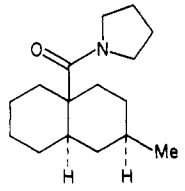
ether by a cationic catalyst system is all the more remarkable in light of the well-known sensitivity of enol ethers toward Lewis acids.[15]

Perhaps the most dramatic entry in the table is the conversion **19** → **20**, with a diastereoisomeric excess of >1000:1.[16] In contrast, hydrogenation with palladium on carbon produces the other three possible diastereoisomers in a ratio of 1:1:11.6. Because of the steric bulk of the carboxamido group in **19**, we assume that the major diastereoisomer from the Pd/C reaction is trans fused **21**. We expect that hydrindanes and other fused ring systems will be similarly available in either cis or trans modification by these complimentary hydrogenation procedures.



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Acknowledgment. We thank the National Institutes of Health (GM 33061) for their support of this work. The purchase of the Nicolet R3m X-ray Diffractometer by Rensselaer Polytechnic Institute is gratefully acknowledged. We thank Dr. Rudolf Kullnig for the X-ray diffraction analysis of **4**.

Supplementary Material Available: Complete listings of positional parameters, bond angles and distances, and thermal parameters for structure **4** (6 pages). Ordering information is given on any current masthead page.

(15) We have found that under carefully defined conditions the enol methyl ether of cyclohexanone is hydrogenated by the iridium catalyst system to give methyl cyclohexyl ether. Although this result requires more detailed study, it does demonstrate that bidentate substrate catalyst coordination is not required for successful enol ether hydrogenation.

(16) Triene **19** is prepared from *o*-anisic acid by the Birch reduction–alkylation procedure, followed by the Lewis acid catalyzed ene methodology described by Snider and co-workers; see: Jackson, A. C.; Goldman, B. E.; Snider, B. B. *J. Org. Chem.* **1984**, *49*, 3988. Details of this synthesis will be published elsewhere.

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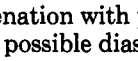
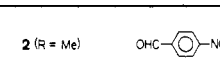
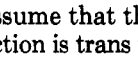
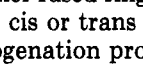
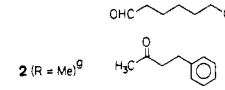
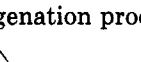
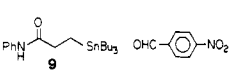
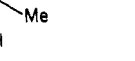
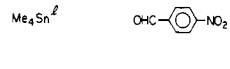
A New Method for Generating Trichlorotitanium(IV) Ester Homoenolates. Direct Tin–Titanium Exchange

Summary: Treatment of the β-tri-*n*-butylstannyl derivatives of esters with titanium tetrachloride in dichloromethane effects tin–titanium exchange to generate trichlorotitanium(IV) homoenolate derivatives of the esters, which may then be used in further reaction with electrophiles.

Sir: Functionalization of β-carbon atoms of carbonyl compounds via carbanion (homoenolate anions) **1** has been of considerable interest to synthetic organic chemists. Many approaches to generate useful homoenolate anion equivalents have been reported.[1] It is well-known that certain types of carbon–tin σ-bonds can be activated by various catalysts to form carbon–carbon bonds with electrophiles.[2] This fact, coupled with the ease with which trialkyltin moieties can be introduced at the β-carbon atoms of carbonyl compounds,[3] prompted us to investigate the possibility of using such β-trialkyltin-substituted carbonyl derivatives as latent homoenolate anions. We report here the generation of trichlorotitanium(IV) ester homoenolate derivatives via direct tin–titanium exchange.

Methyl 3-(tri-*n*-butylstannyl)propionate (**2**, R = Me) can be prepared easily in large quantities by treating tri-*n*-butyltin hydride with methyl acrylate (80 °C, 4 h, 75% yield).[4] Treatment of this methyl ester (**2**, R = Me) with

Table I. Reactions of Tin Compounds with Electrophiles in the Presence of $TiCl_4$[a]

entry	tin substrate	electrophile	reactn condn: temp,[b] °C	reactn condn: time,[c] h	product	yield,[d] %
1	**2** (R = Me)		0	2.5		75
2			20	5.0	 **4**	64
3			−10	5.0		61
4	**2** (R = Me)[g]		−10	24.0	**5**	(50)[h]
5	**2** (R = Me)[i]		−10	24.0		54[j]
6	 **9**		−10	7.0	 **10**	(60)[k]
7	**9**[l]		−10	16.0		83
8	Me_4Sn[l]		−10	48.0	 **11**	47
9	Bu_4Sn[l]		−10	48.0		26[m]

[a] CH_2Cl_2 solvent; unless otherwise mentioned, 1.0 equiv of $TiCl_4$ was used. [b] The initial −78 °C cooling bath was replaced by the specified-temperature bath, and the reaction mixture was allowed to warm to room temperature gradually. [c] The reaction mixture was quenched after the specified time. [d] Unless otherwise mentioned, yield refers to isolated yield of the pure compound. [e] Even at a lower temperature (−30 °C, 20 h), the chloro compound was the major product. [f] Product after lactonization (refluxing in toluene with PTSA as catalyst, 4 h). [g] 2.0 equiv of tin ester and 1.0 equiv of $TiCl_4$ were used in this reaction. [h] A 1:1 mixture of the product and the unreacted ketone was obtained, according to ^1H NMR analysis. [i] 4.0 equiv of tin ester and 2.0 equiv of $TiCl_4$ were used in this reaction. [j] The crude product contained no unreacted ketone, by ^1H NMR analysis. [k] Crude reaction product contained 60% hydroxy amide and 40% *N*-phenylpropionamide; 40% of the aldehyde was unreacted. [l] 2.0 equiv of tin substrate and 2.0 equiv of $TiCl_4$ were used. [m] Much of the unreacted *p*-nitrobenzaldehyde was recovered from the reaction mixture. Based on the recovered *p*-nitrobenzaldehyde, the yield of *p*-nitrobenzyl alcohol was 52%.

(1) For a recent review, see: Werstiuk, N. H. *Tetrahedron* **1983**, *39*, 205.

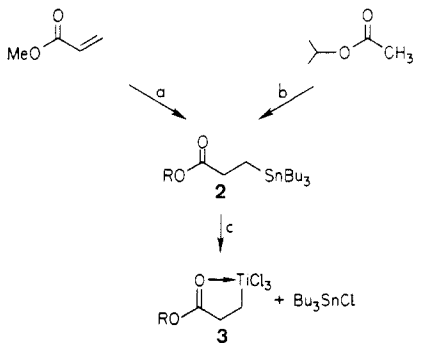
(2) (a) Allyltin compounds: Yamamoto, Y.; Yatagai, H.; Naruta, Y.; Maruyama, K. *J. Am. Chem. Soc.* **1980**, *102*, 7107. Naruta, Y. *Ibid.* **1980**, *102*, 3774. (b) Trialkyltin enolates: Trost, B. M.; Keinan, E. *Tetrahedron Lett.* **1980**, *21*, 2591. Noltes, J. G.; Verbeek, F.; Creemers, H. M. J. C. *Organomet. Chem. Synth.* **1971**, *1*, 57. (c) Intramolecular carbocyclizations: Macdonald, T. L.; Mahalingam, S.; O'Dell, D. E. *J. Am. Chem. Soc.* **1981**, *103*, 6767. (d) Pd(0)-catalyzed reactions: Milstein, D.; Stille, J. K. *J. Am. Chem. Soc.* **1979**, *101*, 4992. Logue, M. W.; Teng, K. *J. Org. Chem.* **1982**, *47*, 2549.

(3) Still, W. C. *J. Am. Chem. Soc.* **1977**, *99*, 4836 and references cited therein.

(4) (a) VanDerkerk, G. J. M.; Noltes, J. G.; Luijten, J. G. A. *J. Appl. Chem.* **1957**, *7*, 356. (b) Hayashi, K.; Iyoda, J.; Shiihara, I. *J. Organomet. Chem.* **1967**, *10*, 81.

0022-3263/85/1950-5907$01.50/0

Scheme I[a]

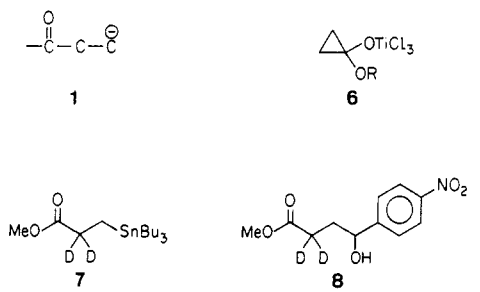


[a] (a) Bu_3SnH, 80 °C, 4 h; (b) THF, $LiN(SiMe_3)_2$, −70 °C, 15 min; ICH_2SnBu_3; (c) $TiCl_4$, CH_2Cl_2.

1.0 equiv of $TiCl_4$ generates the corresponding trichlorotitanium(IV) homoenolate (**3**, R = Me) reported by Nakamura and Kuwajima.[5] This is another example of facile stannylation/destannylation[6] to accomplish the needed "umpolung" to generate ester homoenolate derivatives (Scheme I). We generated the well-characterized isopropyl trichlorotitanium(IV) homoenolate derivative (**3**, R = $CHMe_2$) via the literature method[5] and found that the same species was generated in solution by treating the isopropyltin ester (**2**, R = $CHMe_2$) with 1.0 equiv of $TiCl_4$.[7,8] This isopropyl ester was prepared by reacting the enolate generated from isopropyl acetate with iodomethyltri-*n*-butyltin.[6]

The trichlorotitanium ester homoenolate (**3**, R = Me) generated in situ reacts with various aldehydes (Table I) to produce the γ-hydroxy esters or lactones. With benzaldehyde the benzylic chloro compound **4** was the only adduct isolated. It is well documented that monoalkyltrichlorotitanium reagents, such as $MeTiCl_3$, react only with aldehydes, whereas dialkyldichlorotitanium derivatives, such as Me_2TiCl_2, are more reactive and react with ketones as well as aldehydes.[9] So, it was not a surprise that trichlorotitanium reagent **3** (R = Me) failed to react in any appreciable amount with ketones. By changing the stoichiometry of the ester (**2**, R = Me) and the amount of $TiCl_4$ (2:1 instead of 1:1), we generated a more reactive species, presumably analogous to R_2TiCl_2, which reacted with 4-phenyl-2-butanone (entries 4 and 5, Table I) to produce the γ-lactone **5**.

To examine whether the trichlorotitanium homoenolate **3** is formed via a cyclopropane intermediate such as **6**, we used methyl 3-(tri-*n*-butylstannyl)propionate-2,2-d_2 (**7**) as the precursor.[10] Reaction of **7** with *p*-nitrobenzaldehyde (1.0 equiv $TiCl_4$, CH_2Cl_2, 0 °C, 2.5 h) produced exclusively the hydroxy ester **8**-2,2-d_2. The generation of titanium homoenolate **3** from the corresponding tri-*n*-butyltin compound **2** is, therefore, an example of direct tin–titanium exchange, rather than intramolecular reaction to



form the cyclopropane intermediate, with subsequent ring opening.

Treatment of a mixture of *N*-phenyl-3-(tri-*n*-butylstannyl)propionamide (**9**) and *p*-nitrobenzaldehyde in dichloromethane with 1.0 equiv of $TiCl_4$ gave a product mixture containing 60% hydroxy amide adduct **10** and 40% *N*-phenylpropionamide (protodestannylation product); 40% of the *p*-nitrobenzaldehyde was unreacted (entry 6, Table I). Formation of *N*-phenylpropionamide can be rationalized by the quenching of the reactive trichlorotitanium(IV) derivative (generated in situ) by the relatively acidic proton of the *N*-phenyl amide. By using 2.0 equiv each of **9** and $TiCl_4$, we obtained **10** in 83% isolated yield (entry 7, Table I).

In preliminary experiments we found that even the more common and commercially available tetraalkyltin compounds, such as tetramethyltin and tetrabutyltin, can be activated by addition of $TiCl_4$ to react with *p*-nitrobenzaldehyde. Reaction of tetramethyltin produced 1-chloro-1-(4′-nitrophenyl)ethane (**11**) (entry 8, Table I). The reaction was not as clean with tetrabutyltin. Much of the *p*-nitrobenzaldehyde was recovered unchanged from the reaction mixture. The reduction product, *p*-nitrobenzyl alcohol, was isolated as the major product (entry 9, Table I). We are investigating the possibility that trichlorotitanium(IV) derivatives are involved in these two reactions.

In a typical experiment, a dichloromethane solution containing appropriate amounts of tin compound and the desired electrophile was placed in a two-neck round-bottom flask, fitted with a rubber septum and an argon inlet tube. The solution was cooled to −78 °C in a dry ice/acetone bath. The appropriate amount of $TiCl_4$ (1 M solution in dichloromethane) was slowly added to the reaction mixture, and the resulting dark solution (or suspension) was stirred for 5 min at this temperature. Then the cooling bath was replaced by the appropriate-temperature cooling bath (temperature noted in Table I), and the mixture was gradually allowed to warm to room temperature. The reaction was quenched by slow addition of dilute HCl, and the mixture was extracted with a mixture of ether and ethyl acetate. The organic layer was washed with saturated sodium chloride solution and evaporated under reduced pressure. Excess saturated potassium fluoride solution was added to this residue, and the mixture was triturated with ether. The solid was separated by filtration and discarded. The organic layer was separated, washed with water and then with saturated sodium chloride solution, and evaporated under reduced pressure to give the crude reaction product, essentially free from tributyltin chloride byproduct. When necessary, the product was further purified by flash chromatography on silica gel.

This direct tin–titanium(IV) exchange reaction to generate trichlorotitanium(IV) reagents would make these useful homoenolate reagents more easily accessible to synthetic organic chemists. We are planning to delineate the scope of such tin–titanium exchanges in generating

(5) Nakamura, E.; Kuwajima, I. *J. Am. Chem. Soc.* **1983**, *105*, 652.
(6) Still, W. C. *J. Am. Chem. Soc.* **1978**, *100*, 1481.
(7) The ^{13}C NMR spectrum of a CD_2Cl_2 solution containing isopropyl 3-(tri-*n*-butylstannyl)propionate, $TiCl_4$, and chlorotrimethylsilane (1.0 equiv each) was compared with that of a CD_2Cl_2 solution containing 1-(trimethylsiloxy)-1-isopropoxycyclopropane, $TiCl_4$, and tri-*n*-butylstannyl chloride (1.0 equiv each).
(8) These reactions are stoichiometric rather than catalytic in $TiCl_4$ and do not take place in the absence of $TiCl_4$.
(9) Reetz, M. T.; Steinbach, R.; Westermann, J.; Peter, R. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 1011.
(10) Methyl acetate-d_3 was prepared from acetyl chloride-d_3 (Aldrich Chemicals). Compound **7** was prepared by reacting iodomethyltri-*n*-butyltin with the enolate generated from methyl acetate-d_3.

other useful organotitanium(IV) reagents.[11]

(11) For a review, see: Reetz, M. T. *Top. Curr. Chem.* **1982**, *106*, 1.

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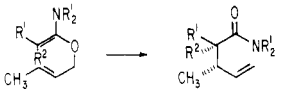
An Accelerated Diastereoselective Variant of the Amide Acetal Claisen Rearrangement

Summary: Salts derived from alkylation of propionamides or fluoroacetamides with methyl triflate or dimethyl sulfate reacted with the lithium alkoxide of (*E*)- or (*Z*)-2-buten-1-ol at room temperature to yield directly the product of 3,3-sigmatropic rearrangement of the corresponding N,O-ketene acetals.

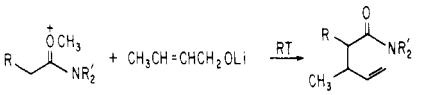
Sir: We have found that propionamides as well as fluoroacetamides may be utilized in a diastereoselective amide acetal Claisen rearrangement at room temperature. The Claisen rearrangement,[1] a powerful synthetic transformation, creates two new asymmetric centers diastereoselectively while concomittantly forming regio- and stereospecifically a new double bond. The sigmatropic rearrangement of N,O-ketene acetals, first developed by Eschenmoser,[2] preceded studies of the ynamine–Claisen rearrangement[3] where the reactive N,O-ketene acetal may be formed at much lower temperatures by treatment of the ynamine with an allylic alcohol.



In our development of new methods for the stereoselective synthesis of fluorinated molecules,[4] rearrangement of a fluorinated N,O-ketene acetal was an attractive approach. However, the necessary fluorinated ynamine was not synthetically accessible and the higher temperatures required for the amide acetal Claisen rearrangement appeared to prohibit the stereoselective formation of the fluoro N,O-ketene acetal by that route.

Three symmetric propionamides, *N*,*N*-dimethylpropionamide, *N*,*N*-diisopropylpropionamide, and *N*-propionylpyrrolidine, were examined in our initial studies. Following alkylation with dimethyl sulfate or methyl triflate, the amides were treated with the lithium salt of (*E*)- or (*Z*)-2-buten-1-ol. After as little as 14 h at room temperature, the rearranged amides were isolated in good yield[5] (See Table I). The observed diastereoselectivity

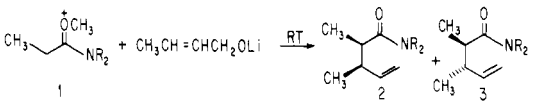
Table I. Amide Acetal Claisen Rearrangement of Propionamides and Fluoroacetamides



amide	alcohol	time,[a] h	diastereoselectivity[b]	yield,[c] %
			2:3	
1a	*E*	18	>10:1	51
1a	*Z*	16[d]	1:8[e]	79[f]
1b	*E*	14	17:1[e]	82
1b	*Z*	18	<1:10	30
1b	*E*	90	>10:1	70[g]
1b	*Z*	21[d]	<1:10	59[f]
1c	*E*	14	15:1[e]	45
1c	*E*	90	>10:1	44[g]
1c	*Z*	25[d]	<1:10	19[f]
			7:8	
5a	*E*	20	1:1.6	50
5a	*Z*	20	2.9:1	23
5b	*E*	14	1:2.7	87
5b	*Z*	18	5.1:1	77
5c	*E*	14	1:5.3	49
5c	*E*	14	1:4.8	40
5c	*E*	70	1:2.6	78
5c	*Z*	70	3.1:1	27
5c	*E*	18[h]	1:1.3	89

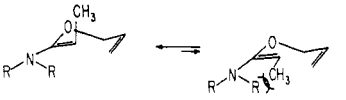
[a] Temperature 25 °C. [b] Determined by NMR spectroscopy at 7.04 T. [c] Determined by gas chromatographic analysis. [d] Temperature 67 °C. [e] Decoupled ^{13}C NMR spectra determined with NOE suppression and 50-s delay. [f] 0.0011 mol of alkoxide. [g] 0.0042 mol of alkoxide. [h] Temperature 42 °C.

was never worse than 8:1 and was as high at 17:1 in some cases as determined by ^1H and ^{13}C NMR spectroscopy.



a. R = CH_3
b. R = $(CH_2)_4$
c. R = $CH(CH_3)_2$

Stereospecificity in the amide acetal Claisen rearrangement has been suggested to result in part from unfavorable steric interactions between the alkyl substituents on nitrogen and the β-substituent of the enamine.[6] The *Z* ketene acetal was also reported to be the thermodynamic intermediate product in the boron trifluoride etherate promoted ynamine–Claisen rearrangement.[3a] With the



less sterically demanding fluorine, it was not clear if selectivity would be possible. *N*,*N*-Dimethylfluoroacetamide, *N*-(fluoroacetyl)pyrrolidine, and *N*,*N*-diisopropylfluoroacetamide were prepared as previously described.[7] Al-

(1) (a) Bennett, G. B. *Synthesis* **1977**, 589–606. (b) Hill, R. K. In "Asymmetric Synthesis"; Morrison, J. D., Ed.; Academic Press: Orlando, 1984; Vol. 3, pp 503–572.

(2) Meerwein, H.; Florian, W.; Schon, N.; Stopp, G. *Justus Liebigs Ann. Chem.* **1961**, *641*, 1–39. (b) Wick, A. E.; Felix, D.; Steen, D.; Eschenmoser, A. *Helv. Chim. Acta* **1964**, *47*, 2425–2429. (c) Felix, D.; Gschwend-Steen, K.; Wick, A. E.; Eschenmoser, A. *Helv. Chim. Acta* **1969**, *52*, 1030–1042. (d) Sucrow, W.; Richter, W. *Chem. Ber.* **1971**, *104*, 3679–3688.

(3) (a) Bartlett, P. A.; Hahne, W. F. *J. Org. Chem.* **1979**, *44*, 882–883. (b) Ficini, J.; Barbara, D. *Tetrahedron Lett.* **1966**, 6425–6429.

(4) (a) Welch, J. T.; Seper, K.; Eswarakrishnan, S.; Samartino, J. *J. Org. Chem.* **1984**, *49*, 4720–4721. (b) Welch, J. T.; Eswarakrishnan, S. *J. Chem. Soc., Chem. Commun.* **1985**, 186–188. (c) Welch, J. T.; Seper, K. *Tetrahedron Lett.* **1984**, *25*, 5247–5250. (d) Welch, J. T.; Samartino, J. S. *J. Org. Chem.* **1985**, *50*, 3663–3665.

(5) **Typical Procedure**: To a magnetically stirred three-necked round-bottom flask under an inert atmosphere, containing 5 mL of anhydrous THF or ether, was added 0.003 mol of (*E*)- or (*Z*)-2-buten-1-ol followed by 0.003 mol of methyl lithium (1.55 M solution in diethyl ether) at room temperature. After the mixture was stirred for 5 min, 0.003 mol of the O-alkylated amide salt, prepared by treatment of the neat amide with a stoichiometric amount of methyl trifluoromethanesulfonate, was added in 4 mL of THF or CH_2Cl_2. The mixture was allowed to stir at room temperature for the specified time, was diluted with 20 mL of CH_2Cl_2, was washed with three 20-mL portions of saturated sodium bicarbonate and one 20-mL portion of saturated sodium chloride solution, was dried over anhydrous magnesium sulfate, and was concentrated in vacuo.

(6) Ziegler, F. E. *Acc. Chem. Res.* **1977**, *10*, 227–232.

(7) Welch, J. T.; Eswarakrishnan, S. *J. Org. Chem.*, in press.

0022-3263/85/1950-5909$01.50/0