Journal of Organometallic Chemistry, 391 (1990) 295–305
Elsevier Sequoia S.A., Lausanne
JOM 20869

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

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(Received February 8th, 1990)

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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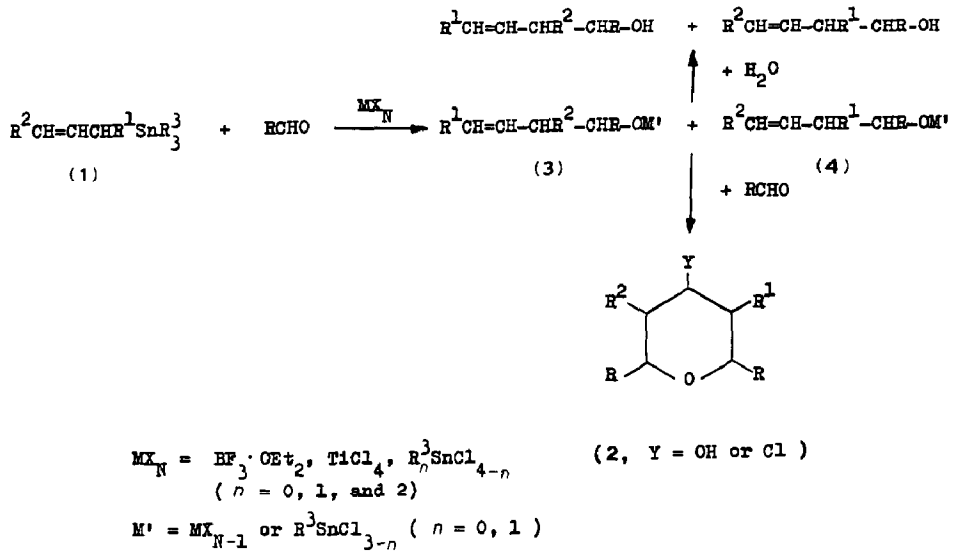


Scheme 1

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 $-78\,^\circ C$, 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 $-78\,^\circ C$.

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 $-78\,^\circ C$) 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)

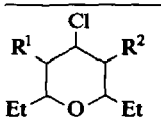
Entry No.	(1) (Sn)	Lewis Acid (LA)	RCHO (A)	Addition sequence reaction conditions	Products [a] (Yields %)	Ref.
1	(*Z*)-1,(R^1 = H, R^2 = Me)	$TiCl_4$	*cyclo*-$C_6H_{11}CHO$	(Sn) to (LA) + (A) CH_2Cl_2, −78 °C	*cyclo*-$C_6H_{11}CHOHCHMeCH{=}CH_2$ (97) *erythro/threo* = 97/7 + cyclo-$C_6H_{11}CHOHCH_2CH{=}CHMe$ (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^{1}CH=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^{1}CH=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, 1½ h	EtCHOHCHR^{1}CH=CHR^2(28) [f] *erythro/threo* = 60/40	[b]
11				(Sn) to (LA) + (A) CH_2Cl_2, −78 °C, 20 min −78 °C → RT, 1½ h	EtCHOHCHR^{1}CH=CHR^2 (39) [f] *erythro/threo* = 64/36	[b]
12		Bu_2SnCl_2	EtCHO [c]	(LA) to (Sn) + (A) RT, no solvent	EtCHOHCHR^{1}CH=CHR^2 (78) *erythro/threo* = 85/35	[b]
13			MeCHO	(A) to premixed (LA) + (Sn) no solvent	MeCHOHCHR^{1}CH=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^{1}CH=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$_2$MgX. [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

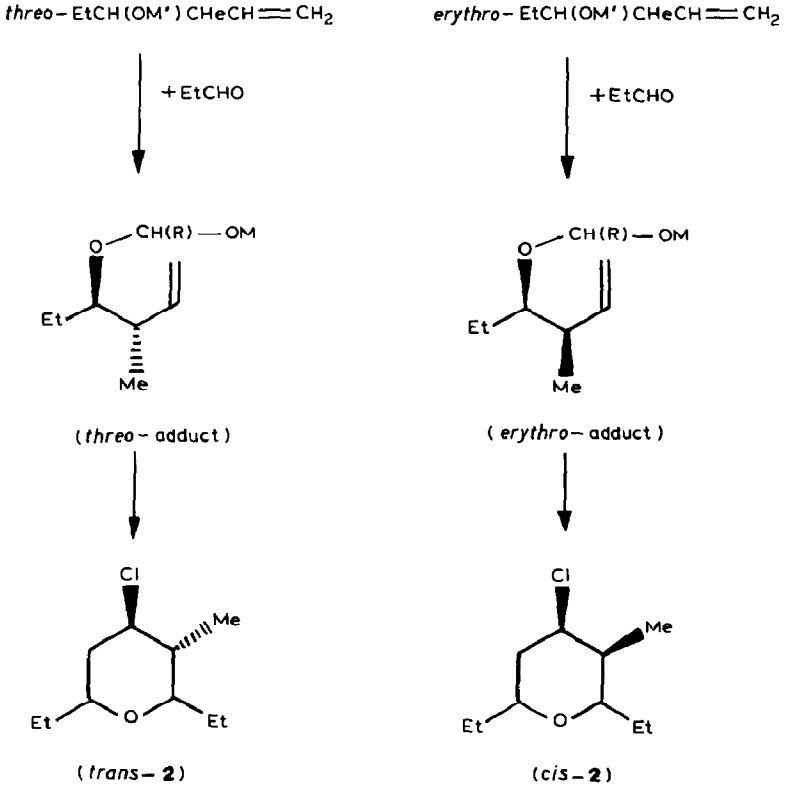
[a] After hydrolysis. [b] 30 mmol. [c] This study. [d] 10 mmol. [e] 40 mmol.

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



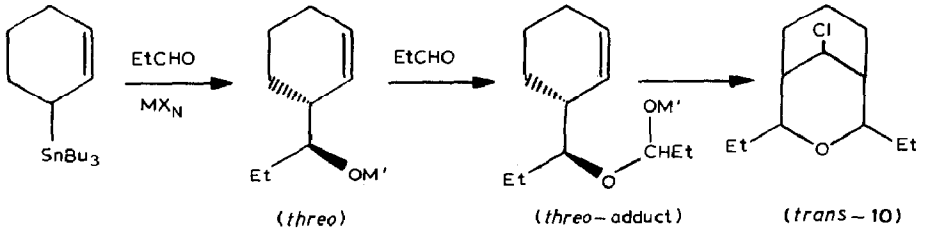
(M' = $TiCl_3$ or $R^3_nSnCl_{3-n}$ (n = 0,1), see ref. 2, 14–16, and BCl_2, see ref. 18)

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′)CHR^{1}CH=CHR^2, 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 1½ 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)CHR¹CH=CHR² (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)CHR¹CH=CHR² (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)CHR¹CH=CHR² (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 1½ h. Total product: 0.5 g. Products: (i) EtCH(OH)CHR¹CH=CHR² (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)CHR¹-CH=CHR² (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)CHR¹CH=CHR² (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)CHR¹CH=CHR² (R^1, R^2 = $(CH_2)_3$), 1 g (79%), *erythro / threo* = 60/40.

Acknowledgements

This work was supported by the C.N.R. (Roma) and the Ministero della Pubblica Istruzione (Roma). A NATO travel grant (to J.L.W./G.T.) is greatefully acknowledged. We thank also for partial support under the "Progetto Finalizzato per la Chimica Fine" CNR, Roma.

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