Available online at www.sciencedirect.com
SCIENCE DIRECT®

Tetrahedron Letters 46 (2005) 8033–8035

Tetrahedron Letters

Diastereoselective addition of silyl- and stannyl metals to γ-alkoxy-alkylidene malonates

Alain Krief,[a,*] Willy Dumont[a] and Diane Baillieul[a,b]

[a]*Facultés Universitaires Notre-Dame de la Paix, 61 rue de Bruxelles, Namur 5000, Belgium*
[b]*Fonds pour la Formation à la Recherche dans l'Industrie et l'Agriculture, 5 rue d'Egmont, Bruxelles 1000, Belgium*

Received 5 July 2005; revised 7 September 2005; accepted 12 September 2005

Abstract—Stereochemical control of the addition of silyl- and stannyl metals to chiral γ-alkoxy-alkylidene malonates proved to be dependant on the nature of the counter ion and of the solvent but in an unpredictable way.

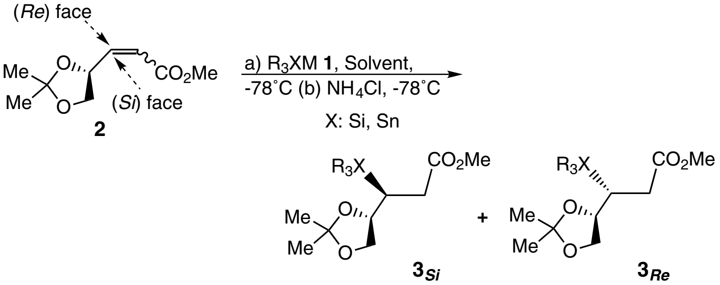
1,4-Addition of nucleophiles[1] including silyl-[2a] and stannyl metals[2b] **1** to chiral enoates, such as γ-alkoxy-α,β-unsaturated esters **2** derived from D-glyceraldehyde acetonide, often takes place with extremely good but unpredictable. This reaction proved to be dependant, upon the case, on almost all the parameters. This includes the nature of the nucleophilic species and of its counter ion, the conditions used and the stereochemistry of the chiral centre as well as that of the C,C double bond of enoate **2** (Scheme 1). Therefore, the stereochemistry of the C,C double bond in **2** has to be perfectly controlled for effective control of the stereochemistry of **3**.

We now report our preliminary results concerning the reaction between silyl metals[4] or stannyl metals[5] **1** and the related chiral alkylidenemalonate **4**[3] which avoids the latter constraints.

The reaction has been carried out at −78 °C in THF or THF–HMPA[6] and usually provides the adduct **5** with equally high (Scheme 2, entries f and k) or better stereocontrol from stannyl than from related silyl reagents (Scheme 2, compare entries g–j to entries a–e).

In both silyl and stannyl series, the counter ion (Li, Cu and Zn) plays a key role in the stereocontrol (Scheme 2). In that respect, the zincates in THF proved to be the most *Re*-face directives reagents (Scheme 2, entries f and k) whereas their lithio analogues usually react by the *Si*-face when the reaction is carried out in the presence of HMPA (Scheme 2, entries d and i).

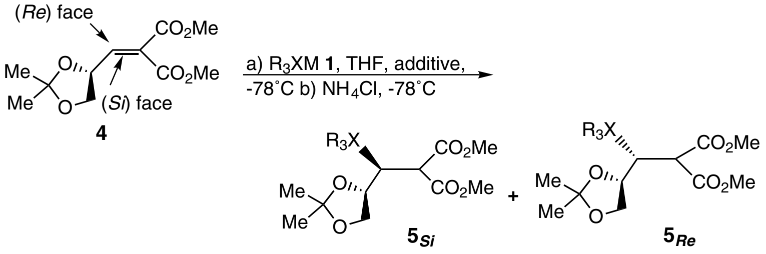
With respect to a solvent, it is worthwhile to mention that in THF, phenyldimethylsilyllithium **1c** and its tributyltin analogue **1g** react in a divergent manner with



Scheme 1.

Keywords: 1,4-Addition; Alkylidene malonates; Stannyl metals; Silyl metals; Facial stereocontrol.
* Corresponding author. Tel.: +32 81 724539; fax: +32 81 724536; e-mail: alain.krief@fundp.ac.be

doi:10.1016/j.tetlet.2005.09.063



Entry	1	R'$_3$XM	Additive	5	5 (%)	5$_{Si}$/5$_{Re}$
a	**1a**	Me_3SiLi	HMPA	**5a**	35	68/32
b	**1b**	$(Me_3Si)_2CuCNLi_2$	HMPA	**5a**	54	31/69
c	**1c**	$PhMe_2SiLi$	-	**5b**	66	30/70
d	**1c**	$PhMe_2SiLi$	HMPA	**5b**	73	82/18
e	**1d**	$(PhMe_2Si)_2CuCNLi_2$	-	**5b**	69	55/45
f	**1e**	$PhMe_2Si(Et_2)ZnLi$	-	**5b**	57	05/95
g	**1f**	Me_3SnLi	-	**5c**	55	79/21
h	**1g**	Bu_3SnLi	-	**5d**	51	91/09
i	**1g**	Bu_3SnLi	HMPA	**5d**	94	92/08
j	**1h**	$(Bu_3Sn)_2CuCNLi_2$	-	**5d**	50	77/23
k	**1i**	$Bu_3Sn(Et_2)ZnLi$	-	**5d**	83	04/96

Scheme 2.

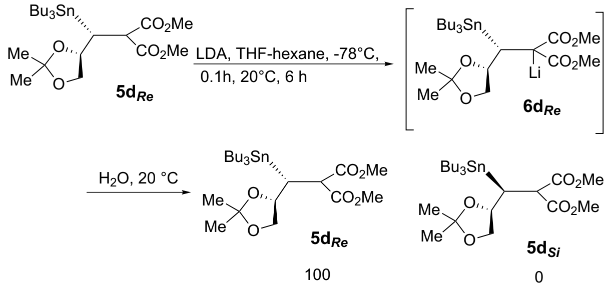
4, since the former mainly attacks **4** by its *Re*-face and the latter by its *Si*-face (Scheme 2, compare entries c and h). Furthermore, whereas the presence of HMPA in the THF solution inverts the stereoisomeric ratio of **5b** from phenyldimethylsilyllithium **1c** (Scheme 2, compare entries d and c), it only substantially improves the yield of **5d** from its tin analogue **1g** (Scheme 2, compare entries i and h).

This preliminary study shows how difficult it is to make accurate comparisons. The substantial enhancement of *Si*-face attack can be related to the increase in the size of the carbon backbone of **1** (Scheme 2, compare entries d to a; h to g) or in the former case to higher softness of the benzylic type reagent (Scheme 2, compare **1c** to **1a**).[5] Also the different behaviours of the silyl **1c** and stannyl **1g** derivatives in THF might be due either to the differences between (i) the nucleophilic atoms (Si/Sn), (ii) the carbon backbone of **1** or to a different control (kinetic vs thermodynamic) of the reaction.

We have proved, in a control experiment, that the reaction between tributylstannyllithium **1g** and alkylidenemalonate **4** proceeds under kinetic control (Scheme 2, entry h or i).

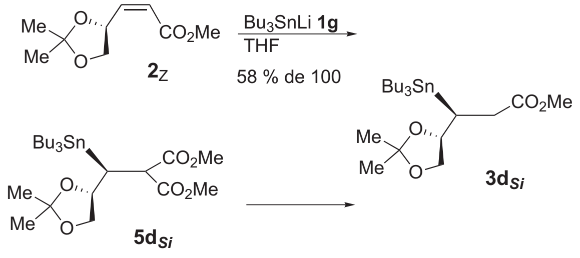
For that purpose, we synthesized the lithio derivative **6** from the γ-stannyl malonate **5d**$_{Re}$, prepared as described in Scheme 2, entry f (1 equiv LDA, THF or THF–HMPA, −78 °C to 20 °C, 6 h; Scheme 3), and recovered after protonation the same diastereoisomer **5d**$_{Re}$. Thus, the γ-stannyl malonate **5d**$_{Si}$ whose synthesis is disclosed in Scheme 2 (entry h or i) does not result from initial formation of **6d**$_{Re}$ which isomerizes then to **6d**$_{Si}$.

We have also confirmed the stereochemistry of 2-[(2,2-dimethyl-[1,3]dioxolan-4-yl)-tributylstannyl-methyl]-malonic acid dimethyl ester **5d**$_{Si}$ by successful comparison of the IR and NMR spectra of **3d**$_{Si}$ resulting from its decarboxy-demethylation with those of the same compound prepared, according to the literature,[2b] from tributylstannyllithium **1g** and methyl *Z*-3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-acrylate **2**$_Z$ (Scheme 4).



Scheme 3.

Surprisingly, decarboxy-demethylation of **5d**$_{Si}$ was not as easy as we expected since neither potassium hydroxide in methanol nor sodium chloride in DMSO which are known to efficiently perform the decarboxy-demethylation of dimethyl malonates, allow the transformation



Scheme 4. Reagents and conditions: (a) KOH, MeOH, 20 °C, 24 h, 0%; (b) NaCl, DMSO, 160 °C, 24 h, 0%; (c) 8 equiv $AcONMe_4$, HMPA, 100 °C, 1.5 h, 53%; (d) 2 equiv, *p*-NH_2PhSH, 0.3 equiv, $CsCO_3$, DMF, 90 °C, 5.5 h, 55%.

of $\mathbf{5d}_{Si}$ to $\mathbf{3d}_{Si}$ (Scheme 4, entries a and b).[7] The reaction, however, proceeds quite efficiently using tetramethylammonium acetate in HMPA at 100 °C (Scheme 4, entry c)[8] or *p*-aminophenylthiol (2 equiv) in the presence of catalytic amounts of caesium carbonate (0.3 equiv) in DMF (90 °C, Scheme 4, entry d).[9]

In conclusion, although we are able to synthesize in quite good yield and good stereocontrol, each of the diastereoisomers of γ-silyl- (Scheme 2, entries d and f) and γ-stannyl- (Scheme 2, entries h and k) malonates **5**, we are unable yet to explain and therefore to predict the behaviour of silyl- and stannyl-metals towards 2-(2,2-dimethyl-[1,3]dioxolan-4-ylmethylene)-malonic acid dimethyl ester **4**. We are working towards this end.

We have previously shown that a series of related nucleophilic reagents such as isopropylidenediphenylsulfurane, isopropylidenetriphenylphosphorane and 2-metallo-2-nitropropanes react in THF almost exclusively by the same *Re*-face of the chiral methyl alkylidenemalonate **4** whereas 2-metallo-2-sulfonyl-propanes in THF react by the *Si*-face of the same electrophilic olefin.[3] In those cases, neither the nature of the counter ion nor the solvent influences the stereochemical outcome of the addition reaction.

References and notes

1. (a) Mulzer, J.; Kappert, M. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 63; (b) Krief, A.; Dumont, W.; Pasau, P.; Lecomte, P. *Tetrahedron* **1989**, *45*, 3039.
2. (a) Krief, A.; Baillieul, D. *Tetrahedron Lett.* **2005**, *46*, 951; (b) Krief, A.; Provins, L.; Dumont, W. *Angew. Chem., Int. Ed.* **1999**, *38*, 1946.
3. (a) Krief, A.; Provins, L.; Froidbise, A. *Tetrahedron Lett.* **1998**, *39*, 1437; (b) Krief, A.; Provins, L.; Froidbise, A. *Synlett* **1999**, 1936; (c) Baudoux, G.; Norberg, B.; Provins, L.; Froidbise, A.; Krief, A.; Evrard, G. *Acta Cristallogr.* **1998**, 834, Section C54; (d) Krief, A.; Froidbise, A. *Tetrahedron* **2004**, *35*, 7637; (e) Krief, A.; Froidbise, A. *Mini-Rev. Org. Chem.* **2005**, *2*, 546.
4. (a) Trimethylsilyllithium has been prepared from hexamethyldisilane and methyllithium in HMPA: Still, W. C. *J. Org. Chem.* **1976**, *41*, 3063; (b) Dimethylphenylsilyllithium has been prepared from dimethylphenylsilyl chloride and elemental lithium in THF: George, M. V.; Peterson, D. J.; Gilman, H. *J. Am. Chem. Soc.* **1960**, *82*, 403; Fleming, I.; Newton, T. W.; Roessler, F. *J. Chem. Soc., Perkin Trans. 1* **1981**, 2527; Fleming, I.; Roberts, R. S.; Smith, S. C. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1209; (c) Dimethylphenylsilylzincate has been prepared from dimethylphenylsilyllithium[4b] and diethylzinc: Crump, R. A. N. C.; Fleming, I.; Urch, C. J. *J. Chem. Soc., Perkin Trans. 1* **1994**, 701.
5. From tin hydrides and LDA: (a) Still, W. C. *J. Am. Chem. Soc.* **1978**, *100*, 1481; From distanannes and alkyllithiums: (b) Still, W. C. *J. Am. Chem. Soc.* **1977**, *99*, 4836.
6. The synthesis of trimethylsilyl lithium cannot be performed in THF alone. It requires the concomitant use of HMPA.[4a]
7. McMurry, J. *Org. React.* **1976**, *24*, 187.
8. (a) Trost, B. M.; Verhoeven, T. R. *J. Am. Chem. Soc.* **1976**, *98*, 630; (b) Johnson, W. S.; Habert, C. A.; Ratcliffe, B. E.; Stipanovic, R. D. *J. Am. Chem. Soc.* **1976**, *98*, 6188; (c) Trost, B. M.; Weber, L.; Strege, P.; Fullerton, T. J.; Dietsche, T. J. *J. Am. Chem. Soc.* **1978**, *100*, 3426; (d) Trost, B. M.; Verhoeven, T. R. *J. Am. Chem. Soc.* **1980**, *102*, 4743.
9. Keinan, E.; Eren, D. *J. Org. Chem.* **1986**, *51*, 3165.