Diversity in the Lewis Acid-induced Reaction of Aldehydes with γ-Substituted Allylstannanes Depending upon the Substituent

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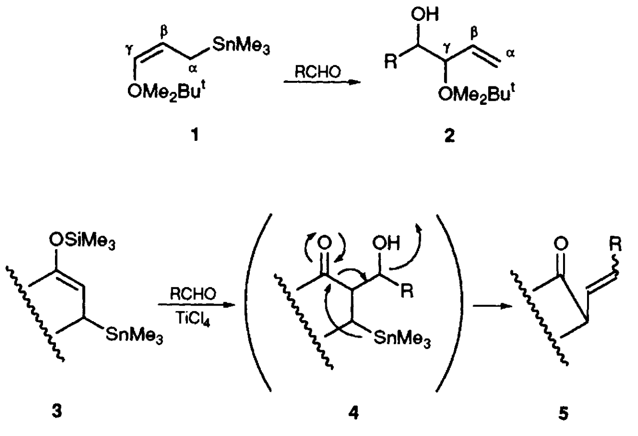
Lewis acid-induced reaction of γ-substituted allylstannanes with aldehydes proceeded at the α-, β- or γ-position, depending upon the nature of the substituents.

It is known that the γ-(*tert*-butyldimethylsilyloxy)allylstannane **1** reacts with aldehydes at the γ-position, and the reaction can be used as a methodology for the synthesis of stereochemically defined 1,2-diols **2**.[1] Previously we reported that the $TiCl_4$-induced reaction of γ-(trimethylsilyloxy)allylstannanes **3** with aldehydes gave β,γ-enones **5** selectively.[2] We thought that the reaction proceeded through the aldol reaction, followed by cyclopropanation and eliminative ring opening as shown in Scheme 1. Obviously the reaction site of **3** with aldehyde is the β-position, in contrast to the γ-position generally observed. In the present study, we found that the Lewis acid-induced reactions of **6** with aldehydes are greatly influenced by the nature of X.

In contrast to the β-substitution of **3**, enol acetates **8** underwent α-substitution to afford **10** as mixtures of diastereoisomers upon treatment with aldehydes **9** in the presence of $TiCl_4$, as shown in Table 1. The starting enol acetates were prepared by the conjugate addition of trimethylstannyllithium to α,β-enones **7**, followed by quenching with acetic anhydride. In view of the fact that the α-substitution of allylstannanes proceeds only through the initial transmetallation,[3] the primary transmetallation of tin with titanium could be responsible for these results. However no further studies have been undertaken on this matter.

We next investigated the reaction of trifluoromethanesulfonates (triflates; Tf = CF_3SO_2) **11a**, obtainable in the same way as above by quenching the lithium enolate with $PhNTf_2$.[4]



Scheme 1

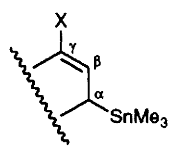
Table 1 Reaction of **8** with aldehydes **9**

Run	**8** R¹	R²	**9** R³	Yield (%) **10**
1	Me	H	Ph	63
2	Me	H	Et	60
3	$-[CH_2]_3-$		Ph	55
4	$-[CH_2]_3-$		Et	37

Treatment of **11a** with aldehydes **12** in the presence of BF_3–Et_2O in CH_2Cl_2, at room temp. to reflux, gave the corresponding **14–16** (Table 2, runs 5–8). Evidently the reaction is a nucleophilic attack of the allylstannanes on aldehydes at the γ-position to produce **13**, followed by a directed pinacol–pinacolone-type rearrangement with 1,2-migration of either R^3 (Type I) or H (Type II).[†] The yields were only moderate or poor, but several attempts at improving the yields were unsuccessful. We attributed the low yields to the sluggish reactivity at the γ-position due to the presence of the strong electron-withdrawing group (OTf), thus preventing the effective generation of a carbanionic character, and inducing side reactions. Actually a large amount of the self-aldol condensation product was obtained in case of propanal (Table 2, run 8). We expected that the yields could be improved by changing the triflate to a substituent with lower electron-withdrawing ability while retaining the good leaving ability.

As is obvious from the results of runs 9–14, better yields were obtained with the γ-chloro allylstannane **11b**,[‡] easily available from 1,3-dichlorobut-1-ene by treatment with Me_3SnLi. Generally $ZnBr_2$ and BF_3–Et_2O (except runs 8 and 12) induced clean reactions, while other Lewis acids such as $TiCl_4$, Me_3SiOTf and $AlCl_3$ gave only complex mixtures of products. The balance between the Type I and Type II reactions seems to be controlled by the migratory aptitudes of R^3 and H in **13**; the Type I reaction predominated with aryl or alkenyl aldehydes, while the Type II reaction predominated with aliphatic saturated aldehydes. A sole exception was the cyclic system in run 7, where H migration predominated over phenyl migration. The selectivity between Types I and II depended upon the Lewis acid. As a general trend, $ZnBr_2$ gave better yields but lower selectivity as compared with BF_3–Et_2O. In the particular case of run 12, BF_3–Et_2O was totally ineffective, probably because of the complexation of the catalyst with the methoxy oxygen.

These reactions are characteristic in that they are formal insertions of allylic carbons into the C–R (Type I) or C–H (Type II) bonds of the aldehydes, and the Type I reaction is particularly attractive from the synthetic viewpoint since it affords compounds having quaternary carbons substituted by



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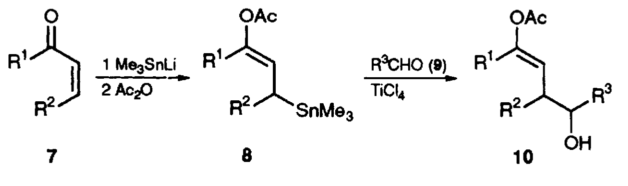
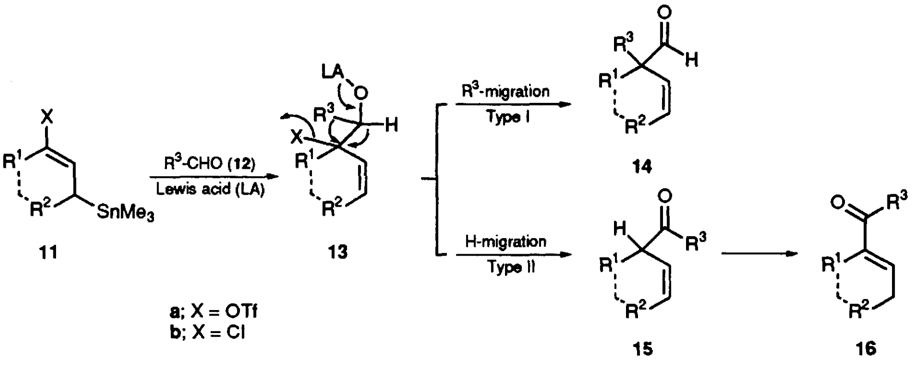


Scheme 2

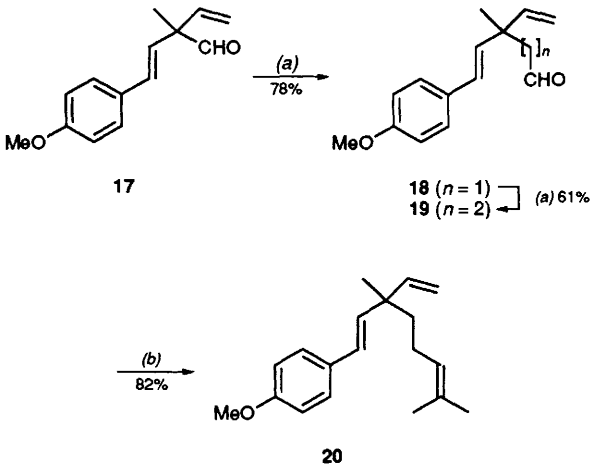
Table 2 Reaction of **11** with aldehydes **12**

	11			**12**	Yield (%)		
Run	X	R^1	R^2	R^3	**14**	**15**	**16**
5	OTf	Me	H	Ph	48	0	0
6	OTf	Me	H	PhCH=CH–	23	0	0
7	OTf	$-[CH_2]_3-$		Ph	0	0	63
8	OTf	Me	H	Et	0	0	13
9	Cl	Me	H	Ph	45 (34)[a]	6 (34)	0 (0)
10	Cl	Me	H	p-MeC_6H_4	53 (59)	0 (18)	0 (0)
11	Cl	Me	H	PhCH=CH–	61 (81)	0 (0)	0 (0)
12	Cl	Me	H	p-$MeOC_6H_4CH{=}CH-$	0 (68)	0 (0)	0 (0)
13	Cl	Me	H	MeCH=CH–	41 (59)	0 (0)	0 (0)
14	Cl	Me	H	n-C_6H_{13}	tr (tr)	53 (52)	0 (0)

[a] Yields in parentheses are those of the $ZnBr_2$-catalysed reaction. Otherwise, the yields are those of the BF_3–Et_2O-catalysed reaction.



Scheme 3



Scheme 4 *Reagents*: (*a*) $[MeOCH_2PPh_3]^+ I^-$, Bu^tOK, then H^+; (*b*) $Ph_3Pr^iP^+ I^-$, Bu^nLi, THF

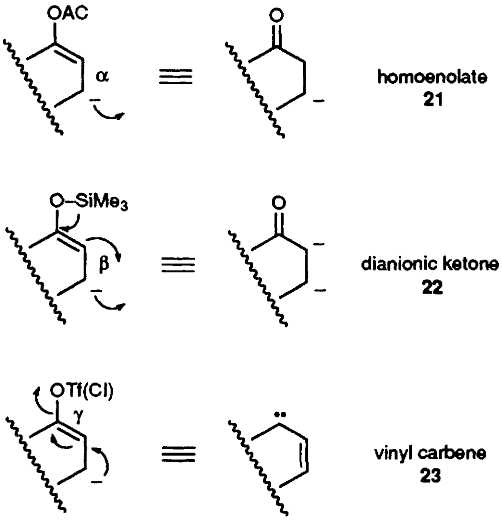


Fig. 1 Summary of reaction types

vinyl and formyl groups, which are potential functional groups for further manipulation. As an example for synthetic application, we utilized the Type I reaction for the synthesis of *rac*-bakuchiol methyl ether **20**. (+)-Bakuchiol is a phenolic monoterpene found in the seeds of *Psoralea corylifolia* Linn.[5,6] As shown in Scheme 4, double homologation of **17**, obtained in run 12, and Wittig reaction with isopropylidenephosphorane gave **20**. The demethylation to bakuchiol has been published.[5]

In view of the respective reaction types mentioned above, the reactions may be summarised as shown in Fig. 1, taking account of the latent carbanionic character of the tin–carbon bond. The enol acetate **21** corresponds to homoenolate, the trimethylsilyl enol ether **22** to dianionic ketone, and the triflate or chloride **23** to vinyl carbene. Evidently the carbenic character arises from the combination of the leaving ability of triflate or chloride with the electron-donating ability of the carbon–tin bond.

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Footnotes

† Reaction schemes involving oxirane formation from **13**, followed by R^3 migration,[7] and HX elimination from **13**, followed by tautomerization, cannot be ruled out for the Type I and Type II reactions, respectively.

‡ *Typical experimental procedure*. A CH_2Cl_2 solution (15 ml) of **11b** (1.00 g, 3.92 mmol) and aldehyde (3.14 mmol) was poured into a suspension of $ZnBr_2$ (0.71 g, 3.15 mmol) in CH_2Cl_2 (10 ml), with a cannula tube at room temp. under N_2. The mixture was then refluxed for 4 h and quenched with sat. aqueous $NaHCO_3$ (10 ml). The mixture was passed through a Celite column to remove the solid materials and extracted with CH_2Cl_2. After drying over $MgSO_4$, the solvent was removed *in vacuo*, and the crude material was purified by column chromatography (silica gel, hexane–ether, 5 : 1) to give the products.

In case of the BF_3-catalysis, the reaction proceeded at room temp. (30 min–2 h, by monitoring the disappearance of the stannane on TLC), using a solution of BF_3–Et_2O (0.45 g, 3.17 mmol) in CH_2Cl_2 (10 ml).

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