*Tetrahedron* Vol 49, No 15, pp 3065-3074, 1993
Printed in Great Britain

0040-4020/93 $6 00+ 00


# Unique Template Effects of Distannoxane Catalysts in Transesterification of Diol Esters

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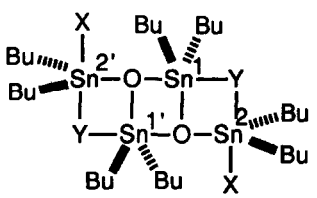
(*Received in Japan* 21 *December* 1992)

**Abstract** 1,*n*-Diol diacetates (n = 2,3,4) are selectively converted into the corresponding monoacetates by distannoxane-catalyzed transesterification Such unique selectivity is not encountered with 1,*n*-diol diacetates where n ≥ 5 A great difference in reactivity is also seen in the transesterifiaction between methyl butyrate and 1,*n*-diol monoacetates the ethylene glycol derivative sluggishly undergoes transesterification whereas higher homologs react smoothly The unique template effects of the catalysts are discussed in terms of cooperation of two different tin atoms which are located in the proximity

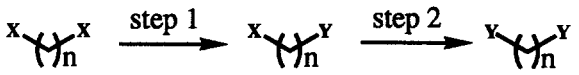
## Introduction

Previously, we disclosed that 1,3-disubstituted tetraalkyldistannoxanes **1** catalyzed transesterification under mild conditions [1] In the continuing study of this subject, we have found that alcoholysis of 1,*n*-diol diacetates (n = 2, 3, 4) provides the corresponding monoacetates selectively [2] Transformation in a selective manner of one of chemically equivalent functional groups is synthetically useful but rather difficult to achieve For instance, attempted monofunctionalization of 1,*n*-diols and dicarboxylic acids leading to versatile key compounds in natural product synthesis is usually accompanied by difunctionalization. To this end, the two successive steps in Scheme 1 need to be differentiated and physical methods were invoked thus far For example, a continuous extraction method was put forth [3] 1,*n*-diols were exposed to acetic acid in the presence of a strong acid catalyst in water-hydrocarbon mixture The monoacetate was extracted to the organic phase before being converted into the




**1a** X = Y = Cl, **1b** X = Y = -NCS, **1c** X = Cl, Y = OH, **1d** X = -NCS, Y = OH

**Scheme 1**




diacetate The polymer support technology was also successful [4] One of the functional groups was attached to the supports allowing the remaining one to be modified selectively. More practically, mineral solid supports were employed by Japanese groups Dicarboxylic acids adsorbed chemically on alumina underwent monoesterification with diazomethane or diols, and dicarboxylic acids were methylated with dimethyl sulfate by analogous procedure [5] 1,*n*-Diols were converted into the monoacetates or the monotetrahydropyranyl ethers by the catalysis of metallic sulfates supported on silica gel [6] Meanwhile, the distannoxane protocol has exemplified that even a homogeneous reaction is workable for this delicate differentiation In this paper, therefore, we present thorough investigations of the catalysis together with results of other transesterifications

## Results and Discussion

A typical reaction is illustrated in Fig 1 Ethylene glycol diacetate (**2a**) (2 mmol) was stirred in methanol (5 ml)-$CHCl_3$ (0 3 ml) in the presence of **1a** (0 2 mmol) $CHCl_3$ was necessary to make the reaction mixture

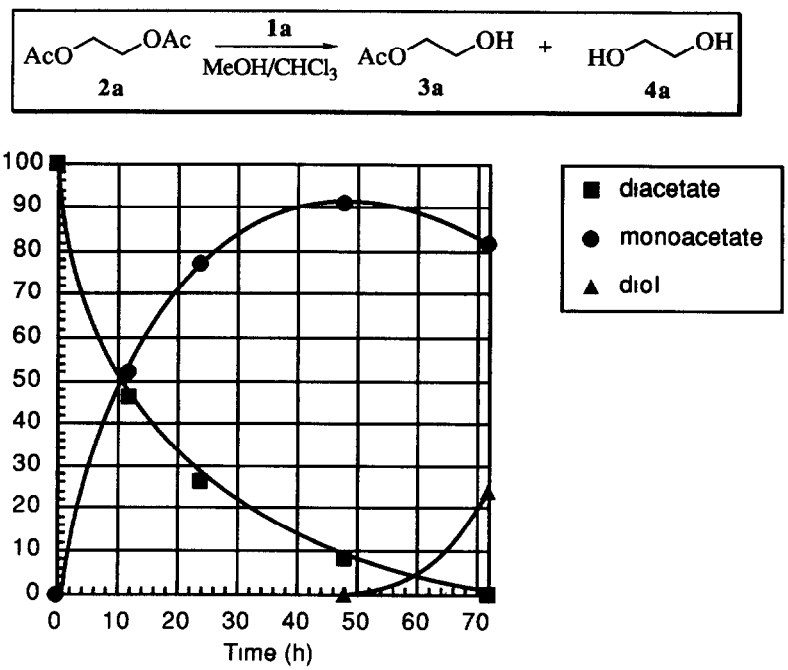
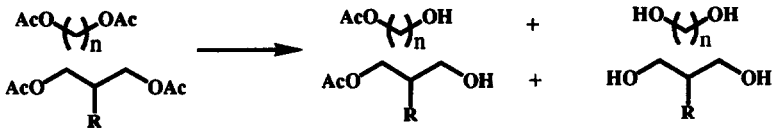
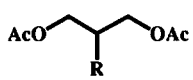



Fig 1 Time conversion curves for the transesterification of **2a**

Table 1 Transesterification of Diol Diacetates Catalyzed by Distannoxane Catalysts[a)]



| diacetate | catalyst | solvent | reaction time (h) | yield(%)[b)] of monoacetate 3 | yield(%)[b)] of diol 4 |
|---|---|---|---|---|---|
|  | | | | | |
| **2a** n = 2 | **1a** | $MeOH-CHCl_3$ | 48 | 91 | <1[c)] |
| | **1b** | $MeOH-CHCl_3$ | 48 | 77 | <1[c)] |
| | **1c** | $MeOH-CHCl_3$ | 96 | 71 | <1[c)] |
| | **1d** | $MeOH-CHCl_3$ | 192 | 48 | <1[c)] |
| | **1a** | $MeOH-CH_2Cl_2$ | 24 | 69 | <1[c)] |
| | | $MeOH-C_6H_6$ | 24 | 81 | <1[c)] |
| | | MeOH-THF | 24 | 82 | <1[c)] |
| | | $EtOH-CHCl_3$ | 216 | 91 | <1[c)] |
| | | $^nBuOH$[d)] | 120 | 85 | <1[c)] |
| **2b** n = 3 | **1a** | $MeOH-CHCl_3$ | 48 | 80 | <1[c)] |
| | | $EtOH-CHCl_3$ | 240 | 78 | <1[c)] |
| | **1b** | $MeOH-CHCl_3$ | 120 | 69 | 5 |
| **2c** n = 4 | **1a** | $MeOH-CHCl_3$ | 48 | 70 | <1[c)] |
| | | $MeOH-C_6H_6$ | 60 | 66 | <1[c)] |
| | | MeOH-THF | 72 | 65 | <1[c)] |
| | | $EtOH-CHCl_3$ | 240 | 72 | <1[c)] |
| **2d** n = 5 | **1a** | $MeOH-CHCl_3$ | 48 | 35 | 29 |
| **2e** n = 6 | **1a** | $MeOH-CHCl_3$ | 48 | 34 | 30 |
| **2f** n = 8 | **1a** | $MeOH-CHCl_3$ | 48 | 40 | 21 |
|  | | | | | |
| R = Me | **1a** | $MeOH-CHCl_3$ | 96 | 70 | <1[c)] |
| | | $EtOH-CHCl_3$ | 120 | 61 | <1[c)] |
| | **1b** | $MeOH-CHCl_3$ | 120 | 49 | 6 |
| R = Ph | **1a** | $MeOH-CHCl_3$ | 48 | 59 | 13 |
| | | $^nBuOH$[d)] | 288 | 63 | 0 3 |
| | **1b** | $MeOH-CHCl_3$ | 48 | 55 | 2 |

[a)] Reaction conditions diacetate (2 mmol), catalyst (0 2 mmol), MeOH or EtOH (5 ml), $CHCl_3$, $CH_2Cl_2$, $C_6H_6$, or THF (0 3 ml)

[b)] Based on GLC

[c)] Diol was not detected on TLC

[d)] $^nBuOH$ (5 ml)

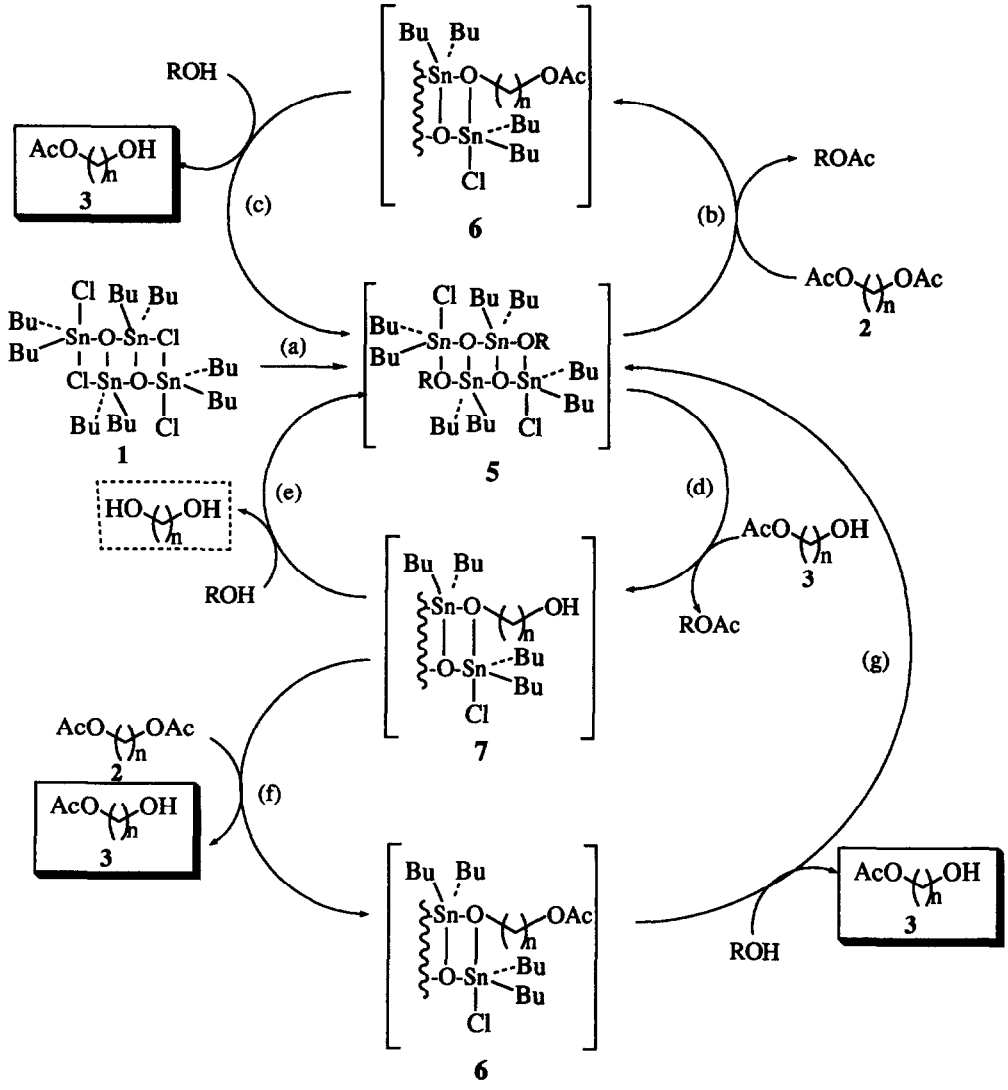
homogeneous because of poor solubility of **1a** in methanol. The solution was stirred at room temperature (standard conditions hereafter) As the reaction proceeds, the GLC monitoring showed exclusive formation of ethylene glycol monoacetate **3a** At the reaction time of 48 h, its yield was 91% and no sign of the diol formation was detected After that stage, the yield of the monoacetate decreased while the diol was gradually formed After 72 h, the yields of the monoacetate and the diol were 77% and 22%, respectively It is remarkable that one of the acetoxy groups is modified in such a selective manner Table 1 summarizes the maximum yields of monoacetates **3** until the stages when diols **4** began to appear on TLC under various conditions The generality of the present procedure is apparent Methanol, ethanol, and 1-butanol are effective The presence of minor amounts of other solvents like $CHCl_3$, $CH_2Cl_2$, benzene, or THF needed to dissolve **1** has no influence on the reaction Addition of the second solvent is not necessary when 1-butanol, a good solvent for **1**, is employed The isothiocyanate derivative **1b** leads to a slightly lower selectivity than **1a** Hydroxydistannoxanes **1c** and **1d** give poorer results with respect to the selectivity and reaction rate There is a distinct gap in the selectivity between butane-1,4-diol and pentane-1,5-diol diacetates The unsubstituted diols with $n \geq 5$ exhibit no selectivity (vide infra) Good selectivities are obtained with 2-substituted propane-1,3-diol derivatives as well

We propose the mechanism depicted in Scheme 2 for the selective monoacetate formation The initial step is the formation of alkoxydistannoxane **5** by replacement of the bridging chlorine in **1** (step a), a fully established process in a variety of distannoxane-catalyzed reactions [1c,7] Then, an acetoxy carbonyl of **2** coordinates on the terminal tin atom Sn (2) Nucleophilic attack of the tin-bonded alkoxy group towards the acetoxy group induces the transesterification to afford ROAc and a new alkoxydistannoxane **6** (step b) Alcoholysis of this intermediate produces the monoacetate **3** and regenerates the catalytically important species **5** (step c) As the amount of the monoacetate increases, this compound interacts with **5** to give the intermediate **7** (step d) Alcoholysis of this intermediate would provide the diol (step e) but this process is actually retarded when the diacetate **2** coexists Transesterification between this alkoxydistannoxane **7** and **2** (step f) predominates over the alcoholysis The intermediate **6** is converted to **5** upon alcoholysis affording the monoacetate **3** (step g) Thus, most crucial for suppressing the diol formation is the retardation of alcoholysis of **7** by the coexisting diacetate The validity of this proposal is deduced from the following observations The first-order rate constants for conversion of ethylene glycol diacetate **2a** to the monoacetate **3a** ($k_{di}$) and of the monoacetate **3a** to the diol **4a** ($k_{mono}$) were compared The rate constants were measured at 25 °C in MeOH-$CHCl_3$ and EtOH-$CHCl_3$ As shown in Table 2, $k_{di}$ is nearly twice as large as $k_{mono}$, implying that the reactivity of the acetoxy group in both compounds is virtually identical As a consequence, one can rule out the possibility that transesterification of diacetates are faster than that of the corresponding monoacetates

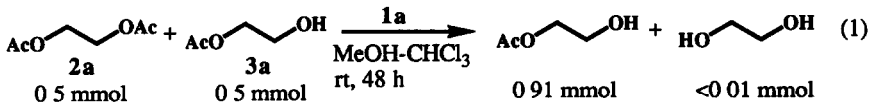
Table 2 First-order Rate Constants of Transesterifiaction of **2a** and **3a** at 25 °C

| solvent | $10^4 \times k_{di}(min^{-1})$ | $10^4 \times k_{mono}(min^{-1})$ |
|---|---|---|
| MeOH-$CHCl_3$ | 6 7 ± 0 5 | 3 6 ± 0 3 |
| EtOH-$CHCl_3$ | 1 4 ± 0 2 | 0 76 ± 0 05 |

**Scheme 2**


ROH
AcO OH
n
3
(c)
Bu Bu
Sn-O OAc
n
O-Sn Bu
Bu
Cl
6
(b)
ROAc
AcO OAc
n
2
Cl Bu Bu
Bu Sn-O-Sn-Cl
Bu
Cl-Sn-O-Sn Bu
Bu
Bu Bu Cl
1
(a)
Cl Bu Bu
Bu Sn-O-Sn-OR
Bu
RO-Sn-O-Sn Bu
Bu
Bu Bu Cl
5
HO OH
n
(e)
ROH
(d)
AcO OH
n
3
ROAc
Bu Bu
Sn-O OH
n
O-Sn Bu
Bu
Cl
7
(g)
AcO OAc
n
2
AcO OH
n
3
(f)
Bu Bu
Sn-O OAc
n
O-Sn Bu
Bu
Cl
6
ROH
AcO OH
n
3

Next, an equimolar mixture of the diacetate **2a** and monoacetate **3a** was subjected to the reaction in MeOH-$CHCl_3$ (eq 1) No diol was produced until a 91% total yield of the monoacetate was obtained 41% from the




**2a** 0 5 mmol **3a** 0 5 mmol 0 91 mmol <0 01 mmol

diacetate and the 50% from the unchanged monoacetate Obviously, the diol was not formed until most of the diacetate had been consumed The suppression of the alcoholysis of **3a** was confirmed more clearly by the competition with propylene glycol diacetate **2b** As seen in Table 3, ethylene glycol began to appear after 25 h when nearly a half of **2b** had been consumed Since exposure of **3a** alone to the standard conditions yielded 41% of ethylene glycol after 25 h, the alcoholysis of **3a** was no doubt retarded by **2b**

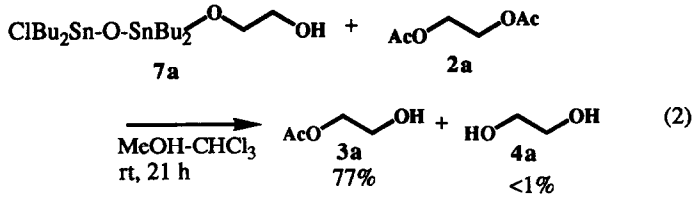
Table 3 Transesterification of an Equimolar Mixture of **2b** and **3a** [a)]


**2b** **3a** **3b** **4a**

| reaction time (h) | distribution of reaction mixture (%)[b)] | | | |
|---|---|---|---|---|
| | **2b** | **3a** | **3b** | **4a** |
| 0 | 50 | 50 | 0 | 0[c)] |
| 5 | 47 | 50 | 3 | 0[c)] |
| 10 | 41 | 50 | 9 | 0[c)] |
| 20 | 33 | 50 | 17 | 0[c)] |
| 25 | 24 | 50 | 26 | 0[c)] |
| 30 | 21 | 44 | 29 | 6[d)] |
| 40 | 17 | 29 | 33 | 21[d)] |

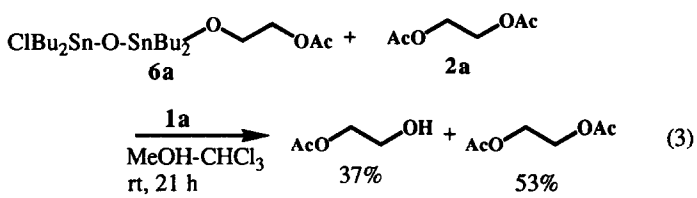
a) Reaction was carried out under the standard conditions
b) Determined by GLC
c) Not detected on TLC
d) Estimated from the decreased amount of **3a**

Finally, a more direct evidence was put forth with **7a** which had been separately prepared by condensation between **1c** and ethylene glycol [8] Reaction of **7a** with an equimolar amount of **2a** in MeOH-$CHCl_3$ at room temperature was monitored by GLC analysis (eq 2) After 21 h, a 77% yield of **3a** was obtained whereas no diol was detected on TLC monitoring Apparently, the transesterification predominated over the alcoholysis even in the presence of a large excess of methanol

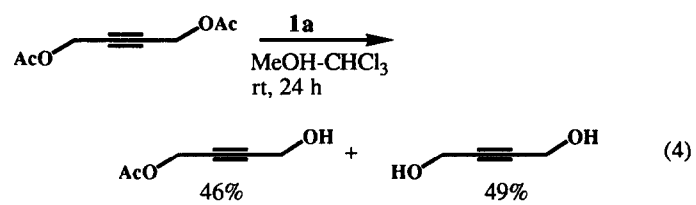



(2)

It should be noted that subjection of **6a** to the same reaction resulted in the formation of the monoaceate (eq 3) If only the transesterification operates in this reaction, the monoacetate would not be formed **2a** is incorporated into **6a** while β-acetoxyethoxy moiety of **6a** is converted to **2a** The monoacetate formation unambiguously arises from methanolysis of **6a** and thus suggests that the terminal hydroxy group in **7a** plays a key role for suppressing the alcoholysis Since the analogous influence of a β-hydroxy group have been observed in distannoxane-catalyzed acetalization,[8] such sort of the hydroxyl participation seems to be one of the fundamental features of the distannoxane catalysts Here, we focus our attention on this issue in more detail Reaction of 2-butyne-1,4-diol diacetate under the standard conditions failed to give rise to the monoacetate preference (eq 4) in sharp contrast to butane-1,4-diol diacetate Apparently, the straight acetylenic skeleton prevents the hydroxy terminal from interacting with the acetoxy group coordinated on Sn (2) Thus, no selectivity encountered with the alkane-1,*n*-diol diacetates with more than four skeletal carbons can be explained by less effective participation of the terminal hydroxy group in **7**




(3)

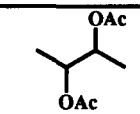
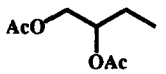
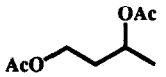



(4)

The competition of the alcoholysis vs the transesterification of the intermediate **7** was further investigated by subjecting secondary alcohol derivatives to the standard reaction conditions (Table 4) No preference for the monoacetate was seen in all cases It is reasonable to assume that the Sn-O bond in **7** derived from the secondary alcohol acetates is more easily replaced by methanol than that in **7** derived from the primary alcohol acetates Accordingly, the alcoholysis competes substantially with the transesterification When butane-1,2- and -1,3-diols

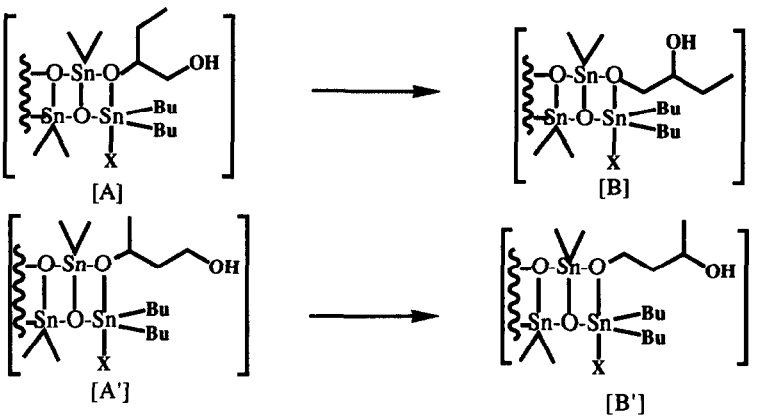
are subjected, the initially formed alkoxydistannoxane [A] or [A'] in which the secondary alkoxy group is bonded to tin may quickly isomerize to another one [B] or [B'] bearing an Sn-primary alkoxyl bond (Scheme 3) Since the reactivity of the secondary alcohol towards the acetoxy carbonyl group is lower than that of a primary one, this may also be responsible for suppressing the transesterification of these unsymmetrical diols

Table 4 Transesterification of Diacetates of Secondary Alcohols [a]

| diol diacetate | reaction time (h) | monoacetate (%) | diol (%) |
|---|---|---|---|
|  | 312 | 39 | 31 |
|  | 120 | 53[b] | 22 |
|  | 120 | 60[b] | 26 |

[a] Reaction conditions diacetate (2 mmol), **1a** (0 2 mmol), MeOH (5 ml), $CHCl_3$ (0 3 ml)
[b] Only primary alcohol was obtained

**Scheme 3**




In relation to the participation of the terminal functional group, we have found remarkable results with transesterification of 1,*n*-diol monoesters (Table 5) $PrCOO(CH_2)_nOH$ was treated with an equimolar amount of PrCOOMe in the presence of **1d** (1 mol%) in refluxing 1,2-dichloroethane After 20 h, most of the diol monobutyrates were converted to the dibutyrates when n = 4,5,6 Conversion of the propane-1,3-diol derivative, on the other hand, was lower and more surprisingly, the ethylene glycol derivative almost remained unchanged This might be accounted for in terms of retardation of the ester exchange by intramolecular coordination of the

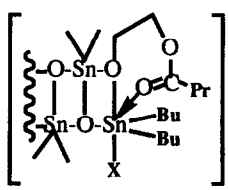
terminal ester group [C] In this model, a seven-membered ring arises from the ethylene glycol derivative but larger rings should be formed from the higher homologs If there is some interaction between the hydroxyl and Sn(2) in the model [D], five- to seven-membered rings are formed in the transesterification of diol diesters **2** when n = 2,3,4 but larger rings should result from **2** with $n \geq 5$ Since there should be significant differences in the coordination mode between the hydroxyl and the carbonyl, it is not appropriate to compare straightforwardly these two models Nonetheless, it follows probably that the participation of the terminal group plays an important role and is associated with effectiveness of the transesterification in terms of the ring size

Table 5 Transesterification of Monobutyrate of 1,*n*-Diols with Methyl Butyrate[a)]

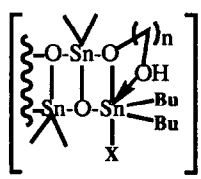
$$PrCOO(CH_2)_nOH + PrCOOMe \xrightarrow[ClCH_2CH_2Cl]{\mathbf{1d}} PrCOO(CH_2)_nOCOPr$$

| n | $PrCOO(CH_2)_nOH$ (%) | $PrCOO(CH_2)_nOCOPr$ (%) |
|---|---|---|
| 2 | 85 | 4 |
| 3 | 13 | 61 |
| 4 | 1 | 70 |
| 5 | 5 | 89 |
| 6 | 1 | 70 |

a) Reaction conditions monobutyrate methyl butyrate **1d** = 1 1 0 01




[C]




[D]

In conclusion, the unique transesterification of one of chemically equivalent acetoxy groups in diol diacetates was realized with the aid of the homogeneous catalysis of the distannoxanes The selectivity is ascribed to the suppression of the alcoholysis of the intermediary β-hydroxyethoxydistannoxanes by the coexisting diacetates The participation of the β-hydroxy group in these intermediates is likely to be responsible for this reaction In other words, cooperation of Sn (1) and Sn (2) in the distannoxane template elaborates on the otherwise difficult-to-achieve transformation

## Experimental

GLC analysis was performed on a Shimadzu GC-8A gas chromatograph with 2% Silicone OV 17 on Chromosorb W ( 3 2 x 2000 mm) or a Shimadzu GC-14A capillary gas chromatograph with ULBON HR-20M (0 2 x 25000 mm) Thin-layer chromatography was carried out on Merk Kieselgel 60 F254 All the solvents

were purified by standard methods Commercially available diols were used as received Diol esters were prepared by conventional methods The monoacetates were confirmed by comparison with authentic specimen The preparation of distannoxanes is described in the literature [1c]

**Transesterification of Diol Diacetate (Standard Conditions)** Diol diacetate (2 mmol), **1** (0 2 mmol), and a hydrocarbon ($C_{10-14}$) internal standard were stirred in methanol (5 ml)-chloroform (0 3 ml) at room temperature At appropiate intervals, the reaction was monitored by GLC The reaction was repeated at least three times and the average values are listed in Table 1 In one experiment, the reaction mixture was evaporated when the maximum yield of the monoacetate was reached The residue was subjected to column chromatography on silica gel The isolated yields were nearly the same as those by GLC analysis within 5% deviation

Other reactions were carried out analogously except in 1-butanol Since the distannoxanes are soluble in this solvent, it was no more necessary to use the minor solvents which were employed to dissolve the catalysts

**Measurements of Rate-Constants of Transesterifiaction** Transesterification of **2a** and **3a** (both 1 mmol) catalyzed by **1a** (0 1 mmol) in methanol (5 ml)-chloroform (0.3 ml) or ethanol (5 ml)-chloroform (0 3 ml) at 25 °C was monitored by GLC The rate constants were calculated by using a first-order equation with respect to the esters

**Transesterification of an Equimolar Mixture of Diacetate and Monoacetate** The ethylene glycol diacetate **2a** and monoacetate **3a** (each 0 5 mmol) were stirred in the presence of **1a** (0 1 mmol) in methanol (5 ml)-chloroform (0 3 ml) at room temperature GLC analysis showed formation of 0 91 mmol of **3a** after 48 h No diol was detected on TLC monitoring

Reaction of propylene glycol diacetate **2b** and **3a** was conducted analogously Even after 25 h, no ethylene glycol was detected

**Reaction of 7a with 2a** β-Hydroxyethoxydistannoxane **7a** was prepared from **1c** and ethylene glycol according to the method described previously [8] A methanol (10 ml)-chloroform (0 6 ml) solution of **7a** (1 mmol) and **2a** (1 mmol) was stirred at room temperature After 21 h, GLC analysis showed formation of **3a** (0 77 mmol) and no diol was detected on TLC

**Reaction of 6a with 2a** β-Acetoxyethoxydistannoxane **6a** was prepared from **1c** and **3a** by the analogous method to **7a** and used without purification because of difficulty to isolate it in a pure form The reaction of this compound with **2a** was conducted as described above for the reaction of **7a**

**Transesterification of Monobutyrate of 1,*n*-Diols with Methyl Butyrate** An equimolar mixture of the monobutyrate and methyl butyrate (each 2 mmol) in the presence of **1d** (0 2 mmol) was heated under reflux in 1,2-dichloroethane After 20 h, the reaction mixutre was analyzed by GLC

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