Pergamon

Tetrahedron Letters, Vol. 35, No. 42, pp. 7767-7770, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $7.00+0.00

0040-4039(94)01716-6

1,2-Metallate rearrangements : Stannyl and (Stannyl)Vinyl Transfers.

Patrick Le Ménez, Valérie Fargeas, Jacques Poisson, Janick Ardisson *.

Laboratoire de Chimie des Substances Thérapeutiques Naturelles associé au CNRS, *BIOCIS*, Centre d'Etudes Pharmaceutiques, 92290, Châtenay-Malabry, France.

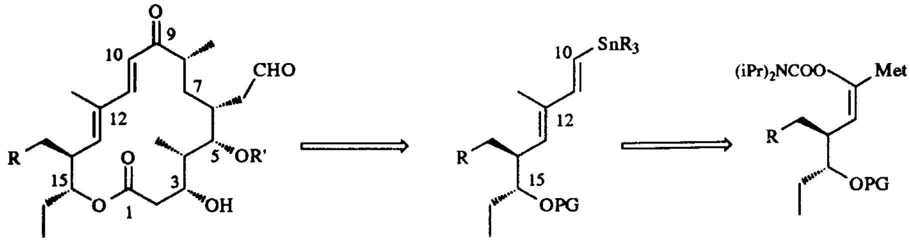
Jean-Yves Lallemand, Ange Pancrazi *.

Laboratoire de Synthèse Organique associé au CNRS, DCSO, Ecole Polytechnique, 91128, Palaiseau, France

Key Words *: 1, 2-Metallate rearrangement, 2-(carbamoyl)alkenyl, vinylstannane, stannyl cyanocuprate, (E)-1,2-bis-(tributylstannyl)ethylene, (E)-2-(tributylstannyl)ethylene cyanocuprate.*

Abstract *: 1,2-Metallate rearrangements were performed on α-(carbamoyl)alkenyl stannane **6** with high yield in alkyl transfer to give **10** after quenching with MeI ; disappointing results were obtained for preparation of **11** and **2b**. Using dihydrofuran **13**, optimized conditions were found to realize 1,2-stannyl and 1,2-(stannyl)vinyl transfers, and methylation, leading to stannyl derivative **15** and stannyl diene **16** in good yields.*

In our project toward the total synthesis of macrocyclic antibiotics such as tylosin **1a** or des-epoxy-rosaramycin **1b**[1] (16 membered macrolides), we took interest in developing a general method for the construction of the western C_{10}-C_{15} moiety **2**. In order to obtain the required fragments **2a** or **2b**, a stereospecific synthesis of trisubtituted alkenes was explored according to Kocienski's procedure,[2] involving a 1,2-metallate rearrangement of a α-(carbamoyl)alkenyl cuprate **3**, or a cyclic α-alkoxyalkenyl cuprate, dihydrofuran series.



tylosin 1a
R = O-mycinosyl, R' = 4-(mycarosyl) mycaminosyl
des-epoxy-rosaramycin 1b
R = H, R' = 4-(mycarosyl) mycaminosyl

western Part
2a R = OH
2b R = H

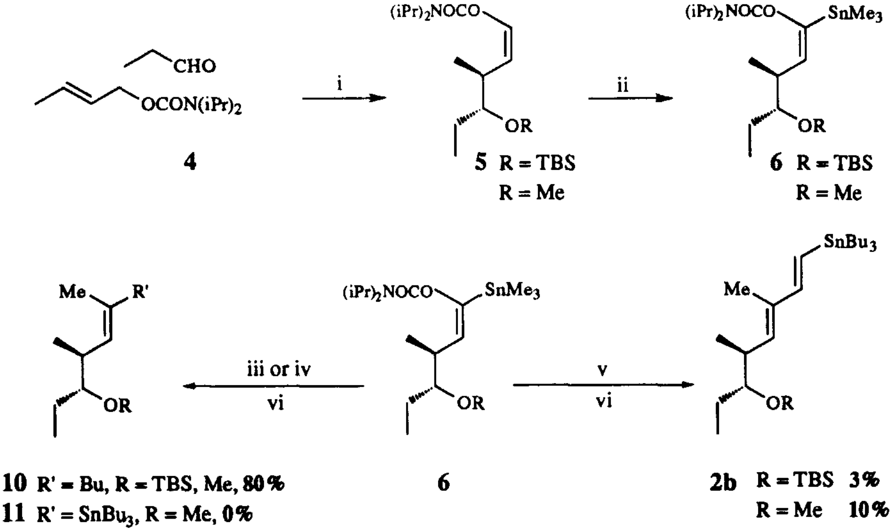
3

Our synthetic interest in this reaction was to realize a (stannyl)vinyl transfer to carbamate enol ether **6** in order to obtain the desired stannyl diene **2** in a stereospecific manner. For an approach of fragment **2b**, the vinyl carbamate precursor **5** was obtained in 90% yield [3] using the Hoppe's homoaldol reaction [4] ; after protection of the secondary alcohol, further lithiation and *trans*-metallation with $SnMe_3$ led to vinyl stannane **6**.

According to Kocienski's results [2], higher order (H.O.), alkylcyanocuprate **7a** [6] reacted with vinylstannane **6** to give pure (*E*) butyl derivative **10** in 80% yield.

When we tried to extend this 1,2-metallate rearrangement to the use of (stannyl)ethylene cuprate **9**, prepared from *trans* 1-lithio-2-tributylstannyl ethylene [5] (*trans*-LiSE), the desired stannyl diene **2b** was produced in poor yields, less than 5% for the OTBS derivative and 10% for the OMe compound.

Thus we decided to look at the reactivity of H.O. stannylcuprate **8a** [7] in order to obtain the vinyl stannane **11** which could be a precursor of stannyl diene **2b**; unfortunately this reaction did not lead to the stannane **11**.



4

5 R = TBS
R = Me

6 R = TBS
R = Me

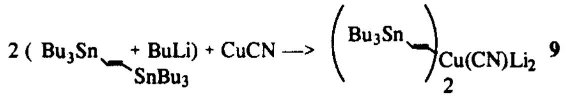
10 R' = Bu, R = TBS, Me, **80%**
11 R' = $SnBu_3$, R = Me, **0%**

6

2b R = TBS **3%**
R = Me **10%**

i) a) n-BuLi, TMEDA, $Ti(OiPr)_4$, EtCHO, 90% ; b) TBSTf, lutidine, >95%, or NaH, MeI, 70%; ii) t-BuLi, Me_3SnCl, 90%; iii) **7a**, THF-Et_2O 1:1, -10°- 5°C—> 5°C, 20min ; iv) **8a**, THF-Et_2O 1:1, -10°-5°C—>5°C, 2h ; v) **9** ,THF-Et_2O 1:1, -20°C—> 5°C, 2h; vi) MeI, -30°C—> rt, 4h.

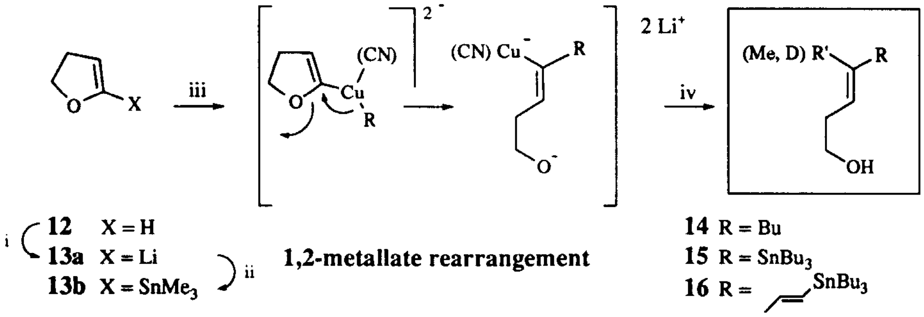
$Bu_2Cu(CN)Li_2$ **7a** ; $(Bu_3Sn)_2Cu(CN)Li_2$ **8a** ;



$$2\,(\,Bu_3Sn\diagdown\!\!\diagdown SnBu_3 + BuLi) + CuCN \longrightarrow \left(Bu_3Sn\diagdown\!\!\diagdown\right)_2 Cu(CN)Li_2 \quad 9$$

These disappointing results constrained us to focus on a dihydrofuran approach. As expected,[2] lithium or stannyl derivatives **13**,[8] obtained from commercial dihydrofuran **12**, gave good yields in alkyl transfers with H.O. or L.O. cyanocuprates **7a** and **7b**, leading to **14** (Entries 1-3, table).

For stannyl transfer, H.O. stannylcuprate **8a**,[7] afforded the desired vinyl stannanne **15** as a single *E* isomer ; yields ranged from 72-77% yields when 1.9 to 3.0 equivalents of Bu_3SnLi were added for the preparation of cuprate **8a**, and increased to 85% when 4 equivalents were used (Entries 6-8, table). Stannyl transfer leading to **15** were also performed in the same manner with Lipshutz's H.O. mixed cyanocuprate **8b**[9] in 75% yield, (Entries 4-5 table).[10]



12 X = H
13a X = Li
13b X = $SnMe_3$

14 R = Bu
15 R = $SnBu_3$
16 R = $SnBu_3$

i) 1.1eq t-BuLi, - 65°C—> 0°C, 1h ; ii) **13a**, Me_3SnCl, - 65°C—> 0°C, 1h ; iii) "cuprate" see table I ;
iv) MeI, -30°C—> rt, 4h, or D_2O, -30°C—> rt, 1h

Having obtained high yields using alkyl and stannyl cuprates, we next turned to the (vinyl)stannyl transfer designed for our synthetic purposes. Therefore we first tried the H.O. cyanocuprate **9** resulting from addition of 1.0 equivalent of CuCN to 1.8 equivalents of *trans*-LiSE; 1,2-metallate rearrangement took place and provided stannyl diene **16** in 66% yield; better yields were obtained when the *trans*-LiSE derivative was prepared by treatment of *trans*-1,2-di(tributylstannyl) ethylene (*trans*-DSE) with 1.4 equivalents of BuLi.

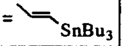
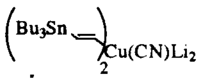
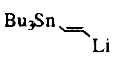
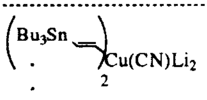
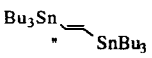
Entry	X	Cuprate*	Yield 12 —>14 R = Bu	Yield 12 —>15 R = $SnBu_3$
1	$SnMe_3$	$Bu_2Cu(CN)Li_2$ **7a** : 1.1eq	R' = Me **85%**	
2	Li	$Bu_2Cu(CN)Li_2$ **7a** : 1.1eq	R' = Me **82%**	
3	Li	$BuCu(CN)Li$ **7b** : 1.1eq	R' = Me **83%**	
4	Li	$(Bu_3Sn)(Bu)Cu(CN)Li_2$ **8b** : 1eq $Bu_2Cu(CN)Li_2$ + 2.0eq Bu_3SnH **		R' = Me **53%**
5	Li	" : " + 2.0eq Bu_3SnH		R' = Me **75%**
6	Li	$(Bu_3Sn)_2Cu(CN)Li_2$ **8a** : 1eq CuCN + 1.9eq Bu_3SnLi		R' = Me **72%**
7	Li	" **8a** : " + 3.0eq Bu_3SnLi		R' = Me **77%**
8	Li	" **8a** : " + 4.0eq Bu_3SnLi		R' = Me **85%**
		Cuprate*		Yield 12 ->16 R = 
9	Li	 **9** : 1eq CuCN + 1.2eq 		R' = D **40%**
10	Li	" **9** : " + 1.8eq "		R' = D **66%**
11	Li	 **9** : 1eq $Bu_2CuCNLi_2$ + 1.8eq 		R' = D **68%**
12	Li	" **9** : " + 4.0eq "		R' = D **82%**
13	Li	" **9** : " + 4.0eq "		R' = Me **77%**

Table * All reactions were carried out in a 1:1 mixture of THF- Et_2O; for stannyl derivatives, yields are given after chromatography (Al_2O_3). For entries 1-3, reaction was performed at -5°C—> 0°C for 30min; for entries 4-8, -5°C —>0°C for 1h 30min ; for entries 9-13, -20°C —> 0°C for 2h. ** For entry 4 pure THF was used.

Finally the easier and more convenient Lipshutz's exchange method [11] was preferred, and 1.8 equivalents of *trans*-DSE were reacted with 1 equivalent of $Bu_2Cu(CN)Li_2$ to afford cuprate **9** which, on reaction with **13**, led to the desired stannyl diene **16** [3]. Yields improved to 80% when 4 equivalents of DSE were used for the preparation of **9** (entries 11-13, table). In good agreement with previous observations in alkyl transfer induced by the $CuBr\text{-}Me_2S$ reagent [12], it seems that the 1,2-metallate rearrangement required four equivalents of the metallated species, with respect to Cu content, to give optimum yields.[13]

Results in this study have shown that the 1,2-metallate rearrangement was efficient when applied to dihydrofuran derivative, instead of (α-carbamoyl)alkenyl stannanes, especially for stannyl or (stannyl)vinyl transfers which afforded pure (E) vinyl stannane 15 and (E,E) stannyl diene 16 in a stereospecific manner.

Applications of this reaction to the synthesis of the western parts of tylosin 1a and des-epoxy-rosaramycin 1b are currently in progress.

Acknowledgements: Thanks are due to Professor Andre Cavé for continual encouragement's.

References and Notes:

1 Tatsuta, K.; Amemiya, Y.; Kanemura, Y.; Takahashi, H.; Kinoshita, M. *Tetrahedron Lett.*, **1981**, *23*, 3375-78; Nicolaou, K. C.; Seitz, S. P.; Pavia, M. R. *J. Am Chem. Soc.*, **1982**, *104*, 2030-31; Masamune, S.; Lu, L. D.- L.; Jackson, W. P.; Kaiho, T.; Toyoda, T. *J. Am. Chem. Soc.*, **1982**, *104*, 5523-26; Grieco, P. A.; Inanaga, J.; Lin, N. H.; Yanami, T. *J. Am. Chem. Soc.*, **1982**, *104*, 5781-84. Tanaka, T.; Oikawa, Y.; Hamada, T.; Yonemitsu, O. *Chem. Pharm. Bull.*, **1987**, *35*, 2219.

2 Kocienski, P.; Barber, C. *Pure & Appl. Chem.*, **1990**, *62*, 1933-40; Takle, A.; Kocienski, P. *Tetrahedron*, **1990**, *46*, 4503-16; Kocienski, P.; Wadman, S. *J. Am. Chem. Soc.*, **1989**, *111*, 2363-65; Kocienski, P.; Dixon, N. J. *Synlett*, **1989**, 52-54; Pimm, A.; Kocienski, P.; Street, D. A. S. *Synlett*, **1992**, 886-88.

3 H^1 and C^{13} NMR spectra of all compounds are consistent with the proposed structures. Studies on the enantioselective synthesis of compound **6** *via* Hoppe's reaction [4] using (-)-sparteine are in progress.

4 Hoppe, D. *Angew. Chem. Int. Ed. Engl.*, **1984**, *23*, 932-948; Zschage, O.; Hoppe, D. *Tetrahedron*, **1992**, *48*, 5657-66.

5 Corey, E. J.; Wollenberg, R. H. *J. Am. Chem. Soc.*, **1974**, *96*, 5581-83; Renaldo, A. F.; Labadie, J. W.; Still, J. K. *Org. Synth.*, **1988**, *67*, 86-97; Seyferth, D.; Vick, S.C. *J. Organomet. Chem.*, **1978**, *144*, 1-12.

6 Lipshutz, B. H.; Kozlowski, J. A.; Wilhelm, R.S. *J. Org. Chem.*, **1984**, *49*, 3943-46.

7 Cuprate **8b** was prepared from $(Bu_3Sn)_2$ + n-BuLi + CuCN as described by Still, W. C. *J. Am. Chem. Soc.*, **1977**, *99*, 4836-38.

8 Kocienski, P J.; Pritchard, M.; Wadman, S. N.; Whitby, R. J., Yeates, C. L. *J. Chem. Soc. Perkin Trans.I.* **1992**, 3419-38.

9 Lipshutz, B. H.; Ellsworth, E. L.; Dimock, S. H.; Reuter, D. C. *Tetrahedron Lett.* **1989**, *30*, 2065-68.

10 Butyl transfer, less than 5%, occurred when the mixed cuprate $(Bu_3Sn)(Bu)Cu(CN)Li_2$ was employed. When cuprate **8b** was prepared using Bu_3SnH + LDA + CuCN as described by Gilbertson, S. R.; Challener, C. A.; Bos, M. E.; Wulff, W. D. *Tetrahedron Lett.*, **1988**, *38*, 4795-98, yields in stannyl transfer leading to **15** were observed to be lower than in other cases (60-67%).

11 Behling, J. R.; Babiak, K. A.; Ng, J. S.; Campbell, A. L.; Moretti, R.; Koerner, M.; Lipshutz, B. H. *J. Am. Chem. Soc.*, **1988**, *110*, 2641-43.

12 Kocienski, P. *Organic Synthesis via Organometallics, OMS 4*, Proceedings of the Fourth Symposium in Aachen, July 15 to 18, **1992**.

13 In our case, for (vinyl)stannyl transfer, the $CuBr\text{-}Me_2S$ reagent was less efficient than CuCN.

(*Received in France* 7 *June* 1994; *accepted* 27 *August* 1994)