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# Efficient acylation and transesterification catalyzed by dilithium tetra-*tert*-butylzincate at low temperatures

Miyuki Oshimura\*, Yuki Oda, Keita Kondoh, Tomohiro Hirano, Koichi Ute

Department of Chemical Science and Technology, Institute of Technology and Science, Tokushima University, 2-1 Minami-josanjima, Tokushima 770-8506, Japan

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### ABSTRACT

The acylation and transesterification of alcohols with vinyl acetate and carboxylic esters were investigated in the presence of a catalytic amount (1–10 mol %) of dilithium tetra-*tert*-butylzincate (TBZL) as a catalyst. The acylation proceeded quantitatively at 0 °C within 1 h. The transesterification occurred for a wide range of combinations of esters and alcohols at 0 to -40 °C. To the best of our knowledge, this is the first successful transesterification at such low temperatures. The time–conversion plots for the transesterification show that the reaction reached equilibrium within 5 min at 0 °C. The reaction proceeded quantitatively by addition of molecular sieves 4A. In addition, the transesterification proceeded even in the presence of H<sub>2</sub>O and amines.

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### Introduction

Transesterification is a useful method for preparing various esters.<sup>1</sup> Acids<sup>2</sup> and bases<sup>3</sup> are commonly used as catalysts to promote these reactions. However, severe conditions are generally required, that is, a high reaction temperature, long reaction time, and large amount of catalyst. Consequently, thermally sensitive functional groups undergo undesirable side reactions during the transesterification.

Effective catalysts for promoting transesterification at room temperature have been developed;<sup>4–9</sup> for example, nitrogenheterocyclic carbenes catalyze transesterification of carboxylic esters and acylation with vinyl acetate.<sup>4</sup> The reactions are complete within a few hours, using catalytic amounts (0.5–5.0 mol %) of the carbenes. Et<sub>2</sub>Zn (10 mol %) catalyzes transesterification (acylation) of benzyl alcohol (BnOH) with vinyl acetate at room temperature in the presence of *N*-phenyldiethanolamine (*N*-PDEA, 5 mol %).<sup>7</sup> A  $\mu$ -oxo-tetranuclear zinc cluster catalyzes acylation of alcohols under reflux conditions even in the presence of amine compounds, which could impede the reaction.<sup>10</sup>

Uchiyama and coworkers<sup>11</sup> reported that dilithium tetra-*tert*butylzincate (TBZL) catalyzed allylations of haloaromatics via halogen–zinc exchange reactions. No protection is required for haloaromatics containing a broad range of functional groups, because of the unusually low basicity of TBZL.<sup>11b,c</sup> The high chemoselectivity of TBZL enables direct polymerization of *N*-isopropylacrylamide in aqueous media.<sup>11a,b</sup>

\* Corresponding author.

http://dx.doi.org/10.1016/j.tetlet.2016.03.096 0040-4039/© 2016 Elsevier Ltd. All rights reserved. Recently, we reported that TBZL catalyzed ring-opening polymerization of  $\varepsilon$ -caprolactone.<sup>11g</sup> In a subsequent study of the copolymerization of  $\varepsilon$ -caprolactone with 2-hydroxylethyl methacrylate (HEMA), TBZL was found to act not only as an anionic initiator but also as a transesterification catalyst.<sup>12</sup> This finding led us to investigate the acylation and transesterification of alcohols with vinyl acetate and carboxylic esters in the presence of a catalytic amount (1–10 mol %) of TBZL (Scheme 1).

### **Results and discussion**

Homopolymerization of HEMA with TBZL in MeOH gave a copolymer composed of two monomeric units, HEMA and methyl methacrylate (Fig. S1). This result indicates that polymerization accompanies transesterification of HEMA with MeOH at 30 °C (Scheme 2). It is interesting to note that the reaction proceeded at a moderate temperature.

The acylation of BnOH with vinyl acetate was examined to investigate the transesterification catalytic ability of TBZL<sup>13</sup> (Table 1).<sup>14</sup> Irreversible transesterification proceeded quantitatively with



**Scheme 1.** Acylation and transesterification of alcohols with vinyl acetate and carboxylic esters in the presence of TBZL.



Scheme 2. Anionic polymerization of HEMA with TBZL in MeOH at 30 °C for 1 h, giving copolymer of HEMA and methyl methacrylate.

#### Table 1

Acylation of alcohols with vinyl acetate in Presence of TBZL or  $Et_2Zn$  with *N*-phenyldiethanolamine (PDEA) as a catalyst<sup>a</sup>



| Run             | Catalyst (mol %)                     | Solvent  | Temp.<br>(°C) | Time<br>(h) | Conv.<br>(%) <sup>b</sup> |
|-----------------|--------------------------------------|----------|---------------|-------------|---------------------------|
| 1               | TBZL (10)                            | Toluene  | 25            | 1           | >99                       |
| 2               | TBZL (10)                            | THF      | 25            | 1           | >99                       |
| 3               | TBZL (10)                            | Toluene  | 0             | 1           | >99                       |
| 4               | TBZL (10)                            | THF      | 0             | 1           | >99                       |
| 5               | TBZL (10)                            | n-Hexane | 0             | 1           | >99                       |
| 6               | TBZL (10)                            | Bulk     | 0             | 1           | >99                       |
| 7               | TBZL (1)                             | Toluene  | 0             | 0.5         | 58                        |
| 8               | TBZL (1)                             | Toluene  | 0             | 1           | 87                        |
| 9               | TBZL (1)                             | Toluene  | 0             | 1.5         | >99                       |
| 10              | Et <sub>2</sub> Zn (10) + N-PDEA (5) | Toluene  | 25            | 1           | >99                       |
| 11              | Et <sub>2</sub> Zn (10) + N-PDEA (5) | THF      | 25            | 1           | 35                        |
| 12              | Et <sub>2</sub> Zn (10) + N-PDEA (5) | Toluene  | 0             | 1           | 67                        |
| 13              | Et <sub>2</sub> Zn (10) + N-PDEA (5) | THF      | 0             | 1           | 6                         |
| 14 <sup>c</sup> | TBZL (2)                             | Bulk     | 0             | 1           | >99                       |

<sup>a</sup> Vinyl acetate (5.0 mmol), benzyl alcohol (1.0 mmol), solvent (2.0 mL).

<sup>b</sup> Conversion was determined by intensities of  $Ph-CH_2-O-$  proton signals of benzyl alcohol and that of benzyl acetate.

<sup>c</sup> <sup>i</sup>PrOH was used as an alcohol instead of benzyl alcohol.

10 mol % TBZL in toluene or THF at 25 °C within 1 h (Runs 1 and 2). Decreasing the reaction temperature to 0 °C or changing the solvent scarcely affected the reaction (Runs 3–6). These results are comparable to those for reactions catalyzed by  $Et_2Zn$  combined with a *N*-PDEA (Runs 10–13).<sup>7a,7b</sup> A decrease in the amount of TBZL to 1 mol % gave quantitative conversion within 1.5 h (Runs 7–9). Acylation of secondary alcohols such as <sup>*i*</sup>PrOH with vinyl acetate also proceeded smoothly in bulk at 0 °C and were complete within 1 h (Run 14 and Fig. S2). These results show that TBZL is a better catalyst than those reported so far.

Irreversible transesterification proceeded quantitatively for the acylation of a wide range of alcohols, except for 3-amino-1-propanol, with vinyl acetate catalyzed by TBZL (Table 2). The acylation of 3-amino-1-propanol was failed because immediate amidation and subsequent cyclization occurred before addition of TBZL due to high reactivity of vinyl acetate with amino group (Run 7).

The transesterification occurred for a wide range of combinations of esters and alcohols, except for <sup>t</sup>BuOH, PhOH, and <sup>t</sup>BuOAc (Table 3).<sup>15</sup> Half the amount of EtOAc was converted to MeOAc in the transesterification of an equimolar mixture of EtOAc and MeOH (Run 1). The time-conversion plots for the transesterification show that the reaction reached equilibrium within 5 min at 0 °C or within 60 min at -20 °C (Fig. 1).<sup>16</sup> The transesterification proceeded at a practical rate even at -40 °C. To the best of our

# Table 2 Acylation of alcohols with vinyl acetate catalyzed by TBZL in Toluene<sup>a</sup>



 $^{a}$  Vinyl acetate (5.0 mmol), alcohol (1.0 mmol), TBZL (0.1 mmol), Toluene (2.0 mL); 0 °C, 1 h.

<sup>b</sup> Conversion was determined by NMR.

<sup>c</sup> Vinyl acetate (10.0 mmol).

knowledge, this is the first successful transesterification at such low temperatures.

Removal of the product alcohol should shift the equilibrium toward complete transesterification; Molecular sieves 4A was therefore added to the mixtures of MeOAc and BnOH at 0 °C to adsorb the MeOH produced via transesterification.<sup>17</sup> The reaction proceeded quantitatively, regardless of the feed ratio of MeOAc to BnOH (Fig. 2). Similar results were observed using MeOBz instead of MeOAc.

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### Table 3

| $R^{1}$ $O^{-}R^{2}$ + $R^{3}OH$ $\xrightarrow{2 \text{ mol% TBZL}}$ $R^{1}$ $O^{-}R^{3}$ + $R^{2}OH$ $R^{1}$ $O^{-}R^{3}$ + $R^{2}OH$ |                  |            |  |                      |             |  |  |  |
|--|------------------|------------|--|----------------------|-------------|--|--|--|
| Run  | Ester            | Alcohol    | Pro  | Product <sup>b</sup> |             |  |  |  |
| 1  | o<br>Lo<br>EtOAc | но<br>МеОН | 0<br>  | +                    | EtOH        |  |  |  |
| 2  | EtOAc            | но         |  | ] +                  | EtOH        |  |  |  |
| 3  | EtOAc            | но         | $\begin{array}{c} 41\% \\ 0 \\ 38\% \end{array}$ | +                    | EtOH        |  |  |  |
| 4  |                  | EtOH       |  | × +                  | но́<br>26 % |  |  |  |
| 5  |                  | MeOH       | MeOAc  | +                    | HO<br>61 %  |  |  |  |
| 6  | °<br>Lo          | MeOH       | MeOAc  | +                    | но<br>55 %  |  |  |  |
| 7  |                  | MeOH       | MeOAc  | +                    | но 51 %     |  |  |  |

Transesterification of equimolar mixtures of ester and alcohol catalyzed by TBZL<sup>a</sup>

 $^{\rm a}$  Ester (5.0 mmol), alcohol (5.0 mmol), TBZL (0.1 mmol); 0 °C, 1 h.  $^{\rm b}$  Conversion was determined by NMR.



**Figure 1.** Time–conversion curves for transesterification of equimolar mixtures of EtOAc and MeOH catalyzed by 2 mol % TBZL at ( $\bullet$ ) 0 °C, ( $\Box$ ) –20 °C, and ( $\blacktriangle$ ) –40 °C.

The transesterification proceeded even in the presence of  $H_2O$  and amines, although slight (about 6%) amidation accompanied transesterification on addition of *n*-propylamine due to lower reactivity of ethyl acetate compared with vinyl acetate (Scheme 3 and Fig. S3, cf. Run 7 in Table 2).<sup>18</sup> The conversions were comparable to that in the absence of additives (cf. Run 1 in Table 3). These results indicate that TBZL catalyzes the transesterification chemoselectively.



Figure 2. Time-conversion curves for transesterification of equimolar mixtures of MeOAc or MeOBz, and BnOH catalyzed by 2 mol % TBZL in presence of molecular sieves 4A.



Scheme 3. Transesterification of equimolar mixtures of EtOAc and MeOH with 2 mol % TBZL at 0  $^{\circ}$ C for 1 h in the presence of H<sub>2</sub>O or amines.

The mechanism of the TBZL-catalyzed transesterification is unclear at this stage. A mechanistic study is therefore in progress. In addition, a study of polymer synthesis using this chemoselective transesterification is now under way.

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### Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2016.03. 096.

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- 13. Titration and inductively coupled plasma optical emission spectroscopy showed that the THF solution of TBZL (base: 0.626 mol  $L^{-1}$ ) contained 3.6 wt % zinc and 1.4 wt% lithium.

- 14. A typical procedure was as follows. Vinyl acetate (5.0 mmol), benzyl alcohol (1.0 mmol), and solvent (2.0 mL) were added to a glass ampoule which had been degassed and filled with nitrogen. A solution of TBZL (0.1 mmol) in THF was added under a nitrogen atmosphere to the ampoule placed in a constant-temperature bath. Then the mixture was kept at 25 or 0 °C and stirred. After a prescribed period, the mixture was diluted with CDCl<sub>3</sub> and transformed in a NMR tube. Conversion of the reaction was determined by <sup>1</sup>H NMR at 400 MHz.
- 15. A typical procedure was as described in Ref. 14. Carboxylic ester (5.0 mmol), alcohol (5.0 mmol), and a solution of TBZL (0.1 mmol) in THF were used. Solvent was not added.
- 16. The initial feeds of EtOAc, MeOH, and TBZL were 50, 50, and 1 mmol, respectively. After initiation for 5 min, an aliquot was removed from the reaction mixture using a syringe by flushing with N<sub>2</sub> gas; the aliquot was mixed with CDCl<sub>3</sub> for NMR spectroscopy. Similar procedures were performed after 10, 20, 30, 60, 120, and 240 min. The conversion was determined from the integral intensities of the NMR signals of the  $CH_3$ -CO-O- methyl protons of EtOAc and MeOAc.
- 17. A typical procedure was as describe in Ref. 14. Molecular sieves 4A (2.5 g) flame-dried in an ampoule were used to adsorb MeOH formed as by-products. Carboxylic ester (5.0 mmol), alcohol (5.0 mmol), and a solution of TBZL (0.1 mmol) in THF were used. THF (2.3 mL) was used as a solvent.
- 18. A typical procedure was as described in Ref. 14. EtOAc (5.0 mmol), MeOH (5.0 mmol), a solution of TBZL (0.1 mmol) in THF, and  $H_2O$  (5.0 mmol) or amines (5.0 mmol) were used. Solvent was not added.