

$\text{CCl}_4$  at room temperature for 3 h gave  $(\text{C}_6\text{F}_{13}\text{CH}_2\text{CH}_2)_2\text{SnBr}_2$  (96%), which was hydrolyzed with aqueous NaOH (4N)/THF at room temperature for 2 h to furnish polymeric  $[(\text{C}_6\text{F}_{13}\text{CH}_2\text{CH}_2)_2\text{SnO}]_n$  (**2**) (93%). Treatment of **2** (5 mmol) with aqueous HCl (4N; 6.5 mmol) in acetone at room temperature for 24 h afforded **1a** in 85% yield: m.p. 90–91 °C ( $\text{CH}_2\text{Cl}_2$ );  $^{119}\text{Sn}$  NMR ( $[\text{D}_6]$ acetone):  $\delta = -178.3, -202.5$ ; elemental analysis: calcd for  $\text{C}_{64}\text{H}_{32}\text{Cl}_4\text{F}_{104}\text{O}_2\text{Sn}_4$ : C 22.44, H 0.94; found: C 22.58, H 0.54.

Fluorous biphasic transesterification: A mixture of ethyl 3-phenylpropionate (356 mg, 2.0 mmol), 1-octanol (260 mg, 2.0 mmol), and **1a** (171 mg, 0.1 mmol) in FC-72 (4.0 mL) was added to a test tube. The test tube was placed in a stainless-steel pressure bottle and heated at 150 °C for 16 h. The reaction mixture was then cooled to room temperature and toluene (5 mL) was added. The FC-72 layer was washed with toluene ( $2 \times 1$  mL) and the combined toluene solution was evaporated to afford pure octyl 3-phenylpropionate (525 mg, 2.0 mmol). The FC-72 solution was used in the next reaction.

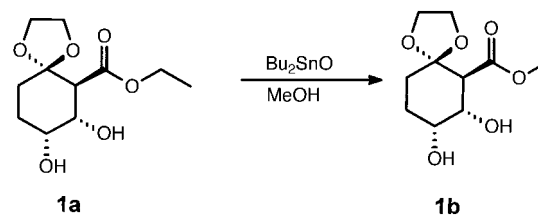
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 [22] The quantitative recovery of the catalyst without depression of the activity is apparent: the reaction shown in Table 1, entry 2 was repeated and gave >99% yield (GC) and 98–100% recovery of the catalyst in every run. For further supporting evidence, see ref. [24].  
 [23] Zhu's conventional transesterification was carried out in refluxing fluoro-carbon solvents in a Dean–Stark trap. The product ester (67–87% yield) was readily separated from the solvent but the catalyst,  $\text{Ti}(\text{O}i\text{Pr})_4$ , remained in the organic layer: D.-W. Zhu, *Synthesis* **1993**, 953.  
 [24] The reaction in Table 2, entry 1 was repeated 20 times. The GC yield was constantly >99% each time, and 91% of the catalyst was recovered after the 20th run, indicative of virtually no loss and no deactivation of the catalyst during the repetition.

## A Mild and Effective Method for the Transesterification of Carboxylic Acid Esters\*\*

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Transesterification is one of the most important transformations in organic synthesis.<sup>[1]</sup> The most important methods, besides acid or base catalysis, employ titanium tetraalkoxides,<sup>[2]</sup> complex tin compounds,<sup>[3]</sup> indium iodide,<sup>[4]</sup> or enzymes.<sup>[5]</sup> During a dibutyltin oxide-mediated selective O-methylation of compound **1a**, we observed the formation of methyl ester **1b** as a side product (Scheme 1). Interestingly,



Scheme 1. Dibutyltin oxide catalyzed transesterification of ethyl ester **1a** into methyl ester **1b**.

neither elimination nor epimerization at the stereogenic center adjacent to the ester moiety was observed. Previous attempts to obtain methyl ester **1b** by using various acids and bases always led either to complete epimerization or to the decomposition of **1a**. Furthermore,  $\text{Ti}(\text{OMe})_4$  was not suitable for this purpose owing to its insolubility in methanol.<sup>[2]</sup>

The significance of the observed side product encouraged us to optimize this reaction and to investigate the scope and limitations of this method. Several simple as well as highly functionalized aliphatic and aromatic esters were treated with catalytic amounts of dibutyltin oxide (1–10 mol%) in different alcohols as solvents. The isolated derivatives corresponded to the product of transesterification with the alcohol that was used as solvent (Table 1). The reaction conditions are very mild and thus the method is tolerant of several functional groups, for example, acetals, ketals, aliphatic bromides,  $\beta$ -ketoesters, and enol ethers. Most significantly, free hydroxy, phenolic, and even amino groups do not affect the reaction.

The potential scope of this method was clear from the treatment of **4a** with dibutyltin oxide in methanol to afford the desired derivative **4b** in an excellent yield (Table 1, entry 4).<sup>[6]</sup> We suppose that the *tert*-butyl ester moiety in **4a** is first transformed into the methyl ester, which is then attacked intramolecularly by the free amino group to afford the final product **4b**. To exclude the possibility that the amide was

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Table 1. Dibutyltin oxide mediated transesterifications.

Entry	Ester	Product	Alcohol	Time [h]	Yield
1			methanol	12	90
2			methanol	12	88
3			methanol	12	90
4			methanol	24	96
5			allyl alcohol	12	87
6			ethanol	12	85
7			methanol	12	89
8			methanol	12	92
9			methanol	12	90
10			methanol	12	80
11			methanol	12	77
12			methanol	5	96
13			allyl alcohol	5	90
14			n-butanol	5	88
15			isopropyl alcohol	5	91
16			benzyl alcohol	5	86

formed directly under dibutyltin oxide mediation, we treated **4a** with dibutyltin oxide in dioxane in the absence of methanol. After 24 h at 90 °C we did not observe the formation of amide **4b**. The transesterification of N-protected amino acid esters also proceeded smoothly without affecting the urethane group (Table 1, entries 5, 6). In this context it is worth noting that Shapiro et al. reported the O-alkyl transesterification of several urethanes by using  $Ti(OiPr)_4$  in the presence of the appropriate alcohols.<sup>[7]</sup>

To test the effect of water on the outcome of the reaction we used a mixture of alcohol and water (4:1) as the solvent and obtained the expected transesterification products in high yields; thus strictly dry reaction conditions are not necessary. The highest turnover numbers were observed in the transesterification reactions of salicylic esters with free phenolic groups, which were converted into the corresponding esters in excellent yields in only five hours (Table 1, entries 12–16). By using this method, esters of primary, secondary, and even tertiary alcohols can be transesterified in high yields. Allyl esters and benzyl esters were also prepared by using this method (Table 1, entries 5, 13, 16). However, *tert*-butyl alcohol cannot be used for transesterification.

In 1979 Poller et al. investigated the activity of dialkyl- and diaryltin oxide compounds as catalysts for the conversion of propyl acetate into methyl acetate.<sup>[8]</sup> On account of our findings we believe that the use of dibutyltin oxide in transesterification reactions deserves more attention, especially because it is comparable with the complex tin compounds introduced by Otera.<sup>[3]</sup> The main advantages of this system are the simple and mild reaction conditions, the inexpensive and commercially available catalyst, the high yields, and especially the compatibility with a variety of functional groups. The method described herein represents a valuable alternative to the known methods and may find a broad application, especially in the field of natural product synthesis.

### Experimental Section

**General procedure:** The carboxylic ester (0.6 mmol) was dissolved in the desired alcohol (5 mL). After the addition of dibutyltin oxide (10 mol%; 15 mg, 0.06 mmol) the mixture was heated at reflux for the time indicated in Table 1 (the reaction was normally complete within 48–72 h when 1 mol% of dibutyltin oxide was used). After completion of the reaction, the mixture was poured into a saturated sodium bicar-

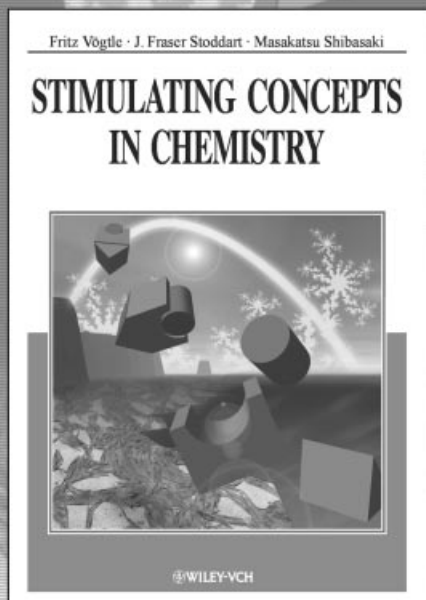
bonate solution (20 mL) and extracted three times with ethyl acetate. The combined organic layers, which contained the dibutyltin oxide as a fine white precipitate, were filtered through celite and dried over sodium sulfate. After removal of the solvent in vacuo, the product was purified by flash chromatography.

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