the corresponding acetates (entries 2 and 3). The reaction of the benzylic alcohol with ester moiety in its molecule required a longer reaction time, but no side product was identified (entry 4). This means that the methyl ester moiety is less reactive compared to the vinyl acetate and does not take part in the transesterification. *ortho*-, *meta*-, and *para*-Methyl benzyl alcohols were also treated with vinyl acetate, which led to high yields. No steric effect was observed, nor did any electronic influence result from the difference of the position of the methyl group (entries 5–7).

We investigated the transesterification of various primary alcohols (Table 4). 1-Naphthalenemethanol was

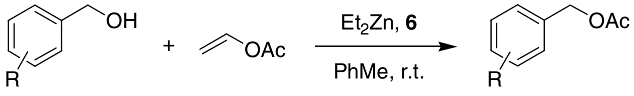
Table 2. Effect of solvent[a]

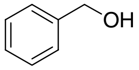
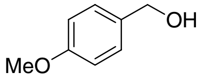
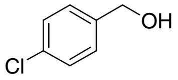
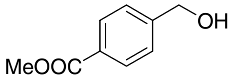
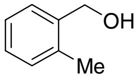
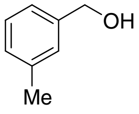
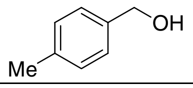


Entry	Solvent	Yield (%)[b]
1	PhMe	99
2	Hexane	81
3	THF	27
4	MeCN	7
5	AcOEt	16
6	$CHCl_3$	1

[a] Reaction conditions: BnOH (1 mmol), vinyl acetate (5 mmol), solvent (2 mL), **6** (0.05 mmol), Et_2Zn (0.1 mmol), rt, 1 h.
[b] Determined by ^{1}H NMR.

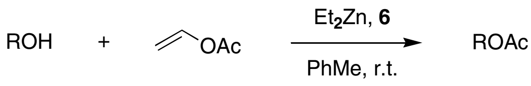
Table 3. Transesterification of various benzylic alcohols with vinyl acetate[a]

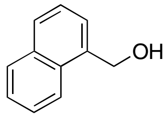
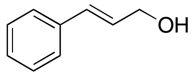
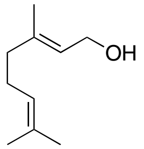
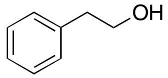
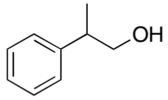
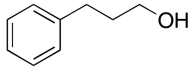
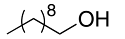
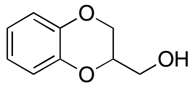


Entry	Alcohol	Time (h)	Yield (%)[b]
1		1	99 (90)
2		3	93 (78)
3		2	94 (90)
4		24	96 (64)[c]
5		3	98 (92)
6		3	93 (88)
7		3	94 (87)

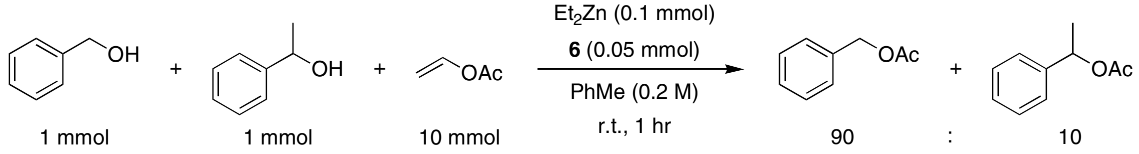
[a] Reaction conditions: alcohol (1 mmol), vinyl acetate (5 mmol), PhMe (2 mL), **6** (0.05 mmol), Et_2Zn (0.1 mmol), rt.
[b] Determined by ^{1}H NMR. Values in parentheses are isolated yields.
[c] **6** (0.1 mmol) and Et_2Zn (0.2 mmol) were used.

Table 4. Transesterification of various primary alcohols with vinyl acetate[a]

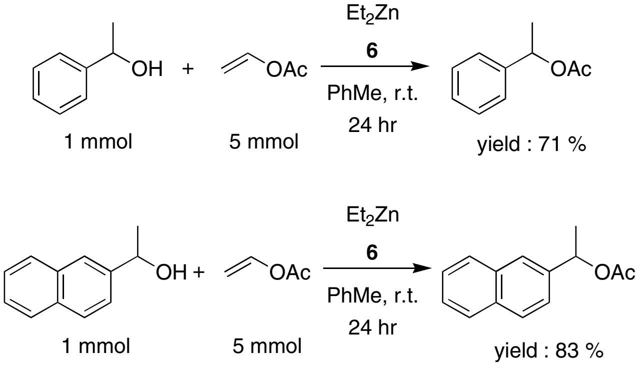


Entry	Alcohol	Time (h)	Yield (%)[b]
1		2.5	97 (97)
2		5	99 (95)
3		4	(97)[c]
4		4	(96)
5		5	(91)
6		6	99 (90)
7		5	(97)[c]
8		24	87 (79)

[a] Reaction conditions: Alcohol (1 mmol), vinyl acetate (5 mmol), PhMe (2 mL), **6** (0.05 mmol), Et_2Zn (0.1 mmol), rt.
[b] Determined by ^{1}H NMR. Values in parentheses are isolated yields.
[c] **6** (0.1 mmol) and Et_2Zn (0.2 mmol) were used.



Scheme 1.



Scheme 2.

easily acylated into the desired ester (entry 1). Allylic alcohols such as cinnamyl alcohol and geraniol also led to good yields (entries 2 and 3). Phenethyl alcohol, 2-phenyl-1-propanol, and 3-phenyl-1-propanol reacted equally well, giving the corresponding acetates in good yields (entries 4–6). Saturated liner alcohol such as decanol, was effectively acylated in high yield (entry 7). The transesterification of alcohols bearing acid-sensitive functional groups, such as 2-hydroxymethyl-1,4-benzodioxane, led to the desired products. There was no side product but the reaction required a much longer reaction time (entry 8).

Selective protection of a primary alcohol versus a secondary alcohol is very useful in natural product synthesis. This can be achieved by using organometallic systems, such as distannoxane/enol ester[5] or $Sc(OTf)_3$/Ac_2O.[8] We attempted selective acylation by employing benzyl alcohol and phenylethyl alcohol (Scheme 1). The reaction was carried out in the presence of excess vinyl acetate and was quenched after 1 h. The conversion for each alcohol was determined by ^1H NMR, and the result clearly indicated that the primary benzyl alcohol was preferentially acylated in this system.

Base on the result of the acylation of various primary alcohols with vinyl acetate, we tested the transesterification of steric hindered secondary alcohols with vinyl acetate (Scheme 2). In the presence of 0.2 mmol of Et_2Zn and 0.1 mmol of **6** at room temperature, benzylic secondary alcohols, such as 1-phenylethanol and 1-(2-naphthyl)ethanol, produced moderate to good yields.

In summary, we found *N*-phenyldiethanolamine (**6**)/Et_2Zn to be an efficient catalyst for transesterification between various alcohols and vinyl acetate. This ligand is inexpensive and the catalyst is easy to prepare. Using this system, a wide variety of alcohols were converted into corresponding acetates at room temperature in good yields.

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