Tetrahedron Letters,Vol.23,No.50,pp 5259-5262,1982 0040-4039/82/505259-04$03.00/0
Printed in Great Britain

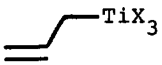
CONTROLLED REVERSAL OF CHEMOSELECTIVITY IN REACTIONS OF ALLYLTITANIUM ATE COMPLEXES WITH CARBONYL COMPOUNDS

M.T.Reetz* and B.Wenderoth

Fachbereich Chemie der Universität, Hans-Meerwein-Str., 3550 Marburg, W-Germany

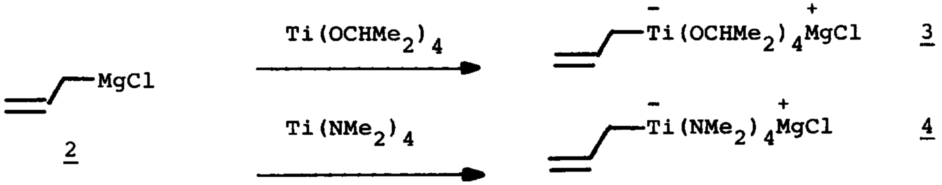
Abstract: Allyltitanium ate complexes react either aldehyde- or ketone-selectively, depending upon the nature of the ligands at titanium.

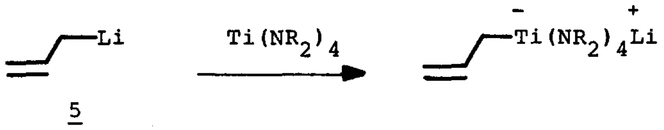
Although nucleophilic addition of carbanions to carbonyl compounds usually proceeds with high yields[1], chemoselectivity is frequently low. For example, Grignard or lithium reagents[2] do not discriminate effectively between ketone and aldehyde functionality. This problem has been solved by converting carbanions into the corresponding organyltitanium compounds, which then display complete aldehyde-selectivity[3,4]. Unfortunately, attempts to extend the list of aldehyde-selective carbon nucleophiles to include synthetically important allyl derivatives such as 1 were unsuccessful[5]. We now report that allyltitanium ate complexes allow for either aldehyde- or ketone-selectivity, depending upon the nature of the ligands at the metal. This class of reagents is also useful in certain diastereoselective C-C bond forming reactions.



1a: X = $OCHMe_2$
1b: X = NMe_2
1c: X = NEt_2

The addition of allylmagnesium chloride 2 or allyllithium 5 to titanium tetraisopropoxide or titanium tetraamides in THF at -78°C led to the ate complexes 3, 4 and 6.

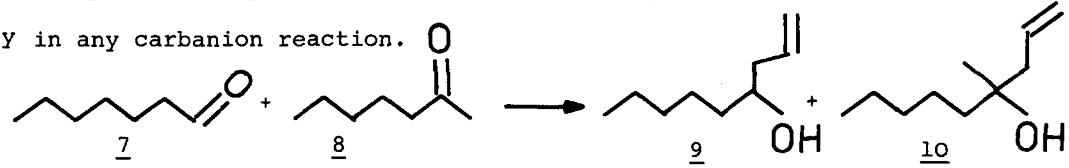




5

6a: R = Me
6b: R = Et

The reaction of a 1:1 mixture of heptanal 7 and 2-heptanone 8 with one part 3 in THF occured smoothly at -78°C (1 h) to afford a 98:2 mixture of 9 and 10 (∿95% conversion). In contrast, the amino titanium ate complexes 4 and 6a-b turned out to be ketone-selective as recorded in Table 1. This means that complete reversal of chemoselectivity is possible simply by switching from alkoxy to amino ligands. The other allyl reagents listed in Table 1 failed to display synthetically useful selectivities. Relevant to these observations is the fact that allylboron[6a] and chromium[6b] reagents are aldehyde-selective, whereas allyltin[6c] analogs provide mixtures in competition experiments. Ketone-selectivity has not been observed previously in any carbanion reaction.



7 8 9 10

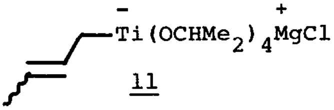
Table 1. Chemoselective Additions[a)]

Reagent	9 : 10
1a (in situ from 2 + ClTi(OCHMe$_2$)$_3$)	86 : 14
1b (in situ from 2 + ClTi(NMe$_2$)$_3$)	13 : 87
1c (in situ from 2 + BrTi(NEt$_2$)$_3$)	22 : 78
1c (distilled sample)	46 : 54
2	29 : 71
3	$\boxed{98 : 2}$
4	4 : 96
6a	$\boxed{2 : 98}$
6b	14 : 86

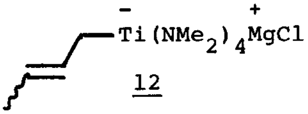
a) Additions were performed at -78°C. Product ratios were determined by GC using internal standards.

In order to test the unique behavior of allyltitanium ate complexes on a wide scale, a different aldehyde/ketone pair was chosen (benzaldehyde / acetophenone).

Indeed, 3 reacts practically only with benzaldehyde (>98% chemoselectivity), while 4 picks out acetophenone (99% chemoselectivity). Comparable results were also obtained using the methallyl analogs of 3 and 4 in combination with aldehyde/ketone pairs. Since crotyl derivatives are sterically more demanding than the parent allyl reagents, we expected difficulties in controlling ketone-selectivity. However, this turned out not to be the case, as shown by competition experiments using the ate complexes 11 and 12. Upon adding 11 to any one of the above mentioned aldehyde/ketone pairs, >98% aldehyde-selectivity was observed, whereas 12 displayed >98% ketone-selectivity. In both cases the reagents react with allyl-inversion to form threo-adducts preferentially[7].

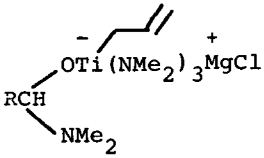


11



12

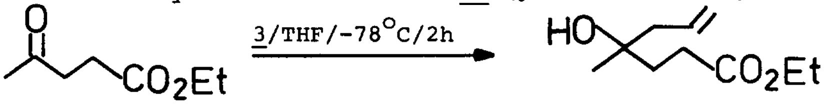
Controlled chemoselective delivery of allyl-type nucleophiles to aldehyde or ketone functionality is synthetically useful because the adducts can be modified chemically by reduction, ozonolysis, epoxidation, etc. Although we prefer to focus on the synthetic implications at present, the results raise interesting questions regarding the mechanism. Control experiments indicate that the reactions are kinetically controlled, i.e., addition is irreversible under the conditions used. An attractive explanation involves chemoselective transfer of an amino ligand onto the aldehyde, which is thereby temporarily protected in the form of species 13, which then allylates the ketone; aqueous workup affords the ketone adduct and regenerates all of the aldehyde. In case of the neutral amino-reagents 1b-c, an analogous MgX_2-mediated and less efficient process is plausible.



13

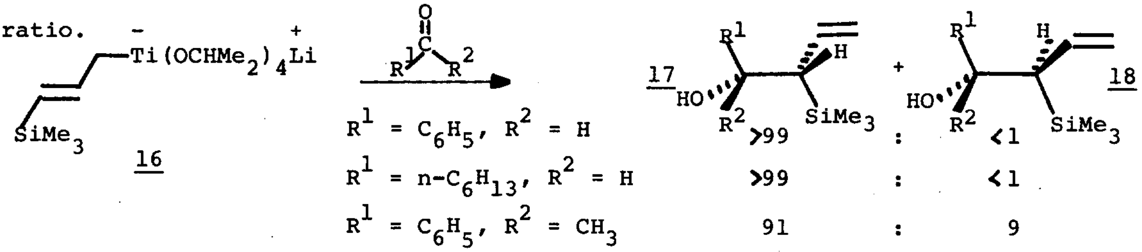
Reagents 1, 2 and 5 failed to react chemoselectively with 14, in contrast to 3, which afforded only the ketone adduct 15 (>95% conversion; 81% isolated) :

14



15

A striking example of diastereoselectivity pertains to the addition of the ate complex 16 (from trimethylsilylallyllithium[8] + $Ti(OCHMe_2)_4$) to aldehydes and ketones to afford the threo and erythro adducts 17 and 18 (~95% conversion at -78°, 2 h; 80-83% isolated by distillation). This one-pot procedure is simpler than related reactions using boron compounds[8]. Adducts of the type 17 have been converted to Z- or E-dienes by the base or acid induced Peterson elimination, respectively[8]. In case of the acetophenone adducts,acid treatment yielded a 91:9 mixture of E- and Z-1-methyl-1-phenyl-1,3-butadiene, which corresponds to the 17:18 ratio.



	17		18
$R^1 = C_6H_5$, $R^2 = H$	>99	:	<1
$R^1 = n\text{-}C_6H_{13}$, $R^2 = H$	>99	:	<1
$R^1 = C_6H_5$, $R^2 = CH_3$	91	:	9

Initial experiments with methyltitanium ate complexes indicate that they do not add as smoothly, yields generally being poor[5]. We are currently trying to solve these problems by using $Ti(NR_2)_4$ as a protective agent. This work was supported by the Fonds der Chemischen Industrie and the Deutsche Forschungsgemeinschaft.

References and Notes:

1. J.C.Stowell, "Carbanions in Organic Synthesis",Wiley, N.Y., 1979.
2. RMgCl and RLi generally react with 1:1 mixtures of aldehydes and ketones to afford about 1:1 adduct mixtures, whereas prior titanation results in >99% aldehyde-selectivity[3,4]. Chemo-random reactions of RMgX have been noted previously:M.S.Kharasch and J.H.Cooper, J.Org.Chem. 10, 46 (1945).
3. Review of Ti-Reagents: M.T.Reetz, Top.Curr.Chem. 106, 1 (1982).
4. M.T.Reetz, R.Steinbach, J.Westermann, R.Urz, B.Wenderoth and R.Peter, Angew. Chem.94, 133 (1982); Angew.Chem.Int Ed.Engl.21, 135(1982);Supplement 1982,258; see also D.Seebach, et al, Helv.Chim.Acta 64, 357 (1981).
5. M.T.Reetz, et al, unpublished results.
6. a) Review of allylmetal reagents: R.W.Hoffmann, Angew.Chem. 94, 569(1982);Angew. Chem.Int.Ed.Engl. 21, 555(1982);b) Y.Okude, et al, J.Am.Chem.Soc. 99, 3179(1977); c) Y.Naruta, S.Ushida and K.Maruyama, Chem.Lett. 1979, 919.
7. E.g., 11 reacts with benzaldehyde to form an 84:16 threo/erythro mixture. 12 shows low diastereoselectivity in reactions with ketones. Threo-selectivity of Ti-crotyl reagents is known[6a]; see also L.Widler and D.Seebach, Helv.Chim. Acta 65, 1085 (1982).
8. D.J.S.Tsai and D.S.Matteson, Tetrahedron Lett. 1981, 2751.

(Received in Germany 17 September 1982)