

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

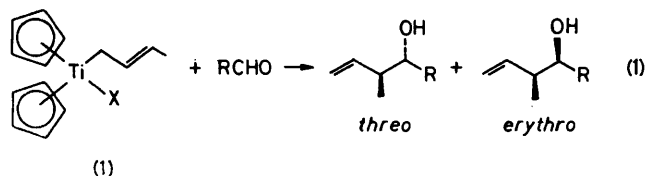
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Summary The diastereoselectivity of the addition of but-2-enyltitanium compounds, $(\eta^5\text{-C}_5\text{H}_5)_2\text{Ti}(\text{CH}_2\text{CH}=\text{CHMe})\text{X}$, to aldehydes is highly dependent on the halide ligand X, and high *threo*-selectivity 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 $(\eta^5\text{-C}_5\text{H}_5)_2\text{Ti}(\text{CH}_2\text{CH}=\text{CHMe})\text{X}$ (**1**; X = halogen)

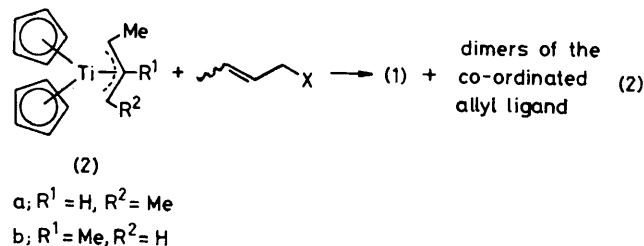
add to aldehydes with high *threo*-selectivity wherein the halogen ligand affects the diastereoselectivity (equation 1).



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 $(\eta^5\text{-C}_5\text{H}_5)_2\text{TiX}_2$ 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 $(\eta^5\text{-C}_5\text{H}_5)_2$ -

† 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 $(\eta^5\text{-C}_5\text{H}_5)_2\text{Zr}(\text{CH}_2\text{CH}=\text{CHMe})\text{Cl}$ and aldehydes were reported to afford *threo*- β -methylhomoallyl alcohols predominantly (K. Maruyama, Y. Ishihara, and Y. Yamamoto).

TiCl₂ and propylmagnesium bromide in the presence of penta-1,3-diene or isoprene, respectively.⁴



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

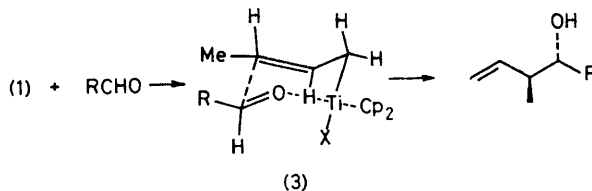
TABLE. Reaction of complexes (1) with aldehydes RCHO (reaction 1).^a

X in (1)	R	<i>threo</i> : <i>erythro</i>	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 ^l	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 (η^5 -C₅H₅)₂TiCl₂ (4.4 mmol), diene (4.2 mmol), and C₃H₇MgBr (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.

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.

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



SCHEME. (Cp = η^5 -C₅H₅)

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 \leftrightarrow 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(π)-mediated reactions of but-2-enyl halides and aldehydes.²

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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.