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Butylstannonic Acid Catalyzed Transesterification of Carboxylic Esters.

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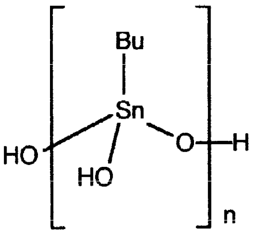
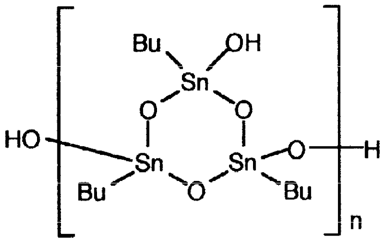
Abstract: Butylstannonic acid is used as catalyst for transesterification of various carboxylic esters. This method is also applicable to acetylation/deacetylation of alcohols.

Transesterification is an equilibrium process where a carboxylic ester is transformed into another through interchange of the alkoxy moiety.[1] One of the most effective methods for carboxylic ester synthesis is generally carried out by heating the substrate carboxylic ester under reflux with a large excess of alcohol in the presence of a Brønsted acid (such as sulfuric acid or p-toluenesulfonic acid) or basic catalysts.[1] This method fails with molecules containing acid- or base-labile functional groups. In contrast, iodotrimethylsilane,[2] bis[1-(hydroxydi-n-butyl)-3-(isothiocyanatodi-n-butyl)distannoxane], bis[1-(hydroxydi-n-butyl)-3-(chlorodi-n-butyl)distannoxane],[3] and a series of mono-organotin (IV) compounds such as butyltin trichloride,[4] as well as a number of titanium tetraalkoxides developed by Seebach *et al.*,[5] have been recommended as exceptionally mild and efficient catalysts for the transesterification of carboxylic esters in the presence of acid-sensitive groups.

In 1966 Luijten[6] first proposed the polymeric structure I for butylstannonic acid [BuSn(O)OH], as well as other alkylstannonic acids. In 1972, based on ^{119}Sn Mössbauer and ^{119}Sn NMR spectra, structure II was suggested by Smith, Smith and Davies.[7] In both structures the tin atom is four-coordinate in a tetrahedral environment of the type $RSnX_3$. Also in 1972, Smith, Smith and Davies first proposed the structure III for the product of the reaction of an organostannonic acid and a carboxylic acid.[7] In 1987, Holmes *et al.* demonstrated by X-ray analysis that the hexameric butyltin oxocyclopentanoate $[n\text{-BuSn(O)O}_2\text{CC}_5\text{H}_9]_6{\cdot}\text{C}_6\text{H}_6$ and the hexameric butyltin oxocyclohexanoate $[\text{BuSn(O)O}_2\text{CC}_6\text{H}_{11}]_6{\cdot}\text{C}_6\text{H}_6$ prepared from butylstannonic acid and the corresponding carboxylic acid have "drum" structures.[8,9] In 1991, Tiekink *et al.* also reported that the reaction of butylstannonic with R'COOH (R' = ^{i}Pr and ^{t}Bu) give hexameric butyltin oxocarboxylates, and these were shown by ^{119}Sn NMR, and later confirmed by X-ray diffraction, to adopt the schematic "drum" structure (IV).[10]



I



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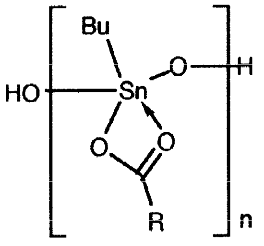

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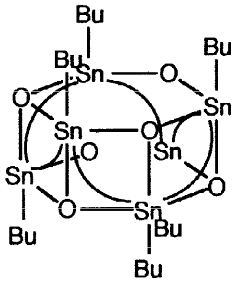

IV

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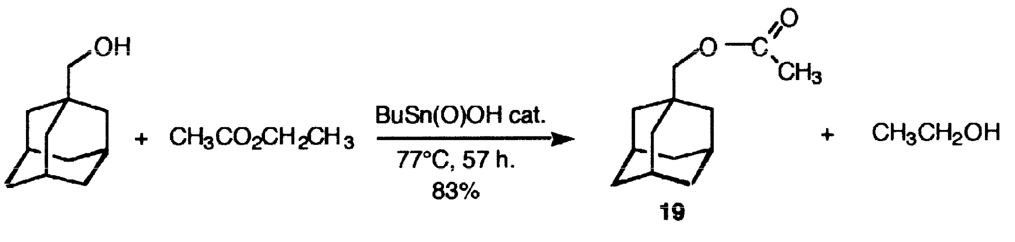
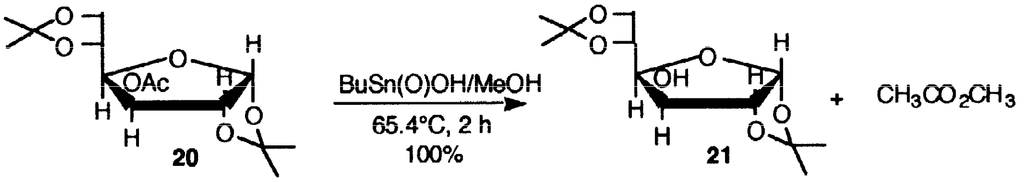
We felt that butylstannonic acid might be a novel transesterification catalyst and have checked its effect on carboxylic esters in alcohol as solvent and also in apolar aprotic solvents with low dielectric constant, such as toluene. We report here that using BuSn(O)OH as a catalyst, an unprecedented transesterification reaction takes place leading to excellent yields of carboxylic esters in the presence of several functional groups, and we also found that this catalyst can be applied for a facile and selective O-acylation/O-deacylation of alcohols.

As reported in Table 1, good yields of transesterified esters were obtained from the 1-adamantanemethyl alcohol (entry 4), secondary (entries 2,6 and 7) and benzyl alcohols (entries 1, 3, 8 and 9). Tertiary alcohols (entry 5) are more sensitive to steric hindrance and are unreactive. The optical purity of chiral alcohols does not decrease during transesterification, for example, (1R,2S,5R)-(-)-menthol and [(1S)-endo-](-)-borneol are recovered without loss of optical purity by the trimethyltin hydroxide cleavage[11] of the transesterification product, bornyl 4-bromocrotonate (**9**) and menthyl 2-butynoate (**11**) (entries 6 and 7). *N*-benzyloxycarbonyl-(Z) and *N*-*t*-butoxycarbonyl (Boc) protected esters of dipeptides (entries 8 and 9) can be transesterified using BuSn(O)OH. This procedure provides a good way of converting methyl esters into their benzyl counterparts; such reactions proceeded in 90% isolated yield. Our attention was then directed towards the reaction of transesterification catalyzed by BuSn(O)OH using the alcohols as solvent. The results for the three examples shown in Table 2 indicate that the ease with which a target ester is formed is dependent upon the combination of alcohol and ester reactants. i) Ethanol (entry 1) has the strongest replacing power. ii) The substitution power of n-propanol, a longer alkyl chain, is lower (entry 2). iii) Branching of the chain (isopropanol) causes a decrease in reactivity (entry 3).

Despite the recent introduction of several useful methods for the protection of hydroxyl groups,[12] there still exists a real need for a highly specific reagent which, in high yield and under mild conditions, will introduce or remove O-acetyl groups. This is highly desirable for synthetic reactions involving multifunctional compounds. The use of BuSn(O)OH as a catalyst and ethyl acetate as an acetylating agent and, conversely, use of methanol as a deacetylating agent, proved to be exceedingly effective. The specific reactions outlined immediately below provide an illustration of the applicability of butylstannonic acid catalysis for the acetylation/deacetylation of alcohols. The acetyl group was introduced in 1-adamantanemethanol in 83% yield (eq. 1). Complementary, the deprotection of 3-acetyl group in 3-O-acetyl-1,2,5,6-di-isopropyliden-α-D-glucofuranose (**20**) with methanol and BuSn(O)OH as catalyst, was accomplished in quantitative yield (eq. 2).



(eq. 1)



(eq. 2)

Table 1. Transesterification mediated by BuSn(O)OH in toluene at reflux.

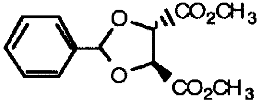
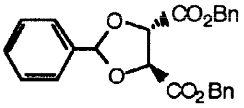
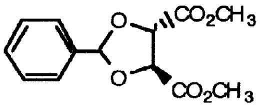
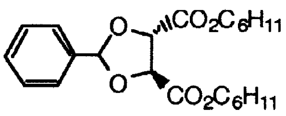
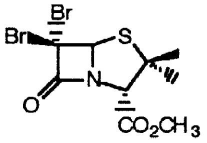
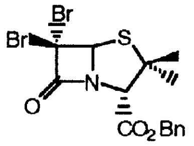
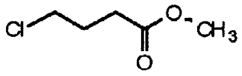
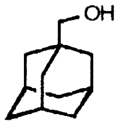
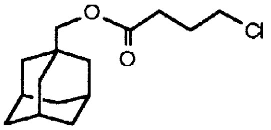
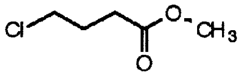
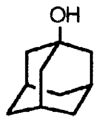
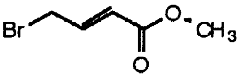
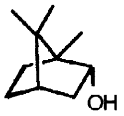
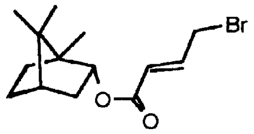
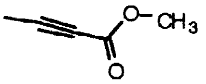
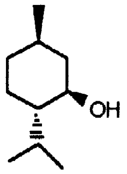
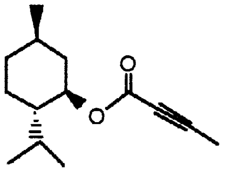
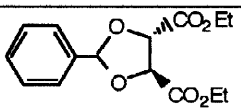
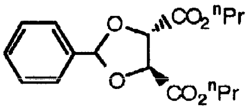
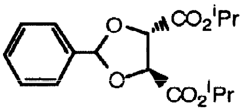
Entry	Substrate		Alcohol	Time (h)	Product		Isolated yield (%)
1		**1**	Benzyl alcohol	19		**2**	90
2		**1**	Cyclohexanol	25		**3**	90
3		**4**	Benzyl alcohol	41		**5**	84
4		**6**		22		**7**	94
5		**6**		40	No reaction		0
6		**8**		21		**9**	87
7		**10**		23		**11**	89
8	Z-Ala-Ala-OCH3	**12**	Benzyl alcohol	64	Z-Ala-Ala-OBn	**13**	90
9	Boc-Phe-Pro-OCH3	**14**	Benzyl alcohol	25	Boc-Phe-Pro-OBn	**15**	90

Table 2. Transesterification mediated by BuSn(O)OH in alcohols at reflux

Entry	Substrate	Alcohol	Time (h)	Product		Isolated yield (%)
1	**1**	CH_3CH_2OH	16		**16**	80
2	**1**	$CH_3(CH_2)_2OH$	16		**17**	65
3	**1**	$(CH_3)_2CHOH$	27		**18**	46

In conclusion, we have developed the first method for transesterification of carboxylic esters using catalytic butylstannonic acid, a commercially available reagent. We believe that this methodology will become a useful tool in the synthesis of carboxylic esters as well as in the acylation and deacylation of alcohols. Notably, this method is applicable to substrates with additional functional groups which would not survive Brønsted acid- or base-catalyzed transesterification conditions, such as triple bonds, acetals, a β-lactam ring, and carbamate groups (Z and Boc).

Further investigation concerning to the scope and mechanism of the present reaction is now in progress.

Representative Experimental Procedures:[13]

Synthesis of (-)-dibenzyl 2,3-O-benzylidene-L-tartrate (2). A toluene solution (4 mL) of (-)-dimethyl 2,3-O-benzylidene-L-tartrate (**1**) (159. 4 mg, 0.59 mmol), benzyl alcohol (0.31 mL, 2.99 mmol), and butylstannonic acid (27.1 mg, 0.13 mmol) was refluxed for 19 h. The excess toluene and benzyl alcohol were evaporated in vacuo. The residue was purified by flash column chromatography on silica gel (hexane-ethyl acetate 80:20) to give compound **2** as a white solid (221 mg, 90%).

Synthesis of (-)-diethyl 2,3-O-benzylidene-L-tartrate (16). Compound **1** (147. 3 mg, 0.55 mmol) was dissolved in ethanol (4 mL), followed by butylstannonic acid (120.6 mg, 0.58 mmol), and the mixture was refluxed for 16 h. The excess ethanol was evaporated in vacuo and the residue was purified by flash column chromatography as above to give compound **16** as a white solid (128 mg, 80%).

Deacylation of 3-O-acetyl-1,2,5,6-di-isopropylidene-α-D-glucofuranose (20). Compound **20** (154.5 mg, 0.533 mmol) was dissolved in methanol (4 mL), followed by butylstannonic acid (56.4 mg, 0.27 mmol), and the mixture was heated to reflux for 2 h. The excess methanol was evaporated and the residue purified as above to give compound **21** as a white solid (133 mg, 100%).

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References and Notes

± Dedicated to Professor Dr. Eduardo G. Gros on the occasion of his 65th birthday

1. For a recent review on transesterification, see: Otera, J. *Chem. Rev.* **1993**, *93*, 1449-1470.
2. Olah, G. A.; Narang, S. C.; Salem, G. F.; Balaram Gupta, B. G. *Synthesis* **1981**, 142.
3. a) Otera, J.; Yano, T.; Kawabata, A.; Nozaki, H. *Tetrahedron Lett.* **1986**, *27*, 2383. b) Otera, J.; Dan-oh, N.; Nozaki, H. *J. Org. Chem.* **1991**, *56*, 5307.
4. Hobbs, L. A.; Smith, P. J. *Appl. Organomet. Chem.* **1992**, *6*, 95.
5. a) Seebach, D.; Hungerbühler, E.; Naef, R.; Schnurrenberger, D.; Weidmann, B.; Züger, M. *Synthesis* **1982**, 138. b) Seebach. D.; Weidmann, B.; Widler, L. *In Modern Synthetic Methods* **1983**, Scheffold, R. Ed.; Otto Salle: Frankfurt, **1983**; Vol. 3, p 217. c) Imwinkelreid, R.; Schiess, M.; Seebach, D. *Org. Syn.* **1987**, *65*, 230.
6. Luijten, J. G. A. *Recl. Trav. Chim. Pays-Bas.* **1966**, *85*, 873.
7. Davies A. G.; Smith, L.; Smith P. J. *J. Organomet. Chem.* **1972**, *39*, 279.
8. Chandrasekhar, V.; Schmid, C. G.; Burton, S. D.; Holmes, J. M.; Day, R. O.; Holmes, R. R. *Inorg. Chem.* **1987**, *26*, 1050.
9. For recent reviews on structural chemistry of organotin carboxylates, see: a) Holmes, R. R. *Acc. Chem. Res.* **1989**, *22*, 190. b) Tiekink, E. R. T. *Applied Organomet. Chem.* **1991**, *5*, 1.
10. Mokal, V. B.; Jain, V. K.; Tiekink. E. R. T. *J. Organomet. Chem.* **1991**, *407*, 173.
11. For a recent review on esterifications, transesterifications and deesterifications mediated by organotin oxides, hydroxides and alkoxides, see: Mascaretti, O. A.; Furlán, R. L. *Aldrichimica Acta* **1997**, *30*, 55.
12. a) Greene, T. W.; Wuts, P. G. M. *Protective groups in Organic Synthesis;* J. Wiley & Sons: New York, **1991**. b) Kocienski, P. J. *Protecting groups*, Georg Thieme Verlag: Stuttgart, **1994**.
13. Products were identified by spectroscopic methods (IR, ^1H and ^{13}C NMR) and by comparison with authentic samples if available.