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LETTERS

Dramatic change of regioselectivity in the addition of silylated organolithium reagents with oxazolidines induced by the presence of a titanium salt

Claude Agami, Sébastien Comesse and Catherine Kadouri-Puchot*

Laboratoire de Synthèse Asymétrique (UMR 7611), Université Pierre et Marie Curie, Case courrier 47,
4 place Jussieu, 75005 Paris, France

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Abstract

Diastereoselective reactions between oxazolidines and organolithium reagents afford β-amino alcohols having chiral vinyl and alkynylsilane moieties. A meaningful change of regioselectivity, from the α- to the γ-position, occurred when these reactions were performed in the presence of titanium isopropoxide, since allyl and allenylsilane derivatives were thus produced. © 2000 Elsevier Science Ltd. All rights reserved.

Much interest has been focused on the preparation of enantio-enriched organosilicon compounds which are very useful reagents in organic synthesis.[1] Most particularly, allyl and vinylsilanes are widely used as intermediates in organic chemistry.[2] On the other hand, diastereoselective additions of organometallic reagents onto imines and oxazolidines are well-documented.[3,4] With a view to synthesizing new optically active β-amino alcohols[5] having an unsaturated silane function,[6] we studied the attack of the allyl and propargyl silylated lithium compounds onto oxazolidines **1a**–**c**. Reactions with the organolithium reagents derived from allyltrimethylsilane **2**[7–9] and 1-(trimethylsilyl)propyn **3**[10] afforded functionalized β-amino alcohols **4** and **5** possessing, respectively, a vinyl or an alkynyl moiety.[11]

Condensation of 2*S*-phenylglycinol and aldehydes gave oxazolidines **1a**–**c**. The vinylsilane moiety of the produced β-amino alcohol **4a**–**c** showed an *E*-geometry (Scheme 1). The diastereoisomeric ratios, determined by ^{1}H NMR analysis of the crude mixture, and the yields are described in Table 1.

A change of regioselectivity was observed when the above reactions were performed in the presence of titanium isopropoxide.[12] As shown on Scheme 2, allylsilane **6** (50% yield, >95/5 dr) and allenylsilane **7** (78% yield, >95/5 dr) were, respectively, produced from oxazolidines **1b** and **1a** under these conditions.

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* Corresponding author. Tel/fax: 33 1 44 27 26 20; e-mail: kadouri@ccr.jussieu.fr

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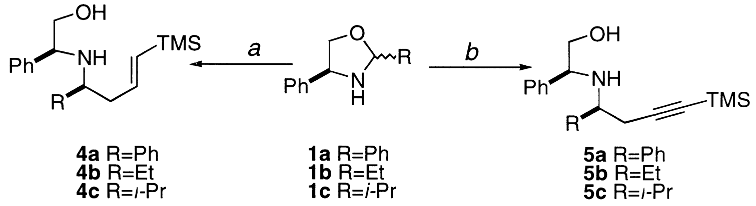


Scheme 1. (*a*) $CH_2{=}CHCH_2SiMe_3$ **2**, *sec*-BuLi (5 equiv.), TMEDA (5 equiv.); (*b*) $CH_3C{\equiv}CSiMe_3$ **3**, *sec*-BuLi (5 equiv.), TMEDA (5 equiv.)

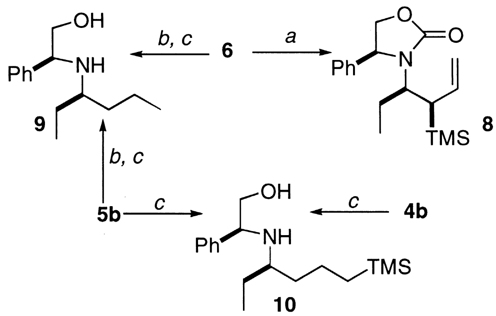
Table 1

Entry	product	R	yield(%)	dr(%)
1	**4a**	Ph	81	92/8
2	**4b**	Et	45	80/20
3	**4c**	*i*-Pr	75	90/10
5	**5a**	Ph	70	80/20
6	**5b**	Et	55	90/10
7	**5c**	*i*-Pr	68	95/5

Scheme 2. (*a*) **2**, *sec*-BuLi (5 equiv.), TMEDA (5 equiv.), Ti(O*i*-Pr)$_4$ (5 equiv.); (*b*) **3**, *sec*-BuLi (5 equiv.), TMEDA (5 equiv.), Ti(O*i*-Pr)$_4$ (5 equiv.)

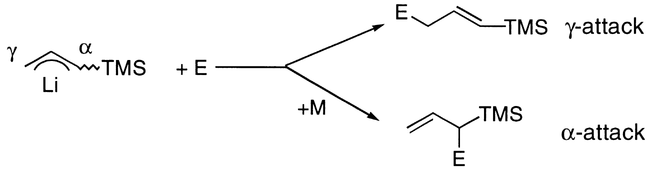
The absolute configurations of β-amino alcohols were determined from three sets of data: (i) X-ray structures of allenyl derivative **7** and of oxazolidinone **8** derived from compound **6**; (ii) desilylation followed by hydrogenation of products **6** and **5b**; and (iii) hydrogenation of compounds **4b** and **5b**. The compound **9** was thus obtained either from **6** or **5b**; this correlation reveals an *R* absolute configuration for the created stereocenter in compound **5b**. Hydrogenation of **4b** or **5b** affords the same product, β-amino alcohol **10**, disclosing, in this case too, an *R* absolute configuration for the stereocenter in **4b** (Scheme 3).

α- versus γ-Regioselectivity shifts in the nucleophilic reactivity of allyl and propargyl silylated lithium reagents pertain to a very intricate field. Many parameters govern this regioselectivity and



Scheme 3. (*a*) $(Cl_3CO)_2CO$, NaOH 6N, CH_2Cl_2 90%; (*b*) *n*-Bu_4NF, THF; (*c*) H_2, Pd, abs. EtOH; 89 and 56% overall from **5b** and **6**; 57 and 75% from **4b** and **5b**

the presence of added metallic salts (M) seems to favor α-attack: this fact has been clearly observed when the electrophile (E) was an aldehyde (Scheme 4).[13,14]



Scheme 4.

Mechanistic studies are currently underway in order to rationalize these results: either an open-chain model or a chelated one are to be considered.[3a] It seems clear, however, that the observed change of regioselectivity must be ascribed to the nature of the organometallic species. Most likely, allyl and allenyl lithium reagents are involved, in their ionic form,[14,15] in the reaction depicted in Scheme 1. Addition of Ti(O*i*-Pr)$_4$ transforms these species into covalent allyl and propargyl titanium derivatives,[16] thus accounting for the formation of compounds **6** and **7**.

Actually, β-amino alcohols are valuable precursors in many enantioselective syntheses. The present methodology is currently being further investigated in order to synthesize new optically active β-amino alcohols and to use them as substrates in asymmetric synthesis.

Acknowledgements

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12. The above representative experimental procedure was used but $\mathrm{Ti(O\textit{i}\text{-}Pr)_4}$ (0.88 mmol) was added at –78°C to the organolithium reagent mixture and this solution was stirred for 1 h before the addition of the oxazolidine.
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