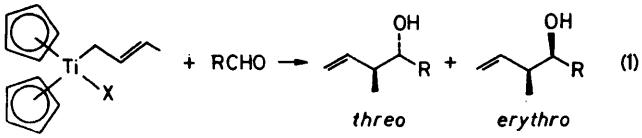
threo-Selective Synthesis of β-Methylhomoallyl Alcohols *via* But-2-enyltitanium Compounds†

By FUMIE SATO,* KATSUMI IIDA, SATOSHI IIJIMA, HIROYUKI MORIYA, and MASAO SATO
(*Department of Chemical Engineering, Tokyo Institute of Technology, Meguro, Tokyo* 152, *Japan*)

Summary The diastereoselectivity of the addition of but-2-enyltitanium compounds, $(\eta^5\text{-}C_5H_5)_2Ti(CH_2CH{=}CHMe)X$, to aldehydes is highly dependent on the halide ligand X, and high *threo*-selectivity is attained when X is Br or I.

RECENTLY, attention has been focused on the diastereoselective synthesis of β-methylhomoallyl alcohols in relation to the synthesis of macrolide antibiotics. The stereoselective addition of allylic organometallic derivatives of but-2-enyl and related systems to aldehydes has afforded an effective solution to this problem,[1,2] and considerable effort has been expended to develop stereoregulated variations of this process. However, little attention has so far been paid to the influence of other ligands in but-2-enyl metal compounds on the diastereoselectivity, although such a factor has been shown to be important in the aldol condensation.[3] The present study demonstrates that the but-2-enyl titanium derivatives $(\eta^5\text{-}C_5H_5)_2Ti(CH_2CH{=}CHMe)X$ (**1**; X = halogen) add to aldehydes with high *threo*-selectivity wherein the halogen ligand affects the diastereoselectivity (equation 1).

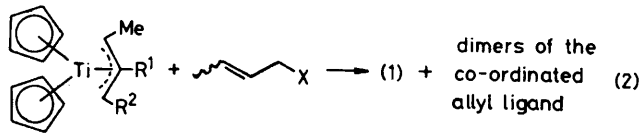


(1) (1)

Compounds (**1**) were prepared by reaction of the η^3-allyltitanium complexes (**2a**) or (**2b**) with but-2-enyl halides (equation 2), or by reaction of an equimolar mixture of $(\eta^5\text{-}C_5H_5)_2TiX_2$ and but-2-enyl magnesium bromide. While the full scope and mechanistic details remain to be further explored, it should be noted that reaction (2) offers a convenient synthesis of (**1**), since (**2a**) and (**2b**) are readily prepared *in situ* quantitatively by the reaction of $(\eta^5\text{-}C_5H_5)_2$-

† Parts of this report were orally communicated at the 43rd Annual Meeting of the Japan Chemical Society, March 1981, Tokyo. The but-2-enylzirconium compound $(\eta^5\text{-}C_5H_5)_2Zr(CH_2CH{=}CHMe)Cl$ and aldehydes were reported to afford *threo*-β-methylhomoallyl alcohols predominantly (K. Maruyama, Y. Ishihara, and Y. Yamamoto).

$TiCl_2$ and propylmagnesium bromide in the presence of penta-1,3-diene or isoprene, respectively.[4]



(2)

a; R^1 = H, R^2 = Me

b; R^1 = Me, R^2 = H

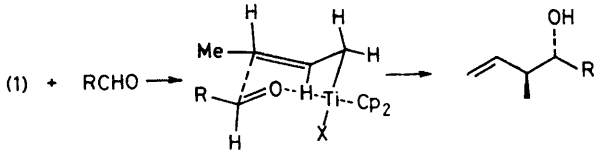
The preparation of complex (**1**) and its reactions with aldehydes were carried out under argon at −30 to *ca.* −35 °C using ether as solvent, and the results are summarized in the Table. As is apparent from the Table, the diastereoselectivity does not vary with the method of synthesis of (**1**) or the stereochemistry of the but-2-enyl unit. It can also be seen from the Table that, for a given aldehyde, a marked enhancement in diastereoselectivity was observed in changing the halide ligand of (**1**) from Cl to Br or I, and excellent diastereoselectivity can be attained in the formation of *threo*-β-methylhomoallyl alcohols when X is Br or I.

TABLE. Reaction of complexes (**1**) with aldehydes RCHO (reaction 1).[a]

X in (**1**)	R	*threo* : *erythro*	Total yield (%)
Cl[b]	Et	64 : 36[f]	99
Cl[b,c]	Et	64 : 36[f]	86
Cl[d]	Et	66 : 34[f]	92
Cl[b]	Ph	60 : 40[g]	96
Br[e]	Et	96 : 4[f]	92
Br[d]	Et	96 : 4[f]	90
Br[e]	Pr^i	99 : 1[f]	87
Br[e]	Bu^t	90 : 10[f]	94
Br[e]	Ph	100 : 0[g]	92
I[e]	Et	93 : 7[f]	86
I[e]	Ph	94 : 6[g]	96

[a] Compounds (**2**) [prepared *in situ* from $(\eta^5\text{-}C_5H_5)_2TiCl_2$ (4·4 mmol), diene (4·2 mmol), and C_3H_7MgBr (8·2 mmol)], 1-halogeno-*trans*-but-2-ene (4·4 mmol), and aldehyde (4·0 mmol) were employed. [b] (**2a**) was used. [c] 1-Chloro-*cis*-but-2-ene was used. [d] Grignard exchange reaction was employed. [e] (**2b**) was used. [f] Determined by g.l.c. (PEG 20M, 5 m). [g] Determined by ^1H n.m.r. spectroscopy.

These results may be explained by assuming a preference for formation of the (*E*)-form of complexes (**1**) and a six-membered transition state (**3**) with a chair conformation in the addition of (**1**) to aldehydes (Scheme). Isomerization



(3)

SCHEME. (Cp = η^5-C_5H_5)

probably occurred in the formation of (**1**) in the case of the Grignard exchange reaction or oxidative addition of 1-halogeno-*cis*-but-2-ene, and afforded the stable (*E*)-isomer. Pseudo-1,3-diaxial R ⟷ X interactions may increase with increasing bulk of the halide ligand and make formation of the transition state (**3**) more favourable in the order Cl < Br or I.

It should be noted that the present reaction offers a convenient general method for the preparation of *threo*-β-methylhomoallyl alcohols irrespective of the bulk of the aldehyde in contrast with the reaction of chromium(II)-mediated reactions of but-2-enyl halides and aldehydes.[2]

This work is supported by Grants-in-Aid for Scientific Research from the Ministry of Education, the Japanese Government.

(*Received*, 27*th July* 1981; *Com.* 898.)

[1] H. Yamaguchi and T. Mukaiyama, *Chem. Lett.*, 1980, 993; F. Sato, S. Iijima, and M. Sato, *Tetrahedron Lett.*, 1981, **22**, 243; R. W. Hoffmann and H.-J. Zeiss, *J. Org. Chem.*, 1981, **46**, 1309; Y. Yamamoto, H. Yatagai, Y. Naruta, and K. Maruyama, *J. Am. Chem. Soc.*, 1980, **102**, 7107, and references cited therein.

[2] T. Hiyama, K. Kimura, and H. Nozaki, *Tetrahedron Lett.*, 1981, **22**, 1037.

[3] D. A. Evans, E. Vogel, and J. V. Nelson, *J. Am. Chem. Soc.*, 1979, **101**, 6120; D. E. Van Horn and S. Masamune, *Tetrahedron Lett.*, 1979, 2229.

[4] H. A. Martin and F. Jellinek, *J. Organomet. Chem.*, 1969, **12**, 149.