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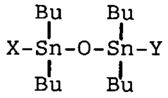
NOVEL DISTANNOXANE-CATALYZED TRANSESTERIFICATION AND A NEW ENTRY TO α,β-UNSATURATED CARBOXYLIC ACIDS

Junzo Otera,* Toru Yano, Atsuya Kawabata, and Hitosi Nozaki
Okayama University of Science, Ridai-cho, Okayama 700, Japan

Summary:Novel distannoxane-catalyzed transesterification reaction has been developed which affords various types of esters under very mild conditions. The reaction was applied to the stereo- and regioselective synthesis of trisubstituted α,β-unsaturated carboxylic acids.

Transesterification reaction, one of the effective methods for ester synthesis, is usually conducted under acidic or basic conditions. Thus, development of a new method which allows for transesterification under milder conditions should heighten the synthetic potentiality of the reaction. In the program of exploring synthetic applications of 1,3-disubstituted tetrabutyldistannoxanes (**1**),[1] we have found a unique catalytic effect of **1**



$$\mathrm{X{-}}\underset{\mathrm{Bu}}{\overset{\mathrm{Bu}}{\mathrm{Sn}}}\mathrm{{-}O{-}}\underset{\mathrm{Bu}}{\overset{\mathrm{Bu}}{\mathrm{Sn}}}\mathrm{{-}Y}$$

1

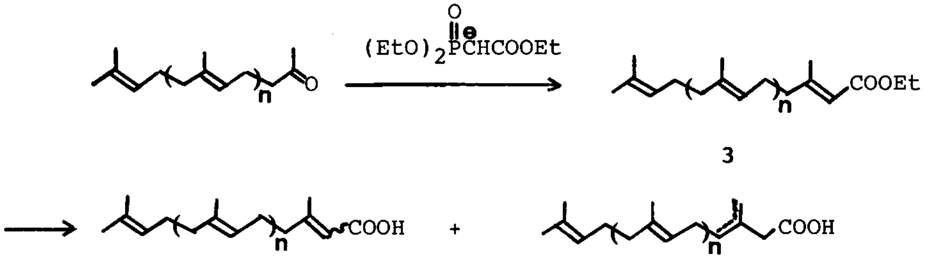
X = Cl, -N=C=S
Y = OH

which affords various esters under nearly neutral conditions in excellent yields (eq 1).

$$\mathrm{RCOOR'} \xrightarrow{\mathrm{R''OH},\ \mathbf{1}} \mathrm{RCOOR''} \qquad (1)$$

The manipulation is quite simple: a toluene solution of esters and alcohols was heated at reflux in the presence of **1** (1-10 mol% relative to esters or alcohols). Evaporation of the solvent and the excessively employed reactant followed by column chromatography on silica gel delivered the desired esters. Table I attests the present method to be applicable to a wide range of compounds. Notable features are as follows. (1) Yields are constantly excellent. (2) A variety of functional groups are tolerated. Of particular interest is that ethyl acetoacetate is successfully transformed into synthetically useful esters although the difficulty of transesterification of β-keto esters has been reported recently.[2] It should be further noted that the present method is effective for non-enolizable β-keto esters as well. (3) Diesters or diols also are employable. (4) Secondary alcohols gave rise to satisfactory results while no reactions occurred with tertiary alcohols.

The synthetic utility of the present method was exemplified by the stereo- and regiospecific synthesis of trisubstituted α,β-unsaturated carboxylic acids (**2**), which are one of the fundamental classes of the terpenoid derivatives, but only difficultly accessible. The skeleton of **2** could be assembled according to the procedure of eq 2. The stereoisomers of the ester **3** thus obtained are easily separable. Unfortunately, however, acid- or base-catalyzed hydrolysis of stereochemically pure **3** results in a mixture of the stereoisomers of **2** and the β,γ-regioisomers **4**. The only precedent successful synthesis of **2** was performed by oxidation of the corresponding alcohol,[3] which impractically demands the use of cyanide ion and silver oxide.[4]

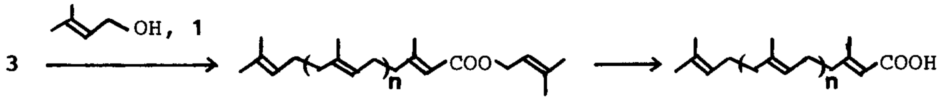


3

2 **4**

(2)

In order to achieve a new effective route, recourse was made to a sequence of the allyl ester formation followed by palladium-catalyzed deprotection (Tsuji's method)[5] (eq 3). Heating the stereochemically pure **3** at

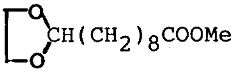
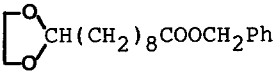
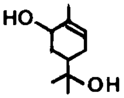
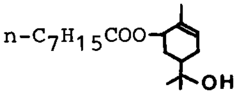
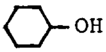
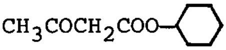
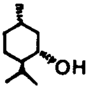
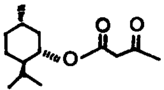
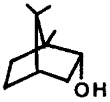
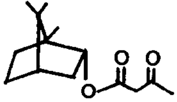
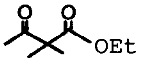
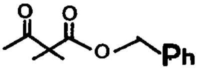
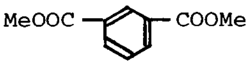
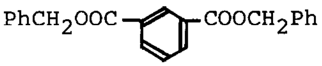
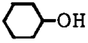
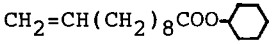


5 **2**

(3)

reflux in 3-methyl-2-buten-1-ol (prenol) for 7 h in the presence of a catalytic amount of $SCNBu_2Sn-O-SnBu_2OH$ furnished the prenyl ester **5** quantitatively without any detectable isomerization. Then, **5** was converted into **2** on

Table 1. Distannoxane-Catalyzed Transesterification [a]

RCOOR'	R"OH	R"OH/RCOOR'	time, h	product,%[b]	
n-$C_7H_{15}COOMe$	$PhCH_2OH$	2	20[c]	n-$C_7H_{15}COOCH_2Ph$	93
PhCOOMe		2	15[c]	$PhCOOCH_2Ph$	92
$CH_2=CH(CH_2)_8COOMe$		2	20[c]	$CH_2=CH(CH_2)_8COOCH_2Ph$	93
$BrCH_2COOMe$	n-$C_8H_{17}OH$	2	20[c]	$BrCH_2COOC_8H_{17}$	93
	$PhCH_2OH$	2	42[c]		90
n-$C_7H_{15}COOMe$	$THPO(CH_2)_6OH$	2	9[c]	n-$C_7H_{15}COO(CH_2)_6OTHP$	94
		1/10	12[d,e]		93
CH_3COCH_2COOEt	$PhCH_2OH$	2	16[c]	$CH_3COCH_2COOCH_2Ph$	96
		2	24[d,f]		91
		1/5	24[d,e]		93
		1/5	42[d,e]		95
	$PhCH_2OH$	10	24[d,e]		88
	$PhCH_2OH$	5	20[d]		86
n-$C_7H_{15}COOMe$	$HO(CH_2)_6OH$	1/6	10[d]	$C_7H_{15}COO(CH_2)_6OOCC_7H_{15}$	99
n-$C_7H_{15}COOMe$	$C_6H_{13}CH(OH)CH_3$	10	22[d,f]	$C_7H_{15}COOCH(CH_3)C_6H_{13}$	88
$CH_2=CH(CH_2)_8COOMe$		10	19[d,f]		93

a) Reaction conditions: toluene, reflux, cat. conc. 1 mol% relative to the minor reactant otherwise noted.

b) Isolated yields after column chromatography on silica gel.

c) $ClBu_2Sn$-O-$SnBu_2OH$ was employed as a catalyst.

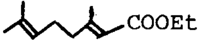
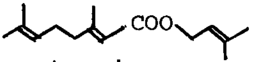
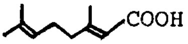
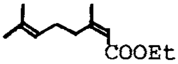
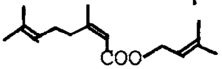
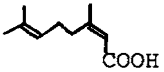
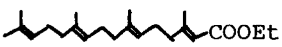
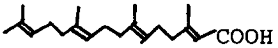
d) $SCNBu_2Sn$-O-$SnBu_2OH$ was employed as a catalyst.

e) Cat. conc. 10 mol%.

f) Cat. conc. 5 mol%.

treatment with $Pd(OAc)_2$-Ph_3P/Et_3N-HCOOH in refluxing dioxane. GLC and NMR analyses confirmed the absence of either the stereoisomer of **2** or regioisomers **4**. Table II shows the efficiency of the present procedure which allows for exclusive formation of (E)- and (Z)-isomers.

Table II. Stereo- and Regiospecific Synthesis of **2**.

3	**5**, yield, %[a,b]	**2**, yield, %[b,c]
	 95	 93
	 90[d]	 90
	 96	 94[e]

a) Reaction conditions: $SCNBu_2Sn$-O-$SnBu_2OH$ (1 mol%), prenol, reflux, 7 h.

b) Isolated yields after column chromatography. No stereo- and regioisomers were detected on the basis of GLC and ^1H NMR spectra.

c) Reaction conditions: $Pd(OAc)_2$(2 mol%)-Ph_3P(24 mol%)/Et_3N-HCOOH, dioxane, reflux, 4.5 h.

d) Reaction time: 43 h

e) $Pd(OAc)_2$: 5 mol%

In conclusion, a novel transesterification reaction has been developed which is promoted by the unique template effect of distannoxanes. The present method proved to be applicable to a wide variety of compounds except for tertiary alcohols, thus offering a versatile synthetic method for otherwise difficult-to-obtain esters.

Acknowledgement:Thanks are due to Prof. Rokuro Okawara for helpful discussions.

References

(1) For a previous study on this subject, see J. Otera, T. Yano, and R. Okawara, Organometallics, in press.

(2) D. F. Taber, J. C. Amedio Jr., and Y. K. Patel, J. Org. Chem. **50**, 3618 (1985).

(3) E. J. Corey, N. W. Gilman, and B. E. Ganem, J. Am. Chem. Soc. **90**, 5616 (1968).

(4) It has also been reported that potassium cyanide catalyzed-transesterification of α,β-unsaturated esters resulted in stereochemical retention with 94% selectivity at best: K. Mori, M. Tominaga, T. Takigawa, and M. Matsui, Synthesis, **1973**, 790.

(5) J. Tsuji and T. Yamakawa, Tetrahedron Lett. **1979**, 613.

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