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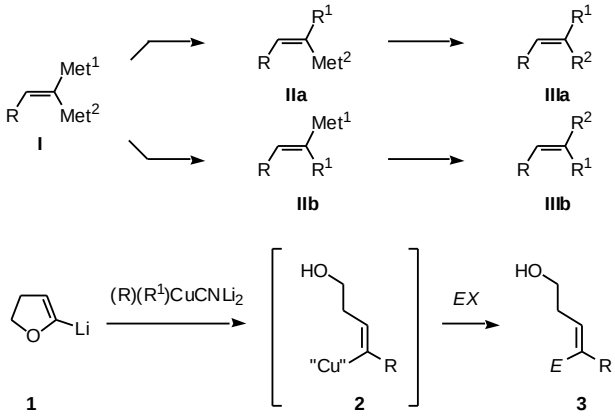
Patrick Le Ménez,[a] Jean-Daniel Brion,[a*] Jean-François Betzer,[b] Ange Pancrazi,[b] Janick Ardisson [b*]

a) *CNRS-BIOCIS*, Université de Châtenay-Malabry, Faculté de Pharmacie, 92296 Châtenay-Malabry, France.
Tel (33) 1 46 83 55 90 -Fax (33) 1 46 83 53 98
b) "*Laboratoire de Synthèse Organique Sélective et Chimie Organométallique*" *CNRS-UCP-ESCOM, UMR 8123*
13 Bd de l'Hautil, 95092 Cergy-Pontoise Cedex, France.
Tel (33) 1 30 75 61 86 - Fax (33) 1 30 75 60 15
E-mail: janick.ardisson@chim.u-cergy.fr

Abstract: Metallate rearrangements performed on 5-lithio-2,3-dihydrofuran **1** gave access to several homo- and hetero-1,1-bimetallated (or pseudo) alkenes **3** upon exposure to a cyanocuprate and quench with an electrophilic reagent *EX*. After metal/halogen exchange, several homo- or hetero-1,1-dihalo-1-alkenes were prepared stereospecifically and in good yields.

Total synthesis in natural compounds involves the stereoselective construction of substituted double bonds.[1] Different methodologies can be applied for this, but stereochemical control remains difficult.



R = Bu_3Sn, TMS, alkyl, aryl ; *E* = Bu_3Sn, TMS, I, Br, Cl, Me

Scheme 1

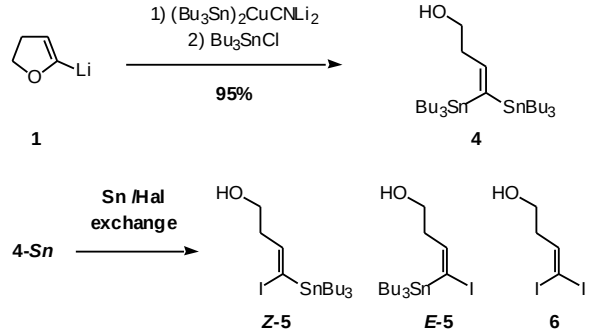
Considering the geminated bimetallic (or pseudobimetallic) olefin **I**,[2] an access to both unsaturated isomeric compound **IIIa** or **IIIb** (Scheme 1) is obtained *via* the monometallated intermediate **IIa** or **IIb** if the two

metallic or pseudometallic atoms Met[1] and Met[2] react selectively with two different electrophilic reagents.

Although 1,1-dibromo-1-alkenes were abundantly used to make substituted double bonds,[3] we wanted to develop a new synthesis of substituted alkenes based on the stereospecific production of hetero-1,1-dihalo-1-alkenes *via* metallate rearrangements. Thus, reaction between a cuprate and lithiodihydrofuran **1** resulted in a rearrangement [4] leading to the vinylcuprate intermediate **2** with complete stereoselectivity (Scheme 1). Subsequent quenching reaction of **2** with several electrophilic agents then delivered the substituted alkenes **3**.[5,6]

We want to present here an extension of our precedent studies [5,6] to the stereoselective preparation of hetero-1,1-dihalo-1-alkenes.

In our initial experiments we tried to functionalize the earlier synthesised **4** ditin compound,[6] using a selective Sn/I exchange (Scheme 2).[7]



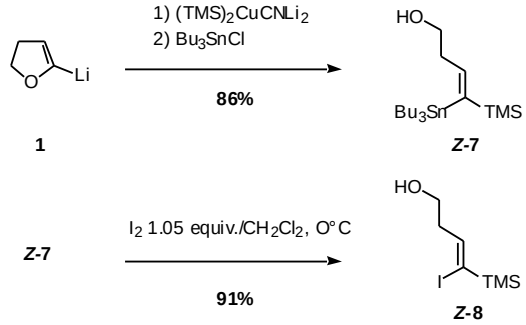
Exchange agent (equiv.)	Conditions	5 (%)	*Z*/*E* ratio	6 (%)
NIS (1.1)	THF, -20°C, 1 h	70	50:50	
NIS (1.1)	CH_2Cl_2, 20°C, 1 h	70	63:37	
I_2 (1.1)	CH_2Cl_2, 20°C, 1 h	82	61:39	
I_2 (1.1)	CH_3CN, 20°C, 1 h	57	34:66	
I_2 (1.1)	THF, 0°C, 1 h	56	80:20	
I_2 (1.1)	Et_2O, 20°C, 1 h	58	46:54	
I_2 (1.1)	Et_2O-THF, -20°C, 1 h	41	87:13	
I_2 (2.2)	CH_2Cl_2, 0°C, 6 h			88

Scheme 2

Unfortunately, and contrasting with results described by Quayle in another series,[8] no selectivity was obtained for the *Z* or *E* tin function exchange. Both ***Z*-5** and ***E*-5** are produced as a 34:66 to 87:13 mixture and in fair yields (41-82%). When 2.2 equivalents of iodine were used, the diiodo derivative **6** was obtained in 88% yield from ditin compound **4**.

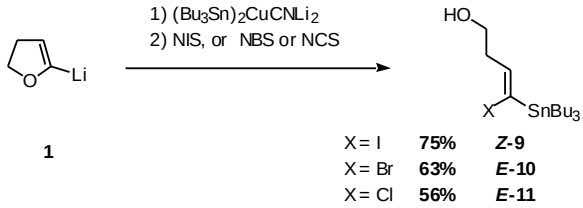
The lack of selectivity of the 1,1-ditin led us to prepare the hetero-1,1-dimetallo or 1,1-dihalo analogues in an indirect way. Starting from the

***Z*-7** vinyltin, obtained in a pure form (86%) from the lithiodihydrofuran **1** *via* a cuprate rearrangement,[9] the Sn/I exchange reaction afforded the ***Z*-8** vinyliodide in 91% yield (Scheme 3).[10] This method could be considered as an alternative to the procedure described by Lautens *et al*.[11]



Scheme 3

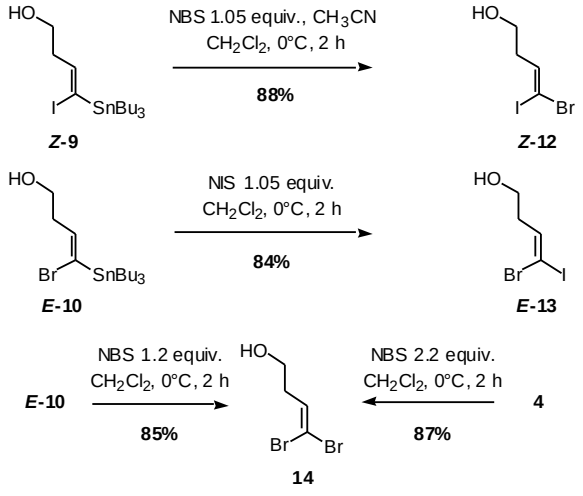
Interestingly, we prepared earlier [12] the halovinyltin derivatives ***Z*-9**, ***E*-10** and ***E*-11** in good yields (75%, 63% and 56%, respectively) *via* cuprate rearrangements effected on **1** (Scheme 4).



Scheme 4

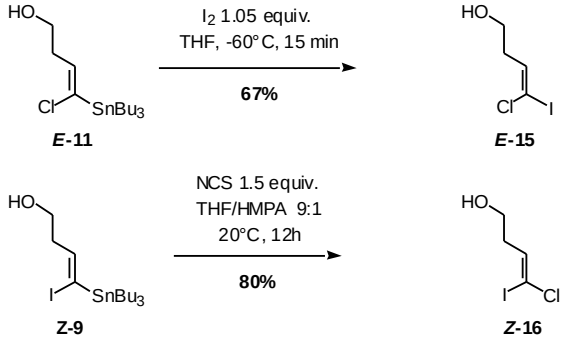
Vinyltin compounds ***Z*-9** and ***E*-10** underwent Sn/Br or Sn/I exchange reactions thereby providing the two stereomeric hetero-1,1-dihalo-1-alkene compounds ***Z*-12** and ***E*-13** in 88% and 84% yields, respectively, as pure isomers.[13]

A Sn/Br exchange could be also performed with the ***E*-10** or **4** compound to produce the dibromoalkene **14** in 85% or 87% yield, respectively (Scheme 5).[13]



Scheme 5

The pure (*E*)-chloroiodo ***E*-15** was smoothly delivered using a Sn-I exchange from the (*E*)-chlorotin ***E*-11** in 67% yield (Scheme 6). Initial attempts to generate the (*Z*)-chloroiodo compound ***Z*-16** were performed on iodotin ***Z*-9** under NCS, CH_3CN, Δ conditions; unfortunately, they afforded a 1:1 mixture of iodochloro ***Z*-15** and ***E*-15** isomers in low yield.



Scheme 6

In contrast, exposure of the (*Z*)-iodotin olefin ***Z*-9** to 1.5 equivalents of NIS in THF/HMPA (9:1) at 20°C for 12 h resulted in its clean conversion to the (*Z*)-chloroiodo derivative ***Z*-16** in 80% yield along with a minor amount (4%) of ***E*-15**.[13]

In this study it was shown that cuprate rearrangement is an efficient and stereoselective method to obtain hetero-1,1-dimetallo-1-alkenes and consequently to form hetero-1,1-dihalo-1-alkenes stereoselectively. Further studies, in connection with their abilities to undergo specific palladium-catalysed coupling reactions, are now under scrutiny.

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9) Preparation of ***Z*-7**: A solution of the 5-lithio-2,3-dihydrofuran derivative **1** (2.5 mmol) [9] in THF (4 mL) was added, *via* cannula, to the solution of the *bis*-(trimethylsilyl) dilithiocyanocuprate [14] at -30-°C (2.75 mmol, 1.1 equiv.) in THF-Et_2O (6 mL/12 mL). The mixture was stirred at -5°- 0 °C for 1 h 30 min. The mixture was then cooled at -40 °C and Bu_3SnCl (4 equiv.) was added. The temperature was allowed to rise to 0 °C for 1 h, stirring was maintained for 4 h, temperature going up to 20 °C. The reaction mixture was poured into a solution of saturated aqueous NH_4Cl/concentrated ammonia (4:1) at 0 °C and stirred for 30 min before extraction with diethyl ether. After purification by chromatography on silicagel compound ***Z*-7** was obtained in 86% yield. IR (Neat) ν^{cm-1}: 3298, 2954, 2923, 2871, 1571, 1463, 1244, 1180, 1046, 960, 871, 830, 743, 685, 620, 591. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.0 (s, 9 H), 0.88 (m, 15 H), 1.32 (m, 6 H + OH), 1.45 (m, 6 H), 2.45 (q, J = 6.5 Hz, 2 H), 3.69 (t, J = 6.5 Hz, 2 H), 6.72 (t, J = 6.5 Hz, 1 H, $J_{H\text{-}^{119}Sn} = J_{H\text{-}^{117}Sn}$ = 170.0 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ - 0.3 (3 CH_3), 11.3 (3 CH_2, $J_{C\text{-}^{119}Sn}$ = 318.0 Hz, $J_{C\text{-}^{117}Sn}$ = 304.0 Hz), 13.6 (3 CH_3), 27.4 (3 CH_2,$J_{C\text{-}^{119}Sn} = J_{C\text{-}^{117}Sn}$ = 58.0 Hz), 29.2 (3 CH_2, $J_{C\text{-}^{119}Sn} = J_{C\text{-}^{117}Sn}$ = 19.0 Hz), 42.4 (CH_2, $J_{C\text{-}^{119}Sn} = J_{C\text{-}^{117}Sn}$ = 57.5 Hz), 62.1 (CH_2), 147.6 (C), 150.7 (CH, $J_{C\text{-}^{119}Sn} = J_{C\text{-}^{117}Sn}$ = 20.0 Hz). MS (CI, CH_4): for major ^{120}Sn isotope, *m/z* 377, 311, 308, 306, 304, 252, 250, 248, 102.

10) To a solution of the vinyltin derivative ***Z*-7** in CH_2Cl_2 (or CH_3CN) at 0°C (or below) was slowly added a CH_2Cl_2 solution of iodine (1.05 equiv.) until persistence of an orange-red colour (1 h at 0°C). The solution was then washed with an aqueous KF and a saturated aqueous Na_2SO_3 solution before evaporation of the solvent and chromatography on silica gel. Compound ***Z*-8** was obtained in 91% yield. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.18 (s, 9H), 2.45 (q, J = 6.5 Hz, 2H), 2.5 (s, 1H), 3.72 (t, J = 6.5 Hz, 2H),

6.57 (t, J = 6.5 Hz, 1H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 1.5 ($3CH_3$), 42.1 (CH_2), 60.6 (CH_2), 116.0 (C), 143.5 (CH). MS (CI, CH_4): *m/z* 181, 143, 103, 91, 73. Anal. calcd for $C_7H_{15}IOSi$: C, 31.12; H, 5.60; I, 46.97; O, 5.92; Si, 10.40; Found: C, 31.32; H, 5.48.

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12) Preparation of ***Z*-9**, ***E*-10** and ***E*-11** derivatives:
A solution of the 5-lithio-2,3-dihydrofuran derivative **1** (2.5 mmol) in THF (4 mL) was added, *via* cannula, to the solution of the *bis*-[(tributyl)stannyl] dilithiocyanocuprate [9] at -30 °C (2.75 mmol, 1.1 equiv.) in THF-Et_2O (6 mL/12 mL). The mixture was stirred at -5°- 0 °C for 1 h 30 min. The mixture was then cooled at -40 °C and a THF solution (1-2 mL) of the quenching agent, NIS,NBS or NCS (4.0 equiv.), was added. The temperature was allowed to rise to 0 °C for 1 h, stirring was maintained for 4 h, temperature going up to 20 °C. The reaction mixture was poured into a solution of saturated aqueous NH_4Cl/concentrated ammonia (4:1) at 0 °C and stirred for 30 min before extraction with diethyl ether. The ***Z*-9** compound was obtained in 75% yield. IR (Neat) ν^{cm-1}: 3324, 2950, 2920, 2870, 2850, 1594, 1461, 1376, 1180, 1044, 907, 733, 690, 664, 597. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.85 (t, J = 8.0 Hz, 6 H), 0.96 (t, J = 8.0 Hz, 9 H), 1.30 (m, 6 H), 1.48 (m, 1 H, OH), 2.45 (q, J = 6.5 Hz, 2 H), 3.69 (t, J = 6.5 Hz, 2 H), 6.14 (t, J = 6.5 Hz, 1 H, $J_{H\text{-}^{119}Sn} = J_{H\text{-}^{117}Sn}$ = 42.0 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ 11.1 (3 CH_2, $J_{C\text{-}^{119}Sn}$ = 348.0 Hz, $J_{C\text{-}^{117}Sn}$ = 332.0 Hz), 13.6 (3 CH_3), 27.2 (3 CH_2, $J_{C\text{-}^{119}Sn} = J_{C\text{-}^{117}Sn}$ = 60.0 Hz), 28.6 (3 CH_2, $J_{C\text{-}^{119}Sn} = J_{C\text{-}^{117}Sn}$ = 20.0 Hz), 42.6 (CH_2, $J_{C\text{-}^{119}Sn} = J_{C\text{-}^{117}Sn}$ = 32.0 Hz), 60.9 (CH_2), 110.0 (C), 145.2 (CH, $J_{C\text{-}^{119}Sn} = J_{C\text{-}^{117}Sn}$ = 20.0 Hz). MS (CI, CH_4): for major ^{120}Sn isotope, *m/z* 377, 322, 307, 252. Anal. calcd for $C_{16}H_{33}IOSn$: C, 39.46; H, 6.83; I, 26.06; O, 3.29; Sn 24.37; Found: C, 39.88; H, 7.09.

13) Selected NMR spectroscopic data
***Z*-12:** ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.22 (q, J = 6.5 Hz, 2H), 3.63 (t, J = 6.5 Hz, 2H), 6.51 (t, J = 6.5 Hz, 1H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 40.4 (CH_2), 55.5 (C), 59.9 (CH_2), 143.5 (CH).
***E*-13:** ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.37 (q, J = 7.0 Hz, 2H), 3.72 (t, J = 7.0 Hz, 2H), 6.90 (t, J = 7.0 Hz, 1H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 37.8 (CH_2), 51.0 (C), 60.3 (CH_2), 143.7 (CH).

14*:* ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.8 (s, 1H), 2.44 (q, *J* = 6.5 Hz, 2H), 3.76 (t, *J* = 6.5 Hz, 2H), 6.48 (t, *J* = 6.5 Hz, 1H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 36.2 (CH_2), 60.3 (CH_2), 90.5 (C), 135.1 (CH).

***E*-15**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.43 (q, *J* = 7.0 Hz, 2H), 3.69 (t, *J* = 7.0 Hz, 2H), 6.51 (t, *J* = 7.0 Hz, 1H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 34.9 (CH_2), 60.5 (CH_2), 68.5 (C), 140.3 (CH).

***Z*-16:** ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.34 (q, *J* = 7.0 Hz, 2H), 3.73 (t, *J* = 7.0 Hz, 2H), 6.18 (t, *J* = 7.0 Hz, 1H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 39.2 (CH_2), 60.4 (CH_2), 75.7 (C), 137.3 (CH).

14) $(Me_3Si)_2CuCNLi_2$ was prepared by reaction of 2 equivalents of MeLi with 2.2 equivalents of $(Me_3Si)_2$ in THF/HMPA (5 mL:1 mL), and 1 equivalent of CuCN at -0°C. For preparation of Me_3SiLi see Lipshutz, B. H.; Sharma, S.; Reuter, D. C. *Tetrahedron Lett*. **1990**, *31*, 7253. Still, W. C. *J. Org. Chem*. **1976**, *41*, 3063.