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Formation of homoallyl alcohols and 4-chlorotetrahydropyrans from allyl-stannanes, aldehydes and $TiCl_4$ or Cp_2TiCl_2

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Abstract

Reactions between $Bu_3SnCHR^1CH{=}CHR^2$ (**1**; $R^1 = H$, $R^2 = H$ or Me; R^1, $R^2 = (CH_2)_3$) and EtCHO in the presence of $TiCl_4$ or Cp_2TiCl_2 are reported. The compound, Cp_2TiCl_2, has been found to be an effective Lewis acid catalyst for the allylation of EtCHO using **1** ($R^1 = H$, $R^2 = Me$) and **1** (R^1, $R^2 = (CH_2)_3$) in CH_2Cl_2 or Et_2O solutions at $-78°C$; the products after hydrolysis are homoallyl alcohols with stereo- and regio-selectivities different from those found for $TiCl_4^-$ reactions. Reactions with an excess of EtCHO in the presence of $TiCl_4$ give 4-Cl-3-R^1-5-R^2-2,6-2Et-tetrahydropyrans (**2**) via insertions of a second EtCHO into the metal–O bond of the initially produced homoallyl alcoholate: the *trans*-**2** compounds are obtained from *threo*-$EtCH(OM')CHR^2CH{=}CHR^1$ and *cis*-**2** from *erythro*-$EtCH(OM')CHR^2CH{=}CHR^1$ (e.g., $M' = TiCl_3$).

Introduction

Homoallyl alcohols can be conveniently prepared by allylation of aldehydes with allylstannanes in the presence of a Lewis acid [1–12]. A second molecule of RCHO can also be incorporated [13–17], via insertion into the M′–O bond of the homoallyl alcoholates **3** and **4**, to give 4-halo- or 4-hydroxy-tetrahydropyrans (**2**), previously obtained from the reactions in the presence of $BF_3 \cdot Et_2O$, tin halides, or BCl_3 [18] (see Scheme 1).

The formation of homoallyl alcohols has been especially well studied, with much attention paid to the factors controlling the stereo- and regio-selectivities. The synthesis of the tetrahydropyrans has been less studied. We present here some observations on the synthesis of 4-chlorotetrahydropyran derivatives (**2**; Y = Cl)

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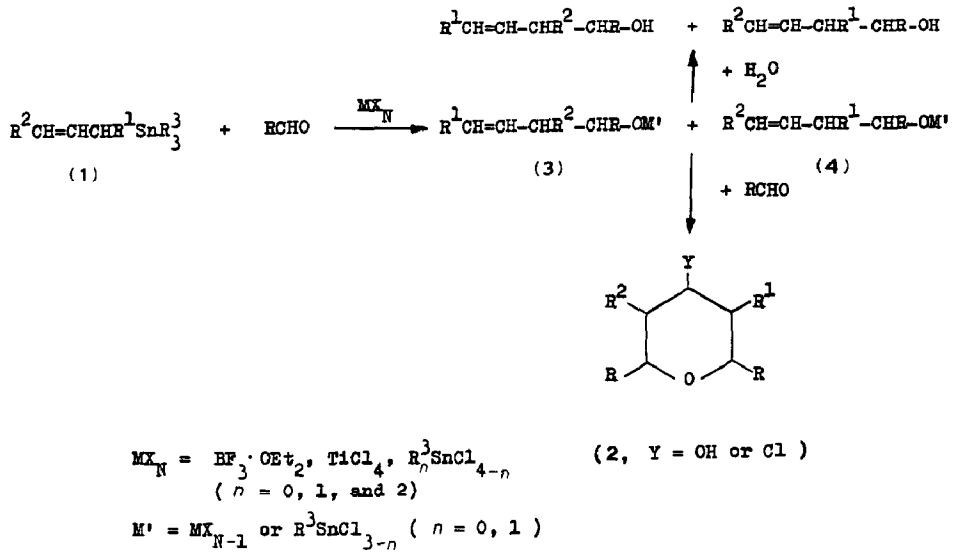


Scheme 1

with $TiCl_4$ as the added Lewis acid. In addition, a comparison has been made of the effects of Cp_2TiCl_2 and $TiCl_4$ as the added Lewis acid in the formation of homoallyl alcohols from crotyl- and cyclohex-2-enyl-stannanes.

Results and discussion

While allylation of RCHO can be brought about by use of an allylstannane **1** alone, on heating or under pressure [19], the presence of a Lewis acid, MX_N, e.g., $BF_3 \cdot OEt_2$, $TiCl_4$ or $R^3_nSnCl_{4-n}$ ($n = 0$–2), allows much milder conditions, e.g., temperatures of $-78°C$, to be employed. Furthermore, the presence of the added Lewis acid can give rise to significantly different selectivities among the homoallyl alcohol products. The added MX_N has been considered to activate the aldehyde, via complexation [7–9], and/or to take part in exchange reactions with **1** to generate new and more active allylating species, $[R^1CH{=}CHCHR^2]MX_{N-1}$. The stereoselectivities of products **3** and **4** (Scheme 1) can depend on the particular allylating agent as well as the structure of the complexed aldehyde. The involvement of a pre-transmetallation step being increasing accepted, especially for the $TiCl_4$ [20] and $R^3_nSnCl_{4-n}$ reactions [10,16,21] (as well as those with BCl_3 [18]). No evidence has yet been found for the occurrence of transmetallations between $BF_3 \cdot OEt_2$ and **1** in solvents such as CH_2Cl_2 at $-78°C$.

Irrespective of the order of mixing of the reagents, mixtures of $BF_3 \cdot OEt_2$, RCHO and either (*Z*)- or (*E*)-crotylstannanes give $CH_2{=}CHCHMeCHROH$ (**5**) with an *erythro*-stereo-selectivity [24]. In contrast $TiCl_4$-promoted reactions have stereo-selectivities markedly dependent on the order of mixing: normal addition (crotylstannane added to $TiCl_4$ and RCHO at $-78°C$) gives **5** with a high *erythro*-selectivity (the active allylating agent is considered to be the allylstannane), whereas inverse addition (RCHO added to pre-equilibrated $TiCl_4$-crotylstannane mixture) gives **5** with a high *threo*-selectivity (a crotyl-titanium species is probably

the active species) [20]. Use of related titanium compounds is known from other studies to lead to products with high *threo*-selectivities [25].

Three allylstannanes **1** were used in this study with $TiCl_4$ or Cp_2TiCl_2 namely (**1**, $R^1 = R^2 = H$), (**1**, $R^1 = H$, $R^2 = Me$) ($E/Z = 40/60$) and (**1**, R^1, $R^2 = (CH_2)_3$). Details of results for the formation of homoallyl alcohols from (**1**, R^1, H, $R^2 = Me$) and (**1**, R^1, $R^2 = (CH_2)_3$) are given in Table 1 for reactions involving $TiCl_4$ or Cp_2TiCl_2 and some other selected Lewis acids.

The halide Cp_2TiCl_2 is as an effective Lewis acid in these reactions. There are however clear differences (compare entries 1–3) between the results for Cp_2TiCl_2 (using the so-called normal addition) and for $TiCl_4$ (using either the normal or inverse addition) [20] in CH_2Cl_2 solution, initially at $-78°C$, in terms not only of the *erythro/threo* selectivities observed for $EtCH(OH)CHMeCH{=}CH_2$ (**6**) but also of the high yield (42%) of (*Z*)-$EtCH(OH)CH_2CH{=}CHMe$ (**7**) * obtained from the Cp_2TiCl_2 reaction. The formation of **7** suggests the involvement of $CH_2{=}CHCHMe$-metal allylating agents as well of $MeCH{=}CHCH_2$-metal species (for formation of **6**). High yields of **7** were obtained from reactions involving the addition of **1** ($R^1 = H$, $R^2 = Me$) and EtCHO to Bu_2SnCl_2, in which $Bu_2ClSnCHMeCH{=}CH_2$ is the actual allylating species [10]. The *erythro/threo* ratio for **6** obtained in the Cp_2TiCl_2 (**1**, $R^1 = H$, $R^2 = Me$; $E/Z = 40/60$) reaction (entry 3) is similar to that for reaction in Et_2O at $-35°C$ using Cp_2TiCl(crotyl) (**8**), pre-formed [26] from (*E*)-$MeCH{=}CHCH_2MgBr$ and Cp_2TiCl_2 (entry 5). It appears that stereoselectivities in reactions of **8** in Et_2O solution are somewhat temperature-dependent [26,27] (entries 4 and 5).

As shown by entries 10 and 11 in Table 1, Cp_2TiCl_2 is mildy in the reaction of tributylcyclohex-2-enyltin (**1**, R^1, $R^2 = (CH_2)_3$) with EtCHO in both CH_2Cl_2 and Et_2O solutions. As well as the homo allyl alcohol, $EtCH(OH)CHR^1CH{=}CHR^2$ (**9**, R^1, $R^2 = (CH_2)_3$), produced in modest yields (28 and 39%), products of decomposition of **1** (R^1, $R^2 = (CH_2)_3$) viz. cyclohexenone and cyclohexenol, were also isolated. Similar *erythro/threo* ratios (ca. 60/40) for **9** were observed in both reactions. This ratio was also observed when Bu_2SnCl_2 was used at 25 °C in the absence of solvent (entry 12) and also in one of the two $TiCl_4$ reactions involving **1** (R^1, $R^2 = (CH_2)_3$) (entry 8). A similar *erythro/threo* ratio (for $MeCH(OH)CHR^1CH{=}CHR^2$) was also observed in the Bu_2SnCl_2, MeCHO and **1** (R^1, $R^2 = (CH_2)_3$) reaction. Only the $BF_3 \cdot OEt_2$ reaction [18] (entry 14) showed a higher *erythro*-selectivity.

Compound **1** (R^1, $R^2 = (CH_2)_3$) can exist only as a (*Z*)-alkene, and no apparent allyl migration or isomerization occurs in exchange reactions with MX_N. The involvement of the Lewis acid thus can only provide a new allyl-metal species, $X_{N-1}M\overline{CHCH{=}CH(CH_2)_3}$ and/or a complexed aldehyde.

The Bu_2SnCl_2 reactions (with MeCHO or EtCHO) and **1** (R^1, $R^2 = (CH_2)_3$) give the same *erythro/threo* ratio for the homo-allyl alcohols even when different sequences of adding reagents were utilized. Use of these different sequences gave rise to quite distinct *erythro/threo* ratios when crotyl$SnBu_3$ was used.

The different stereoselectivities obtained in the two $TiCl_4$, EtCHO and **1** (R^1, $R^2 = (CH_2)_3$) reactions (entries 8 and 9) indicate the importance of the reaction

* Species 7 was the major homoallyl alcohol product from such reactions.

Table 1

Products of reactions between equimolar amounts of RCHO(A), $Bu_3SnCHR^1CH{=}CHR^2$ (1; Sn) and Lewis acid (LA)

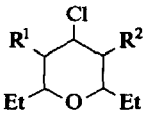
Entry No.	(1) (Sn)	Lewis Acid (LA)	RCHO (A)	Addition sequence reaction conditions	Products [a] (Yields %)	Ref.
1	(*Z*)-1,(R^1 = H, R^2 = Me)	$TiCl_4$	*cyclo*-$C_6H_{11}CHO$	(Sn) to (LA) + (A) CH_2Cl_2, −78 °C	*cyclo*-$C_6H_{11}CHOHCHMeCH{=}CH_2$ (97) *erythro/threo* = 97/7 + cyclo-$C_6H_{11}CHOHCH_2CH{=}CHMe$ (3) *Z/E* = 81/19	20
2		$TiCl_4$	*cyclo*-$C_6H_{11}CHO$	(A) to premixed (LA) + (Sn)	*cyclo*-$C_6H_{11}CHOHCHMeCH{=}CH_2$ (95) *erythro/threo* = 5/95 + (*E*)-*cyclo*-$C_6H_{11}CHOHCH_2CH{=}CHME$ (5)	20
3	1 (R^1 = H, R^2 = Me) (*E*):(*Z*) = 40:60	Cp_2TiCl_2 [c]	EtCHO	(Sn) to (LA) + (A) CH_2Cl_2	EtCHOHCHMeCH=CH_2 (58) *erythro/threo* = 40/60 + (*Z*)-EtCHOHCH$_2$CH=CHMe (42)	[b]
4	$Cp_2TiCl(CH_2CH{=}CHMe)$ [d]		PhCHO	Et_2O, −78 °C	PhCHOHCHMeCH=CH_2 *erythro/threo* = 20/80	27
5	$Cp_2TiCl(CH_2CH{=}CHMe)$		RCHO	Et_2O, −35 °C	RCHOHCHMeCH=CH_2 R = Ph; *erythro/threo* = 40/60 R = Et, *erythro/threo* = 36/64	26
6	1 (R^1 = H, R^2 = Me) (*E*):(*Z*) = 33:66	Bu_2SnCl_2	EtCHO	(Sn) + (A) to (LA) Neat, 25 °C	EtCHOHCHMeCH=CH_2 (4–13) *erythro* ⩾ *threo* + (*Z*)-EtCHOHCH$_2$CH=CHMe (87–96)	28
7		Bu_2SnCl_2	EtCHO	(A) to equilibrated (Sn) + (LA) Neat, 25 °C	EtCHOHCHMeCH=CH_2 (80) *erythro/threo* = 38/62	10

8	**1** (R^1, $R^2 = (CH_2)_3$)	$TiCl_4$	EtCHO [c]	(Sn) to (LA) + (A) CH_2Cl_2 (i) −79 °C, 20 min (ii) −78 °C → RT in 3 h	$EtCHOHCHR^1CH{=}CHR^2$ (50) *erythro/threo* = 3/97	[b]
9			EtCHO [e]	(Sn) to (LA) + (A) CH_2Cl (i) −78 °, 30 min (ii) −50 °C, 30 min (iii) −30 °C 1 h	$EtCHOHCHR^1CH{=}CHR^2$ (53) *erythro/threo* = 60/40	[b]
10		Cp_2TiCl_2	EtCHO [c]	(Sn) to (LA) + (A) Et_2O, −78 °C, 20 min −78 °C → RT, $1\frac{1}{2}$ h	$EtCHOHCHR^1CH{=}CHR^2$(28) [f] *erythro/threo* = 60/40	[b]
11				(Sn) to (LA) + (A) CH_2Cl_2, −78 °C, 20 min −78 °C → RT, $1\frac{1}{2}$ h	$EtCHOHCHR^1CH{=}CHR^2$ (39) [f] *erythro/threo* = 64/36	[b]
12		Bu_2SnCl_2	EtCHO [c]	(LA) to (Sn) + (A) RT, no solvent	$EtCHOHCHR^1CH{=}CHR^2$ (78) *erythro/threo* = 85/35	[b]
13			MeCHO	(A) to premixed (LA) + (Sn) no solvent	$MeCHOHCHR^1CH{=}CHR^2$ (70) *erythro/threo* = 60/40	[b]
14		$BF_3{\cdot}OEt_2$ [h]	EtCHO [c]	(A) to premixed (LA) + (Sn) −78 °C, 20 min −78 °C → RT	$EtCHOHCHR^1CH{=}CR^2$ (76) *erythro/threo* = 77/23	18

[a] After hydrolysis. [b] This study; [c] 10 mmol. [d] Obtained in situ from $Cp_2TiCl_2 + MeCH{=}CHCH_2MgX$. [e] 20 mmol. [f] Other products cyclohexenone and cyclohexenol. [g] Excess MeCHO (3 equivalents) was used to allow for polymerization of MeCHO. [h] 2 equivalents $BF_3{\cdot}OEt_2$.

Table 2

Products of reaction of $Bu_3SnCHR^1CH{=}CHR^2$ (1; Sn). Lewis acid (LA) and an excess of EtCHO (A) (2.2 equivalents)

Entry No.	(1; Sn)	Lewis acid (LA)	Addition sequence reaction conditions	Products [a] (Yield %)		Ref.
					Other	
1	1 ($R^1 = R^2 = H$)	$TiCl_4$ [b]	(Sn) to (A) + (LA) no solvent, −50 °C	$R^1 = R^2 = H$ (66)		[c]
2		BCl_3 [d]	(Sn) to (A) + (LA) CH_2Cl_2, −78 °C → RT	$R^1 = R^2 = H$ (68)		18
3	1 (R^1 = H, R^2 = Me) (*E*)/(*Z*) = 40/60	$TiCl_4$ [b]	(Sn) + (A) → (LA) Et_2O, −78 °C → RT	R^1 = H, R^2 = Me (80) *trans*/*cis* = 27/73		[c]
4		$TiCl_4$ [b]	(A) to (Sn) + (LA) Et_2O, −78 °C → RT in $1\frac{1}{2}$ h	R^1 = H, R^2 = Me (78) *trans*/*cis* = 28/72	(*E*)-EtCH=CMeCHO (20)	[c]
5		$TiCl_4$ [b]	(A) to (Sn) + (LA) CH_2Cl_2, −78 °C → RT in $1\frac{1}{2}$ h	R^1 = H, R^2 = Me (51) *trans*/*cis* = 88/12	$EtCHOHCHMeCH{=}CH_2$ (12) (*E*)-EtCH=CMeCHO (36)	[c]
6		$TiCl_4$ [b]	(LA) to (Sn) + (A) no solvent, −78 °C → RT	R^1 = H, R^2 = Me (49) *trans*/*cis* = 45/55	$EtCHOHCHMeCH{=}CH_2$ (47)	[c]
7		BCl_3 [d]	(Sn) to (A) + (LA) CH_2Cl_2, −78 °C → RT in $1\frac{1}{2}$ h	R^1 = H, R^2 = Me (46) *trans*/*cis* = 30/70		18
8	1 (R^1, $R^2 = (CH_2)_3$)	$TiCl_4$ [b]	(Sn) + (A) to (LA) Et_2O, −78 °C, 30 min −78 °C → RT	R^1, $R^2 = (CH_2)_3$ (28) only *trans*		[c]
9		$BF_3{\cdot}OEt_2$ [d]	(Sn) to (A) + (LA) CH_2Cl_2, −78 °C, 30 min −78 °C → RT		4-HO-3-Me-2, 6-Et-tetrahydropyran (63) *trans*/*cis* = 12/88 (*E*)-EtCH=CMeCHO, cyclohexenol	18
10		BCl_3 [d]	(Sn) to (A) + (LA) CH_2Cl_2, −78 °C → RT	R^1, $R^2 = (CH_2)_3$ (17) *trans*/*cis* 55/45	$EtCHClCHR^1CH{=}CHR^2$ (78)	18
11		$BuSnCl_3$ [c]	(A) to equilibrated (Sn) + (LA) no solvent, −20 °C	R^1, $R^2 = (CH_2)_3$ (70) *trans*/*cis* = 75/25	$EtCHOHCHR^1CH{=}CHR^2$	17

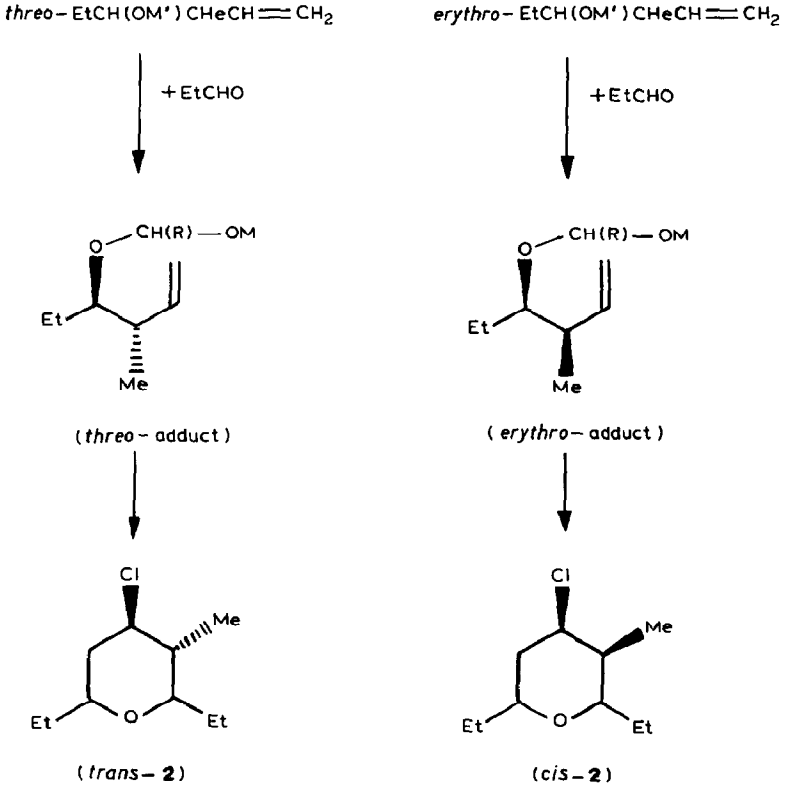
[a] After hydrolysis. [b] 30 mmol. [c] This study. [d] 10 mmol. [e] 40 mmol.

temperature. The so-called normal addition was used in both cases and under these conditions there is generally a high *erythro*-selectivity. However, a high *threo*-selectivity (97/3) was observed (entry 8) when the reaction temperature, after being kept at −78°C (for 20 min), was allowed to rise in steadily to room temperature. The *erythro*-product was the major product when the reaction temperature was raised from −78°C to ambient in several distinct steps. The results for the cyclohex-2-enyltin derivative **1** (R^1, $R^2 = (CH_2)_3$) suggest that reactions are not complete within the short periods during which the mixtures are kept at −78°C and that the exchange reactions, equilibrations, etc., must occur at higher temperatures.

Formation of 4-Chlorotetrahydropyrans

Only one stereoisomer of **2** (X = Cl, $R^1 = R^2 = H$, R = Et) is obtained from reaction of **1** ($R^1 = R^2 = H$), EtCHO (excess) and $TiCl_4$ at −50°C without solvent. A similar result was obtained when either BCl_3 in CH_2Cl_2 at −78°C or a tin halide was used.

From **1** ($R^1 = H$, $R^2 = Me$) ($E/Z = 40/60$), EtCHO (excess) and $TiCl_4$, two isomers (*trans* and *cis*) were obtained in ratios dependent on the solvent and other



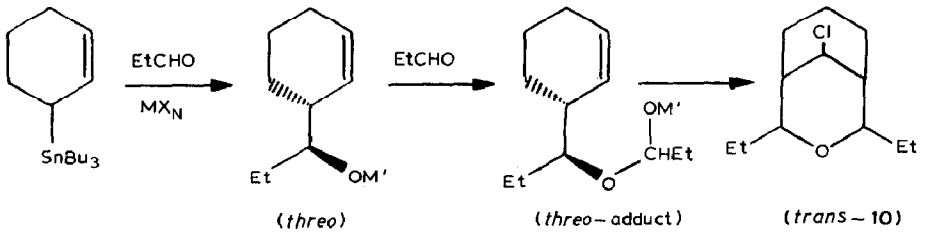
(M' = $TiCl_3$ or $R^3_nSnCl_{3-n}$ (n = 0,1), see ref. 2, 14–16, and BCl_2, see ref. 18)

Scheme 2

conditions. Under the conditions which lead to a high *threo/erythro* ratio for EtCH(OH)CHMeCH=CH_2, i.e. inverse addition of EtCHO to premixed **1** (R^1 = H, R^2 = Me) and $TiCl_4$ in CH_2Cl_2 at −78°C, (see entry 2 in Table 1) the second EtCHO molecule is incorporated to give a high *trans/cis* ratio (of 88/12) for **2** (X = Cl, R^1 = H, R^2 = Me, R = Et) (entry 5 in Table 2). Thus *trans*-**2** must be formed [15] from *threo*-EtCH(OM′)CHMeCH=CH_2 and *cis*-**2** from *erythro*-EtCH(OM′)CHMeCH=CH_2 (M′ = MX_{N-1} or $R^3_nSnCl_{3-n}$, n = 0, 1) (see Scheme 2) as was judged to be the case for reactions provided by tin halides [15]. The yield of **2** (X = Cl, R^1 = H, R^2 = Me, R = Et) is only 51%, owing partly because condensation of EtCHO to (*E*)-EtCH=CMeCHO (36%) also takes place.

Production of **2** (X = Cl, R^1 = H, R^2 = Me, R = Et) in Et_2O at −78°C leads (in contrast to that in CH_2Cl_2) to high *cis/trans* ratio, irrespective of the order of mixing reagents. This suggests that in Et_2O there is no *trans*-metallation of **1** (R^1 = H, R^2 = Me) probably owing to the lower Lewis acidity of $TiCl_4(Et_2O)$ and also that the first molecule of EtCHO (probably complexed with $TiCl_4$) reacts with **1** (R^1 = H, R^2 = Me) to give preferentially *erythro*-EtCH(OH)CHMeCH=CH_2. The reaction between $TiCl_4$, **1** (R^1 = H, R^2 = Me) and an excess of EtCHO in the absence of solvent gives **2** with an intermediate selectivity. The result for the reaction in presence of BCl_3 is also included in Table 2 (entry 7); the *trans/cis* ratio of 30/70 for **2** is difficult to correlate with the products from the incorporation of the first EtCHO molecule owing to the more complex nature of the BCl_3 reactions [18]. The outcome of the reactions of the cyclohex-2-enylstannyl derivative **1** (R^1, R^2 = $(CH_2)_3$) is also indicated in Table 2. The reaction with $TiCl_4$ and an excess of EtCHO provides *trans*-9-chloro-2,4-diethyl-*cis*-3-oxabicyclo[3.3.1]nonane (**10**) [17]* stereospecifically in Et_2O at −78°C (Scheme 3). This indicates that the initial reaction of EtCHO gives *threo*-EtCH(OM′)CHR¹CH=CHR², a similar result was found for reaction in CH_2Cl_2 at this temperature (entry 8 in Table 1).

Results for reactions involving other Lewis acids $BF_3 \cdot OEt_2$, BCl_3 and $BuSnCl_3$ are listed in Table 2 and show that there are differences in the *trans/cis* ratios. It is noteworthy that $BF_3 \cdot OEt_2$ is alone among the Lewis acids in yielding 4-hydroxy-tetrahydropyran derivatives; all the others give rise to the 4-halo-analogues.



MX_N = $TiCl_4$ (or BCl_3 and $BuSnCl_3$)

M′ = $TiCl_3$ (or $BuSnCl_2$, see ref. 17, and BCl_2, see ref. 18)

Scheme 3

* The description of the ring as *cis* is according the nomenclature of N.P. Volynskii (see ref. 5 in ref. 29. See also ref. 29 for the designation of the *trans*-isomerism.

Experimental

Organotin compounds **1** were made by standard methods [10]. Titanium tetrachloride and Cp_2TiCl_2 were commercial samples. Aldehydes were distilled prior to use.

General reaction procedure

The reagents were mixed in a particular sequence in a given solvent at −78°C (or another temperature) under N_2. The mixtures were kept at set temperatures for a specified period. After hydrolysis with saturated aqueous NH_4Cl, the organic material was extracted with CH_2Cl_2, the extracts dried, and the organic products separated by fractional distillation. Identification of products was by GC and ^{13}C NMR and IR spectroscopy, and comparison with authentic products obtained in previous studies.

Reaction of EtCHO and 1 ($R^1 = R^2 = H$)

(a) Compound **1** ($R^1 = R^2 = H$, 30 mmol) and EtCHO (30 mmol) was added to $TiCl_4$ (30 mmol) in CH_2Cl_2 (20 ml) at −78°C. Product: $EtCH(OH)CH_2CH{=}CH_2$ (2.4 g, 80%); identical to an authentic sample.

(b) A mixture of **1** ($R^1 = R^2 = H$, 30 mmol) and EtCHO (66 mmol) was added to $TiCl_4$ (30 mmol) at −50°C under N_2. Product: 4-Chloro-2,6-diethyltetrahydropyran (3.5 g, 66%); identical to an authentic sample.

Reaction of EtCHO and 1 ($R^1 = H$, $R^2 = Me$; $Z/E = 40/60$)

(a) To the solid mixture obtained from **1** ($R^1 = H$, $R^2 = Me$; 30 mmol) and $TiCl_4$ (30 mmol) under N_2 at −78°C was added Et_2O (20 ml). The temperature was increased to −20°C to aid dissolution and the dark-brown solution then recooled to −78°C and treated with EtCHO (66 mmol). The solution was allowed to reach room temperature during $1\frac{1}{2}$ h. Total product: 4.6 g. Products: (i) 4-chloro-3-methyl-2,6-diethyltetrahydropyran (78%): *trans / cis* = 28/72; identical with authentic samples, and (ii) (*E*)-EtCH=CMeCHO (20%), identified by GC.

(b) A solution of $TiCl_4$ (30 mmol) and **1** ($R^1 = H$, $R^2 = Me$; 30 mmol) in CH_2Cl_2 (20 ml) at −78°C under N_2 was kept at −78°C for 30 min and EtCHO (66 mmol) was then added. The mixture was allowed to warm to room temperature in $1\frac{1}{2}$ h, then kept at room temperature for 2 h before work-up. Total products 2.6 g. Products: (i) 4-chloro-3-methyl-2,6-diethyltetrahydropyran (51%): *trans / cis* = 88/12, (ii) $EtCH(OH)CHMeCH{=}CH_2$ (12%): mixture of *threo-* and *erythro*-isomers, and (iii) (*E*)-EtCH=CMeCHO (36%), all identical to authentic samples.

(c) To a solution of $TiCl_4$ (30 mmol) in Et_2O (20 ml) at −78°C under N_2 was added a mixture of **1** ($R^1 = H$, $R^2 = Me$; 30 mmol) and EtCHO (66 mmol). The mixture was allowed to warm to room temperature during $1\frac{1}{2}$ h then kept at room temperature until work-up. Product: 4-chloro-3-methyl-2,6-diethyltetrahydropyran (5.2 g, 80%): *trans / cis* = 27/73.

(d) Compound $TiCl_4$ (30 mmol) was added to **1** ($R^1 = H$, $R^2 = Me$; 30 mmol) and EtCHO (66 mmol) at −78°C without a solvent. An exothermic reaction ensued, with development of a bright-orange colour. The mixtures was allowed to warm to room temperature during $1\frac{1}{2}$ h and then kept at room temperature for 1 h before

work-up. Total product 3.7 g. Products: (i) 4-chloro-3-methyl-2,6-diethyltetrahydropyran (49%), *trans / cis* = 45/55, and (ii) $EtCH(OH)CHMeCH{=}CH_2$ (47%).

(e) To a mixture of Cp_2TiCl_2 (10 mmol) and EtCHO (10 mmol) in CH_2Cl_2 (20 ml) at −78 °C was added **1** (R^1 = H, R^2 = Me; 10 mmol). The mixture was allowed to warm to room temperature during $1\frac{1}{2}$ h and left overnight at that room temperature. Total products 0.45 g. Products: (i) $EtCH(OH)CHMeCH{=}CH_2$ (58%), *erythro / threo* = 40/60, and (ii) (*Z*) = $EtCH(OH)CH_2CH{=}CHMe$ (42%).

Reaction of EtCHO and 1 (R^1, $R^2 = (CH_2)_3$)

(a) Compound **1** (R^1, $R^2 = (CH_2)_3$; 10 mmol) was added to a solution of $TiCl_4$ (10 mmol) and EtCHO (10 mmol) in CH_2Cl_2 (20 ml) at −78 °C. The solution was kept at −78 °C for 20 min and then allowed to warm to room temperature during 3 h. Product: $EtCH(OH)CHR^1CH{=}CHR^2$ (R^1, $R^2 = (CH_2)_3$; 0.7 g), *erythro / threo* = 5/95.

(b) As in (a) but with 20 mmol reagents, and 1 h from −78 °C to room temperature. Product: $EtCH(OH)CHR^1CH{=}CHR^2$ (R^1, $R^2 = (CH_2)_3$; 1.0 g), *erythro / threo* = 2/98.

(c) Compound **1** (R^1, $R^2 = (CH_2)_3$; 20 mmol) was added to $TiCl_4$ (20 mmol) and EtCHO (20 mmol) in CH_2Cl_2 (40 ml) at −78 °C. The solution was kept (i) at −78 °C for 30 min, then (ii) at −50 °C for 30 min (colour yellow-brown), and finally (iii) at −30 °C for 1 h (colour ochre). Product: $EtCH(OH)CHR^1CH{=}CHR^2$ (R^1, $R^2 = (CH_2)_3$; 1.5 g), *erythro / threo* = 60/40.

(d) To a solution of $TiCl_4$ (30 mmol) in Et_2O (20 ml) at −78 °C was added a mixture of **1** (R^1, $R^2 = (CH_2)_3$; 30 mmol) and EtCHO (66 mmol). The mixture was kept at −78 °C for 30 min and then allowed to warm to room temperature during 3 h. Product: *trans*-9-chloro-2,4-diethyl-*cis*-3-oxabycyclo[3.3.1]nonane (1.8 g, 28%). B.p. 80 °C/0.1 mmHg (Lit. value, 135 °C/10 mmHg) [17].

(e) To a mixture of EtCHO (10 mmol) and Cp_2TiCl_2 (10 mmol) in Et_2O (20 ml) at −78 °C was added **1** (R^1, $R^2 = (CH_2)_3$; 10 mmol). The mixture was kept at −78 °C for 20 min and then allowed to warm to room temperature during $1\frac{1}{2}$ h. Total product: 0.5 g. Products: (i) $EtCH(OH)CHR^1CH{=}CHR^2$ (R^1, $R^2 = (CH_2)_3$ 28%), *erythro / threo* = 60/40, (ii) cyclohex-2-enol (50%), and (iii) cyclohex-2-enone, all identical with authentic samples.

(f) Repeated (e) using CH_2Cl_2 as solvent. Products: (i) $EtCH(OH)CHR^1$-$CH{=}CHR^2$ (R^1, $R^2 = (CH_2)_3$; 39%), *erythro / threo* = 64/36, (ii) cyclohex-2-enol (46%), and (iii) cyclohex-2-enone (15%).

(g) An equimolar mixture of **1** (R^1, $R^2 = (CH_2)_3$) and EtCHO (10 mmol) was added, with stirring to solid Bu_2SnCl_2. The mixture was stirred for 4 h. Product: $EtCH(OH)CHR^1CH{=}CHR^2$ (R^1, $R^2 = (CH_2)_3$), 1.1 g (78%); *erythro / threo* = 65/35.

Reaction of 1 (R^1, $R^2 = (CH_2)_3$) and MeCHO

An equimolar mixture of **1** (R^1, $R^2 = (CH_2)_3$) and Bu_2SnCl_2 (10 mmol) was stirred for 3 h before MeCHO (30 mmol) was added. The mixture was stirred for 6 h. Product: $MeCH(OH)CHR^1CH{=}CHR^2$ (R^1, $R^2 = (CH_2)_3$), 1 g (79%), *erythro / threo* = 60/40.

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References

1 Y. Yamanoto, Accouns. Chem. Res., 20 (1987) 243. see also Aldrichimica Acta, 30 (1987) 45.
2 G. Tagliavini, Reviews Silicon, Germanium, Tin and Lead Cmpds., 8 (1985) 237.
3 C. Hull, C.V. Mortlock, and E.J. Thomas, Tetrahedron, 45 (1989) 1007.
4 J.-P. Quintard, G. Dumartin, B. Elissondo, A. Rahm and M. Pereyre, Tetrahedron, 45 (1989) 1017.
5 J.M. Coxon, S.J. van Eyk, and P.J. Steel, Tetrahedron, 45 (1989) 1029.
6 J.A. Marshall and M.Y. Gung, Tetrahedron, 45 (1989) 1043.
7 S.E. Denmark, E.J. Weber, T.M. Wilson, and T.M. Willson, Tetrahedron, 45 (1989) 1053.
8 S.E. Denmark, B.R. Henke, and E. Weber, J. Am. Chem. Soc., 109 (1987) 2512, and reference therein.
9 Y. Yamamoto, S. Hatsuya, and J.I. Yamada, J. Chem. Soc. Chem. Comm., (1987) 561.
10 A. Boaretto, D. Marton, G. Tagliavini, and P. Ganis, J. Organomet. Chem., 321 (1987) 199.
11 H.T. Reetz, M. Hüllmann, W. Massa, S. Berger, p. Rademacher, and P. Heymanns, J. Am. Chem. Soc., 108 (1986) 2405.
12 G.E. Keck and E.J. Enholm, J. Org. Chem., 50 (1985) 147.
13 A. Gambaro, A. Boaretto, D. Marton, and G. Tagliavini, J. Organomet. Chem., 288 (1983) 283.
14 A. Boaretto, D. Marton, G. Tagliavini, and A. Gambaro, Inorg. Chim. Acta, 77 (1983) L153.
15 A. Gambaro, A. Boaretto, D. Marton, and G. Tagliavini, J. Organomet. Chem., 260 (1984) 255.
16 A. Boaretto, D. Furlani, D. Marton, and G. Tagliavini, J. Organomet. Chem., 299 (1986) 157.
17 D. Marton, D. Furlani and G. Tagliavini, Gazz. Chim. It., 117 (1987) 189.
18 D. Marton, G. Tagliavini, M. Zordan, and J.L. Wardell, J. Organomet. Chem., 390 (1990) 127.
19 Y. Yamamoto, H. Yatagai, Y. Ishihara, and K. Maruyama, Tetrahedron, 40 (1984) 2239.
20 G.E. Keck, D.E. Abbott, E.P. Buden, and E.J. Enholm, Tetrahedron Lett., 25 (1984) 3927.
21 Y. Naruta, Y. Nishigaichi, and K. Maruyama, Tetrahedron, 45 (1989) 1067; see also J. Org. Chem., 33 (1988) 1192.
22 P. Harston, J.L. Wardell, D. Marton, G. Tagliavini, and P.J. Smith, Inorg. Chim. Acta, 162 (1989) 245.
23 S.E. Denmark, T.M. Wilson, and T.M. Willson, J. Am. Chem. Soc., 110 (1988) 984.
24 Y. Yamamoto, H. Yatagai, Y. Naruta, and K. Maruyama, J. Am. Chem. Soc., 102 (1980) 7107.
25 B. Weidmann and D. Seebach, Angew. Chem. Int. Ed. Engl., 22 (1983) 31.
26 F. Sato, K. Iida, S. Iijima, H. Moriya and M. Sato, J. Chem. Soc. Chem. Comm., (1981) 1140.
27 Y. Yamamoto and K. Maruyama, J. Organomet. Chem., 284 (1985) C45.
28 A. Gambaro, P. Ganis, D. Marton, V. Peruzzo and G. Tagliavini, J. Organomet. Chem., 231 (1982) 307.
29 D.R. Stapp, and J.C. Randall, J. Org. Chem., 35 (1970) 2948.