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TITANIUM-MEDIATED AND NEIGHBORING-GROUP ASSISTED δ-METHYLATION OF HOMOALLYL ALCOHOLS : A NEW REGIO- AND STEREOSELECTIVE CC-LINKING REACTION

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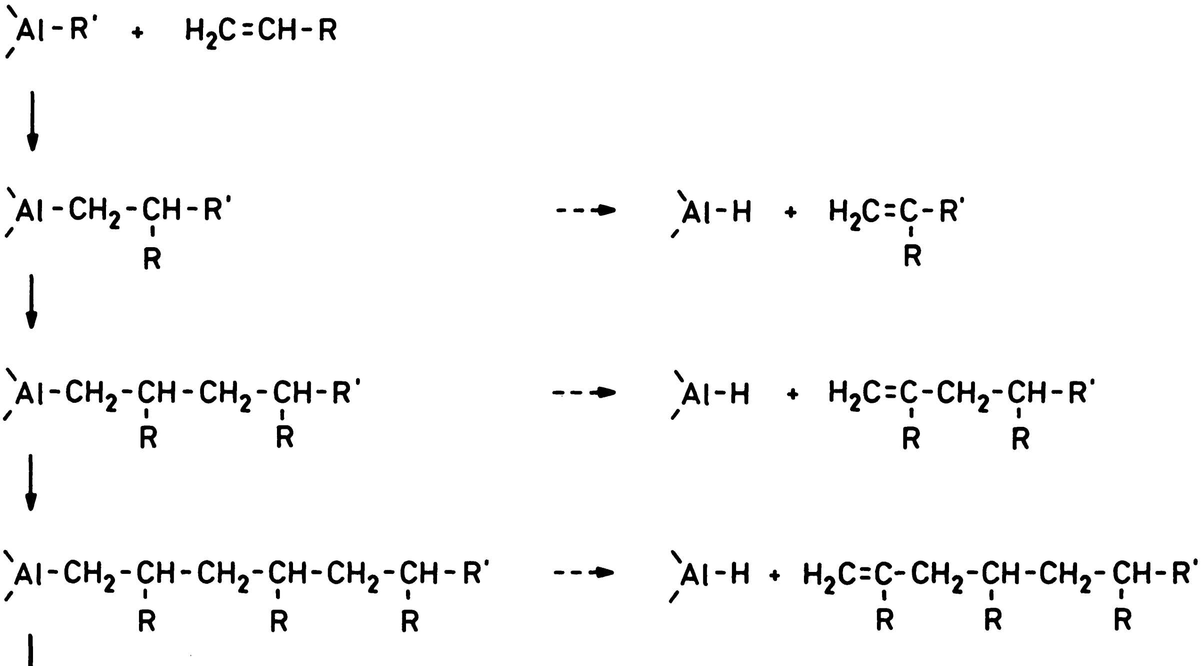
Upon treatment with dimethyltitanium dichloride or trimethylaluminum in the presence of titanium tetrachloride, a hydrogen atom at the olefinic 4-position is replaced by a methyl group. Terminal homoallyl alcohols afford (*E*)-isomers. If the double bond is an internal one, the carbon chain (at the other side of the hydroxy group) leaves its original position to the entering methyl group and switches to the other one at the same carbon atom.

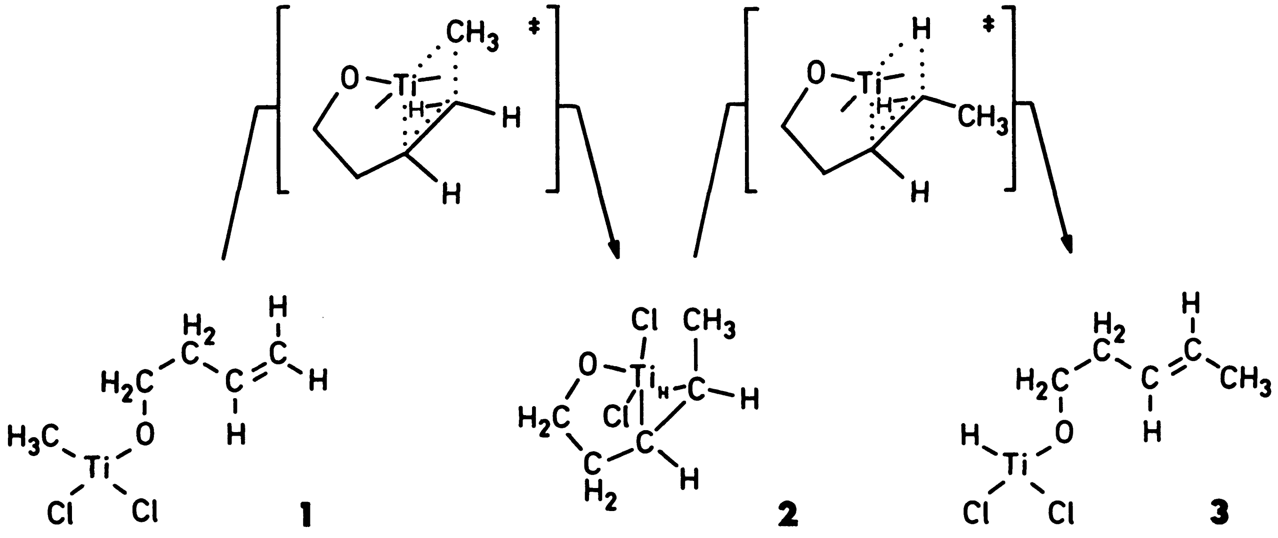
At temperatures above 100°C, trialkylaluminum compounds add slowly onto ethylene and some other olefins having a terminal double bond. If the olefin is present in excess, consecutive addition reactions will produce oligomers, but no polymers of high molecular weight. As a matter of fact, competitive elimination of dialkylaluminum hydride sooner or later interrupts the chain growth [2].



From a synthetic point of view it would be extremely useful, if immediately after the first addition step the reaction sequence could be terminated by an irreversible hydride elimination. This would permit to elaborate a practical method for the nucleophilic displacement of an olefinic hydrogen by an alkyl, alkenyl or aryl group. Here we give a first account of our efforts made toward this goal. So far, we have confined ourselves to a special case, the δ-methylation of homo-allyl alcohols. The mixture of trimethylaluminum and titanium tetrachloride, a typical ZIEGLER catalyst for ethylene polymerization, or dimethyltitanium dichloride in the presence of lithium halides were found efficient to bring about the desired substitution reaction.

When under nitrogen a solution of trimethylaluminum (40 mmol), titanium tetrachloride (20 mmol) and 3-buten-1-ol (20 mmol) in tetrahydrofuran was evaporated to dryness and the residue kept 3 h at 120°C, 35% of (*E*)-3-penten-1-ol were formed. The yield increased to 51% when the heating was prolonged to 40 h at 100°C and to 57% when methyllithium (40 mmol) was used to replace the organoaluminum reagent. Secondary or tertiary homoallyl alcohols gave again satisfactory results, whereas any branching of the carbon backbone in the vicinity of the double bond diminished the reaction rates and even more the yields (see table).

Presumably, the sequence of transformations is initiated by an acid-base reaction between dimethyltitanium dichloride and butenol producing a titanium alkoxide **1** along with methane. As one would expect then, methyltitanium trichloride and lithium 3-butenoxide, which can combine to produce the same titanium alkoxide, give identical results. The subsequent step is the intramolecular *syn*-addition of the titanium moiety and a methyl group onto the double bond. The orientation of the



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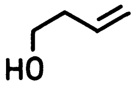
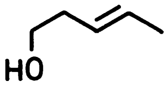
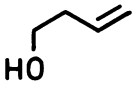
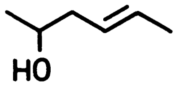
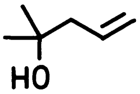
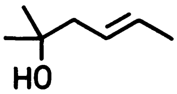
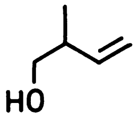
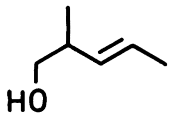
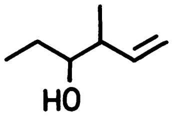
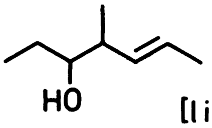
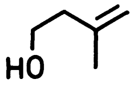
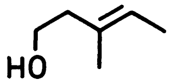
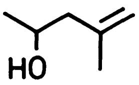
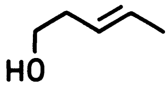
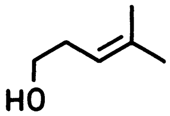
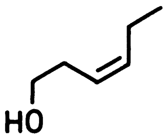
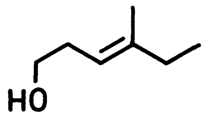
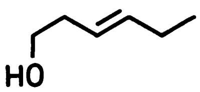
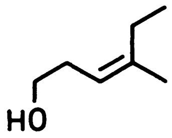
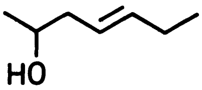
	26 %		57 %	
	26%		23 %	*(Z)*-isomer 1%
	60 %		10%	*(Z)*-isomer 2 %
	33 %		27 %	
	43%	 [lit.6]	32%	
	62%		6%	 12 %
	70%		20%	
	63%		23%	*(Z)*-isomer 1 %
	56%		12 %	*(E)*-isomer 1%  7%

metal towards the nearer olefinic carbon atom, giving rise to a five-membered ring 2 , finds an analogy in the similar behavior of organomagnesium and -lithium compounds 3). Obviously, the intramolecular elimination of titanium hydride again follows a *syn*-mode. Under these circumstances the formation of a *trans*-substituted product 3 should be highly favored 4). Indeed, in all cases studied so far, only trace amounts of *cis*-configurated products were detected, it at all.

When homoallyl alcohols having an internal rather than a terminal double bond serve as substrates, the succession of *syn*-addition and *syn*-elimination brings about an inversion of the double bond configuration. Thus, when treated with dimethyltitanium dichloride, (*Z*)-3-hexen-1-ol affords (*E*)-4-methyl-3-hexen-1-ol and (*E*)-3-hexen-1-ol yields the corresponding (*Z*)-isomer (see table, last entries). Since *cis*- and *trans*-3-alkenols are readily available 5), the titanium-mediated δ-methylation offers a simple and, inspite of the poor yields, efficient access to β,β-disubstituted homoallyl alcohols with high stereoselectivity.

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References

1) The permission for a scientific leave of K.F. From Sumitomo Chemical Company, Takaratsuka-Shi, is gratefully acknowledged.
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