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1983Regio- and Stereo-selective Reaction of 1,3-Disubstituted Allyl Anions with Aldehydes via η^3 -Allyltitanium Compounds

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The regio- and stereo-chemistry in reactions of 1,3-disubstituted allyl anions with aldehydes via η^3 -allyltitanium compounds and this provides a simple method for the preparation of *threo*-4-hydroxy-3-methyl-*cis*-1-phenoxyhex-1-ene (3b) and *threo*-4-hydroxy-3-trimethylsilyl-*trans*-1-trimethylsilylhex-1-ene (3d).

Regio- and stereo-chemical control in reactions of allyl anions with aldehydes is an important subject in organic chemistry. There have been several reports of the selective addition of monosubstituted allyl anions to aldehydes.^{1,2} However, few studies have been done on the addition of 1,3-disubstituted allyl anions to aldehydes.^{3,4}

We have recently reported that the regio- and stereo-chemistry in reactions of monosubstituted allyl anions such as the but-2-enyl- and 1-trimethylsilyl-allyl anions with aldehydes can be controlled using the η^3 -allyltitanium compound, $(\eta^3\text{-C}_6\text{H}_5)_2\text{Ti}(\eta^3\text{-allyl})$.⁵ Here we describe the application of η^3 -allyltitanium chemistry to the problem of regio- and/or stereo-chemical control of reactions of 1,3-disubstituted allyl anions with aldehydes.

The η^3 -allyltitanium compounds (2a–c), prepared *in situ* by the reaction of $(\eta^3\text{-C}_6\text{H}_5)_2\text{TiCl}$ ⁶ with the corresponding heterosubstituted allyl anion derived from (1a–c), reacted with propionaldehyde regiospecifically to afford (3a–c) (Scheme 1). The structures of (3a–c) were determined by ¹H n.m.r. and mass spectroscopy and by correlation with known

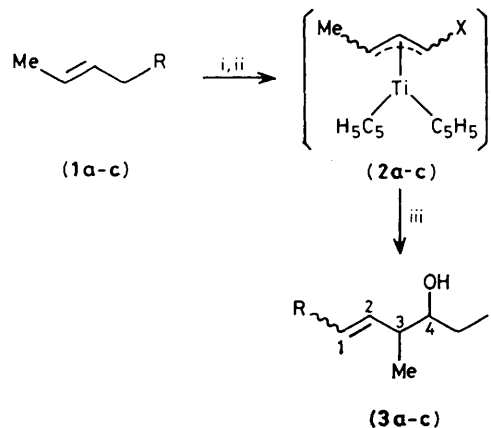
compounds. The stereochemistry of the C(1)=C(2) double bond was ascertained from the ¹H n.m.r. coupling constant between the vinylic protons (Table 1).⁷ The stereochemistry of the C(3)–C(4) bond in (3) was established by converting (3a–c) into mixtures of the 4-hydroxy-3-methylhex-1-enes (Scheme 2).

As is apparent from Table 1, the selective formation of the *threo*-configuration for the C(3)–C(4) single bond is general

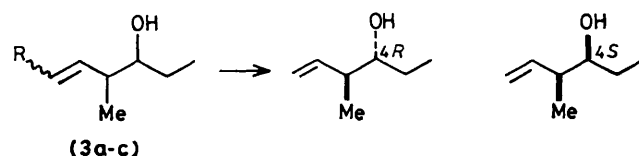
Table 1. Reaction of complexes (2) with propionaldehyde.^a

Complex ^b	Product (3) ^c	Yield ^d /%	¹ H N.m.r., <i>J</i> (vinylic protons)/Hz
(2a)	(3a)(4 <i>R</i> :4 <i>S</i> , 86:14, <i>trans</i>) ^{e,t}	85	19.0
(2b)	(3b)(4 <i>R</i> , <i>cis</i>) ^g	88	6.3
(2c)	(3c)(4 <i>R</i> :4 <i>S</i> , 66:34) ^{e,h}	93	{ 9.0 (<i>cis</i>) 16.3 (<i>trans</i>)
(2d) ⁱ	(3d)(4 <i>R</i> , <i>trans</i>) ^g	85	18.9

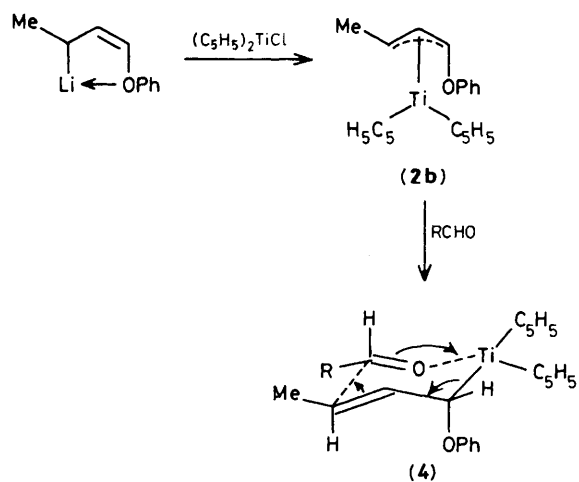
^a Carried out at -78°C for 30 min and then at room temp. for 1 h in THF under argon. ^b Prepared at -78°C by the reaction of $(\text{C}_6\text{H}_5)_2\text{TiCl}$ with the corresponding allyl anions which were generated from (1a,d) ($\text{Bu}^t\text{Li-HMPA}$, -40°C) and (1b,c) ($\text{Bu}^t\text{Li-HMPA}$, -78°C). ^c Products were characterized by ¹H n.m.r. and mass spectral analysis, and also by comparison with known compounds (see text). ^d Total yield, isolated by column chromatography. ^e Ratios were determined by g.l.c. analysis after conversion into the 4-hydroxy-3-methylhex-1-enes (ref. 5). ^f G.l.c. analysis also supported the ratio. ^g ¹³C N.m.r. spectra (CDCl_3) showed the product to be essentially a single compound. ^h Mixture of almost equal amounts of *cis*- and *trans*-isomers. ⁱ Reaction with isobutyraldehyde also afforded $>98\%$ pure *trans,threo*-product in 78% yield.



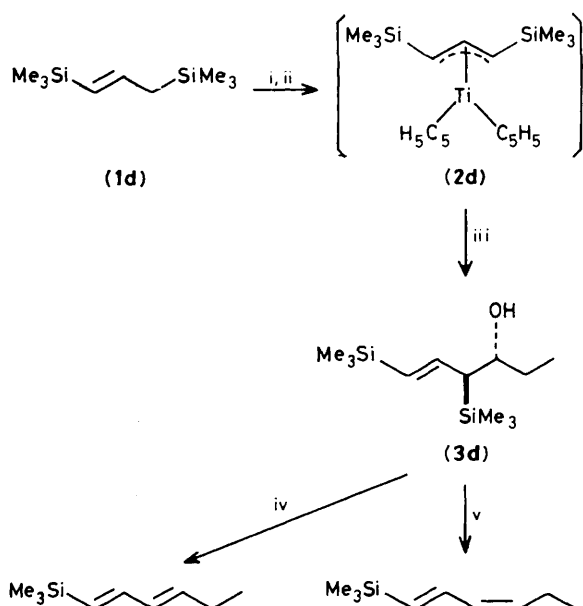
Scheme 1. Reagents: i, Bu^tLi -hexamethylphosphoramide (HMPA); ii, $(\text{C}_6\text{H}_5)_2\text{TiCl}$; iii, EtCHO ; a, $\text{R} = \text{SiMe}_3$; b, $\text{R} = \text{OPh}$; c, $\text{R} = \text{SPh}$.



Scheme 2. For (3a), protodesilylation with $\text{I}_2\text{-C}_6\text{H}_6$ (ref. 8); for (3b), treatment with 2,3-dihydro-4*H*-pyran, ozonolysis of the tetrahydropyranyl ether, and Wittig reactions with $\text{Ph}_3\text{P}=\text{CH}_2$ followed by deprotection; for (3c), protodesulphurization with $\text{Me}_2\text{CHMgBr-Ni}(\text{PPh}_3)_2\text{Cl}_2$ (r.f. 9).



Scheme 3



Scheme 4. Reagents: i, Bu^tLi -HMPA; ii, $(C_5H_5)_2TiCl$; iii, EtCHO; iv, H_2SO_4 -THF; v, KH -THF.

regardless of the substituent X. However, the degree of diastereoselectivity is dependent on X, and is moderate for (2c), good for (2a), and excellent for (2b). The stereochemistry of the double bond, though, is very dependent on X, and varies from completely *trans* in (3a) to completely *cis* in (3b). Of particular note is the formation of (3b) with exclusive *threo-*

and *cis*-geometry, which implies that (2b) can be used as a *threo*-selective homo-enolate synthetic equivalent.³

The selective production of (3b) may be explained by assuming that the allyl moiety of (2b) had a *syn,anti*-type form because of the chelated structure of the lithium precursor, and that the reaction proceeded *via* a 6-membered transition state (4) with a chair conformation (Scheme 3). In the case of (2a), the allyl moiety probably had a *syn,syn*-type form owing to steric repulsion, and thus afforded the *threo,trans* product (3a).

The compound (2d), prepared *in situ* by the reaction of 1,3-bis(trimethylsilyl)prop-1-enyl-lithium and $(\eta^5-C_5H_5)_2TiCl$, reacted with propionaldehyde stereoselectively giving an 85% yield of (3d) with *trans,threo*-stereochemistry (>98% purity) (Scheme 4 and Table 1). The configuration and purity of (3d) were determined by converting it into either the (1E,3E)- or (1E,3Z)-diene by the Peterson olefination reaction. Thus, treatment of (3d) with potassium hydride or sulphuric acid in tetrahydrofuran (THF) afforded a >98% pure (judged by 200 MHz 1H n.m.r. spectroscopy) (1E,3Z)- or (1E,3E)-diene in >80% yields, respectively.

The selectivity of the reaction of (2d) with an aldehyde is higher than that of the analogous reactions of the boron reagent.⁴ The reaction described here provides a stereoselective synthesis of 1-trimethylsilylalka-1,3-dienes.

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