Regioselective Hydrostannation of Highly Hindered Arylalkynes under Ortho Directing Effects

Abdallah Hamze, Patrick Le Menez, Olivier Provot, Estelle Morvan,
Jean-Daniel Brion, Mouad Alami

► To cite this version:

Abdallah Hamze, Patrick Le Menez, Olivier Provot, Estelle Morvan, Jean-Daniel Brion, et al.. Regioselective Hydrostannation of Highly Hindered Arylalkynes under Ortho Directing Effects. *Tetrahedron*, 2010, 66 (45), pp.8698-8706. 10.1016/j.tet.2010.09.010 . hal-02394476

HAL Id: hal-02394476

<https://hal.science/hal-02394476>

Submitted on 4 Dec 2019

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Graphical Abstract

To create your abstract, type over the instructions in the template box below.
Fonts or abstract dimensions should not be changed or altered.

Regioselective Hydrostannation of Highly Hindered Arylalkynes under Ortho Directing Effects

Leave this area blank for abstract info.

Abdallah Hamze, Patrick Le Menez, Olivier Provot, Estelle Morvan, Jean-Daniel Brion and Mouâd Alami
Univ Paris-Sud, CNRS, BioCIS, UMR 8076, Laboratoire de Chimie Thérapeutique, Faculté de Pharmacie, rue J.B. Clément F-92296 Châtenay-Malabry, France.

Regioselective Hydrostannation of Highly Hindered Arylalkynes under Ortho Directing Effects

Abdallah Hamze, Patrick Le Menez, Olivier Provot, Estelle Morvan, Jean-Daniel Brion and Mouâd Alami*

Univ Paris-Sud, CNRS, BioCIS, UMR 8076, Laboratoire de Chimie Thérapeutique, Faculté de Pharmacie, rue J.-B. Clément F-92296 Châtenay-Malabry, France.

Abstract

Palladium-catalyzed hydrostannation reactions of ortho-disubstituted arylalkynes were achieved with total stereo- and regioselectivity in THF at room temperature. The regioselectivity was found to be under the control of the ortho-substituents (ortho-directing effects, ODE) and pure α -vinyl stannanes are produced in good yields and as single isomers regardless of the substituents' nature. These hydrostannation α -products are precursors of choice for the preparation of stereodefined triarylolefins. © 2019 Elsevier Science. All rights reserved

Keywords: Alkynes, Palladium, *Ortho*-Directing Effects, Regioselectivity.

1. Introduction

Organostannanes, and particularly vinylstannanes are of increasing importance as synthetic intermediates in organic chemistry due to the large number of carbon-carbon bond forming reactions available to these substrates.¹ As a result of their synthetic utility, considerable effort has been expended toward their preparation² and the addition of tributyltin hydride to alkynes remains the most simple and straightforward route to these vinylstannanes intermediates.³ The challenge in the hydrostannation of unsymmetrical alkynes is to directly produce vinylstannanes of high purity with a total regio- and stereoselectivity because mixtures of vinyl stannanes are tedious to separate (destannylation, non polar isomers,...). For palladium-catalyzed hydrostannation of alkynes, control of stereoselectivity is not a problem since the addition of tributyltin hydride proceeds in a *syn* manner (*cis*-addition).^{2d,4} In contrast, the regiochemical control of this reaction appears to be dependent on steric,^{2d,4,5} electronic^{2d} and chelating^{2d,6} factors of the alkyne substituents. We previously described the regioselective palladium-catalyzed hydrostannation of conjugated alkynes. With (*Z*)-enyne⁷ and (*Z*)-enediynes⁸ substrates, the regioselectivity of the H-Sn bond addition was found to be totally controlled by the geometry of the double bond (*Z*-Directing Effect, ZDE) rather than the nature of its substituents (Cl, alkyl, aryl,...) to give exclusively α -vinylstannanes (Scheme 1). With ortho substituted internal⁹ and terminal¹⁰ arylalkyne derivatives, we demonstrated that an ortho substituent delivered the Bu₃Sn group on the carbon atom (C _{α}) whatever the electronic nature of the substituent, electron withdrawing or electron donating (e.g.; CO₂R, COR, OR, Cl...). This trend in α -regioselectivity was also observed with substrates having ortho nonchelating alkyl substituents (e.g.; CH₃, *i*Pr,...), clearly indicating that coordinating

factors were not at the origin of this remarkable regioselectivity (Scheme 1). The results have been rationalized in terms of electronic polarization across the alkyne bond, induced by the ortho substituent whatever its electronic nature.^{9b} Although at the moment, we did not succeed in correlating the α -selectivity observed with the triple bond polarization, this ortho-directing effect (ODE) has been successfully extended to control the regiochemistry of the platinum-catalyzed hydrosilylation of internal aliphatic arylalkynes as well as diarylalkynes.¹¹

Although it was clearly established that the regioselectivity of the Pd-catalyzed hydrostannation of aliphatic alkynes is very sensitive to the steric hindrance,^{2d,5a,5b} we showed previously in the case of internal ortho substituted diarylalkynes^{9b} that increasing steric hindrance of ortho substituent provides better α -regioselectivities (anti steric effects) as depicted in Scheme 2.

Table 1. Hydrostannation of highly hindered arylalkynes **1** under palladium catalysis.

Entry	Alkyne 1	α/β ratio ^a	Vinyl Stannane 2	Yield ^b (%)
1		1a 90/10		2a 94
2		1b 100/0		2b 86
3		1c 100/0		2c 90
4		1d 100/0		2d 65
5		1e 100/0		2e 71
6		1f 100/0		2f 55
7		1g 100/0		2g 70
8		1h 81/19		2h 86
9		1i 100/0		2i 88
10		1j 100/0		2j 98
11		1k 100/0		2k 98
12		1l 100/0		2l 48
13		1m 95/5		2m 97
14		1n 100/0		2n 81
15		1o 100/0 100/0		2o 91 ^c

^a Ratio was determined by ¹H NMR analysis.^b Yields were given for isolated products.^c 3.0 equiv. of Bu₃SnH were used.

These findings clearly highlighted the role of steric hindrance of substituent in directing the α -addition of the metals to the more hindered alkyne carbon atom (C_α). To the best of our knowledge there has been no systematic study on metal-catalyzed hydrometallation of highly hindered arylalkynes **1** having ortho/ortho' substituents. Herein, the results of these studies are reported using tributyltin hydride or triethylsilane in order to determine the impact of ortho/ortho' substituents of **1** on the α -regioselectivity.

1. Results and Discussion

At the beginning of this work, hindered ortho/ortho'-diarylalkynes **1** were prepared according to Sonogashira-Linstrumelle (SL) couplings¹² using $\text{PdCl}_2(\text{PPh}_3)_2$ (5 mol%), CuI (10 mol%), piperidine as the base in THF, in good to excellent yields. The hydrostannylation of diarylalkynes **1** was conducted under standard conditions using $\text{PdCl}_2(\text{PPh}_3)_2$ (5 mol%) and Bu_3SnH (1.3 equiv) in THF. The results of this study are summarized in Table 1. In order to establish a baseline regioselectivity control, 1-(2-methoxyphenyl)-2-phenylacetylene **1a** bearing a single ortho MeO substituent was evaluated. Under the above conditions, **1a** was hydrostannylated to give a diastereomeric mixture of non separable α and β vinylstannanes with an excellent but not total α -preference (entry 1, α -**1a**/ β -**2a**: 90/10). For comparison, by switching the MeO substituent from the ortho to the para position on the aromatic, an equimolar isomeric α -**2**/ β -**2** product distribution was obtained (data not shown). More interestingly, hydrostannylation of ortho-disubstituted arylalkyne **1b**, **1c** and **1d** bearing on the same aromatic nucleus two ortho electron-donating substituents was totally regioselective¹³ furnishing α -vinylstannanes **2b-d** in good yields (entries 2-4). As expected for electronic considerations, hydrostannylation of ortho/ortho' disubstituted diarylalkynes **1e-g**, bearing a para MeO substituent on the second aromatic nucleus, furnished vinylstannanes **2e-g**, again with a total α -regioselectivity (entries 5-7). The example depicted in entry 8 with "push-pull" diarylalkyne **1h** is particularly interesting. In this case, where ODE is opposed by a strong electronic effect (induced by the para-CN), the α -regioselectivity was less spectacular and β -vinylstannane was obtained as minor products together with α -adduct (entry 8, α -**2h**/ β -**2h**: 81/19). By replacing the ortho and ortho' electron-donating substituents with chlorine atoms, the α -regioselectivity is entirely governed by ODE rather than the *p*-CN induced polarization of the triple bond (entry 9). For substrate **1j-1l**, ODE and electronic factors cooperate to give α -substituted vinylstannanes **2j-l** exclusively in good yields (entries 10-12). We next tested the ortho-directing effect on the distribution products with arylalkynol **1m**. It was found that hydrostannylation of **1m** proceeded with an excellent α -regioselectivity in a nearly quantitative yield (entry 13, α -**2m**/ β -**2m**: 95/5). As it was observed for diarylalkynes **1b-g**,

1i-l, the hydrostannylation of arylalkynols **1m** and **1n** bearing two substituents on the ortho position was totally regioselective and produced α -vinyl stannanes **2m** and **2n** in good yields. The last example, described in entry 15 sums up this study. The two triple bonds of alkyne **1o** were successfully hydrostannylated with a total regioselectivity furnishing a single compound α,α -**2o** in an excellent isolated yield. In this case, if ortho substituents are at the origin of the α -regioselectivity observed for the hydrostannylation of the hindered alkyne, the exclusive α -stannylation of the alkynol moiety is not immediately clear.

The success of this ortho/ortho'-substituent regiocontrol prompted additional investigations with ortho-disubstituted terminal aryl alkynes. The results of this study are abstracted in Scheme 3. Hydrostannylation of electron-rich arylalkyne **1p** as well as electron deficient arylalkyne **1q** was achieved and again, a total regioselectivity was observed. In these cases, exclusive α -isomers **2p** and **2q** were produced in excellent yields (**2p**: 92%, **2q**: 98%).

Scheme 3 Hydrostannylation of terminal ortho/ortho' disubstituted arylalkynes **1p** and **1q**.

Reagents and conditions. (i) Bu_3SnH (1.3 equiv), $\text{PdCl}_2(\text{PPh}_3)_2$ (5 mol %), 20 °C, THF, 0.5 h.

Next, to examine the synthetic utility of α -vinylstannanes of type **2**, we first evaluated the Stille coupling of 4-iodoanisole with **2k** and **2o**. However, the coupling products **4a** and **4b** were not obtained in satisfactory yields. Therefore, a second synthetic approach involving an iododestannylation-Negishi sequence was explored (Scheme 4).¹⁴ Thus, stereospecific iodo-destannylation of **2k** and **2o** with molecular iodine (1 equiv) in CH_2Cl_2 at 20°C provided cleanly and rapidly the suitable electrophilic vinyl iodides **3a** and **3b** in quantitative yields. Further coupling with 4-methoxyarylzinc chloride in the presence of $\text{PdCl}_2(\text{PPh}_3)_2$ (5 mol%) furnished the triarylated ethylenic compounds **4a-b** with a total stereospecificity in good yields (Scheme 4).

Finally, we wanted to examine if this total α -selectivity could be successfully extended to the hydrosilylation of various ortho-disubstituted alkynes. Preliminary results are presented in Table 2. Reaction of ortho-disubstituted diarylalkyne **1b** with triethylsilane in THF in the presence of PtO_2 (5 mol%) at 70 °C for 1 h afforded regioselectively an inseparable 90/10 mixture of the vinylsilanes α -**3a** and α -**3b** in 90% yield (entry 1, Table 2). For comparison, the hydrosilylation of alkyne **1a** bearing a single MeO substituent on the ortho position, (baseline control)

afforded a mixture of α - and β -vinylsilanes but with a lower α -selectivity (α/β : 80/20).

Scheme 4 Iododestannylation of **2k** and **2o** followed by Negishi Cross-coupling reactions under palladium catalysis.

Reagents and conditions. (i) I_2 , CH_2Cl_2 . (ii) 4-MeOC₆H₄ZnCl, $PdCl_2(PPh_3)_2$ 5 mol %, THF.

A similar α -preference was also observed with alkyne **1e** bearing two MeO-substituents on the ortho and ortho' position (97%, entry 2). As previously observed for the hydrostannylation of **1j** (entry 10, Table 1), the hydrosilylation of **1j** bearing two chlorine atoms on the ortho positions was totally regioselective. Again, electronic factors, generated by the chlorine atoms, and ODE cooperate and the reaction produced a single α -vinylsilane **3c** in a nearly quantitative yield (98%, entry 3, Table 2).

Table 2 Hydrosilylation of ortho disubstituted arylalkynes **1**.

Entry	Alkyne 1	Selectivity α/β^a	Vinylsilane α -3	Yield ^b (%)
1	1b	90/10		90
2	1e	92/8		97
3	1j	100/0		98

^a Ratio was determined by 1H NMR analysis.

^b Yields were given for isolated products.

3. Conclusion

In summary, we demonstrated that hydrostannylation of hindered arylalkynes bearing on the same aromatic nucleus two ortho-substituents give exclusively the α -vinylstannanes in good yields whatever the electronic nature and steric hindrance of substituents. Moreover, preliminary results indicate that the PtO_2 -catalyzed hydrosilylation of these hindered alkynes was also highly regioselective. The factors governing this total α -selectivity would be close to those observed in the hydrostannylation or hydrosilylation of arylalkynes bearing on the ortho position a single substituent (ODE). This study shows that it is possible to predict the exclusive α -isomers formation even if the exact origin of this regioselectivity remains unclear. Interestingly, the products of the hydrostannylation reaction can be efficiently used as versatile substrates in iododestannylation-Negishi sequences to afford stereo-defined triarylelefins of therapeutic interest.¹⁵

4. Experimental

General comments

All glassware were oven-dried at 140°C and all reactions were conducted under a nitrogen atmosphere. Solvents: cyclohexane, ethyl acetate (EtOAc), for chromatography were technical grade. Diethylether (Et₂O) and tetrahydrofuran (THF) were distilled under argon from sodium-benzophenone ketyl, piperidine, triethylamine from potassium hydroxide. $PdCl_2(PPh_3)_2$ and Bu_3SnH ¹⁶ were prepared following literature procedure. All new compounds were characterized by 1H -NMR, ^{13}C -NMR, IR spectroscopy and elemental analysis. 1H and ^{13}C NMR spectra were measured in $CDCl_3$ with a Bruker ARX 400 or Bruker Avance 300. 1H chemical shifts are reported in ppm from an internal standard TMS or of residual chloroform (7.27 ppm). The following abbreviation are used: m (multiplet), s (singlet), br s (broad singlet), d (doublet), t (triplet), dd (doublet of doublet), q (quadruplet), sextet (sextuplet). ^{13}C chemical shifts are reported in ppm from the central peak of deuteriochloroform (77.14). IR spectra were measured on a Bruker Vector 22 spectrophotometer (neat, cm^{-1}). Elemental analyses were performed with a Perkin-Elmer 240 analyzer. Analytical TLC was performed on Merck precoated silica gel 60 F-254 plates. Merck silica gel 60 (230-400 mesh) was used for column chromatography. The plates were visualized by either UV light (254 nm), or by a solution of phosphomolybdic acid in ethanol. Melting points (m.p.) were recorded on a Büchi B-450 apparatus and were uncorrected.

General procedure for the synthesis of diarylalkynes **1** procedure for the synthesis of diarylalkynes (A)

To a flame-dried flask under a nitrogen atmosphere were added $PdCl_2(PPh_3)_2$ (120 mg, 0.17 mmol), CuI (76 mg, 0.4

mmol), aryl iodide (4.0 mmol), piperidine (1.2 mL, 12.0 mmol) in THF (12 mL). To this solution was added dropwise 1-alkyne (6.0 mmol). After stirring at room temperature for 12 h, the mixture was diluted in Et₂O (25 mL), and then washed with a saturated NH₄Cl solution (20 mL). After extraction with Et₂O (25 mL) the combined organic layers were dried over MgSO₄. After concentration under reduced pressure, the residue was purified by column chromatography over silica gel, to yield the desired ortho-disubstituted alkyne **1**.

1,3-Bis(benzyloxy)-2-(phenylethynyl)benzene (1c)

White solid, mp: 106-108 °C. (90 %). *R_f* = 0.23 (Et₂O/Cyclohexane, 5/95, SiO₂). ¹H NMR (CDCl₃, 300 MHz): δ 5.14 (4H, s), 6.54 (2H, d, *J* = 8.4 Hz), 7.11 (1H, t, *J* = 8.4 Hz), 7.15-7.54 (15H, m). ¹³C NMR (75 MHz, CDCl₃): δ_c 70.6 (2CH₂), 82.6 (C), 98.4 (C), 103.7 (C), 106.0 (2CH), 124.3 (C), 126.9 (4CH), 127.8 (2CH), 127.9 (CH), 128.3 (2CH), 128.5 (4CH), 129.6 (CH), 131.6 (2CH), 137.2 (2C), 160.6 (2C). IR (cm⁻¹, neat): 1582, 1474, 1446, 1375, 1261, 1116, 771, 732, 690. Anal. Calcd for C₂₈H₂₂O₂ (390.47): C 86.13, H 5.68, found C 85.91, H 5.70.

2-(Phenylethynyl)-1,3-phenylene diacetate (1d)

Brown solid, mp: 106-108 °C. (65 %). *R_f* = 0.40 (Et₂O/Cyclohexane, 30/70, SiO₂). ¹H NMR (CDCl₃, 300 MHz): δ 2.37 (6H, s), 7.06 (2H, d, *J* = 8.2 Hz), 7.40-7.32 (4H, m), 7.51-7.43 (2H, m). ¹³C NMR (75 MHz, CDCl₃): δ 20.9 (2CH₃), 79.7 (C), 98.8 (C), 112.5 (C), 119.9 (2CH), 122.7 (C), 128.5 (2CH), 128.9 (CH), 129.2 (CH), 131.5 (2CH), 152.3 (2C), 168.5 (2C). IR (cm⁻¹, neat): 1761, 1494, 1457, 1371, 1182, 1026, 882, 758, 690. Anal. Calcd for C₁₈H₁₄O₄ (294.30): C 73.46, H 4.79, found C 73.74, H 4.65.

1,3-Dimethoxy-2-((4-methoxyphenyl)ethynyl)benzene (1e)

Brown solid, mp: 142-144 °C. (71 %). *R_f* = 0.15 (Et₂O/Cyclohexane, 10/90, SiO₂). ¹H NMR (CDCl₃, 300 MHz): δ 3.82 (3H, s), 3.91 (6H, s), 6.56 (2H, d, *J* = 8.4 Hz), 6.86 (2H, d, *J* = 8.4 Hz), 7.24 (1H, t, *J* = 8.4 Hz), 7.53 (2H, d, *J* = 8.4 Hz). ¹³C NMR (75 MHz, CDCl₃): δ 55.3 (CH₃), 56.2 (2CH₃), 80.4 (C), 97.9 (C), 102.0 (C), 103.6 (2CH), 113.9 (2CH), 116.2 (C), 129.5 (CH), 133.2 (2CH), 159.4 (C), 161.3 (2C). IR (cm⁻¹, neat): 1579, 1513, 1472, 1252, 1103, 826, 778, 726. Anal. Calcd for C₁₇H₁₆O₃ (268.31): C 76.10, H 6.01, found C 76.25, H 5.84.

2-((4-Methoxyphenyl)ethynyl)-1,3-phenylene bis(oxy)bis(methylene)dibenzene (1f)

Brown solid, mp: 89-91 °C. (55 %). *R_f* = 0.20 (Et₂O/Cyclohexane, 5/95, SiO₂). ¹H NMR (CDCl₃, 300 MHz): δ 3.84 (3H, s), 5.21 (4H, s), 6.61 (2H, d, *J* = 8.3 Hz), 6.87 (2H, d, *J* = 8.8 Hz), 7.17 (1H, t, *J* = 8.3 Hz), 7.66-7.25 (12H, m). ¹³C NMR (75 MHz, CDCl₃): δ 55.4 (CH₃), 70.7 (2CH₂), 81.1 (C), 98.4 (C), 104.1 (C), 106.1 (2CH), 114.0 (2CH), 116.6 (C), 127.0 (4CH), 127.8 (2CH), 128.5 (4CH),

129.2 (CH), 133.0 (2CH), 137.3 (2C), 159.4 (C), 160.4 (2C). IR (cm⁻¹, neat): 1574, 1509, 1449, 1378, 1247, 1087, 1028, 830, 780, 727, 692. Anal. Calcd for C₂₉H₂₄O₃ (420.50): C 82.83, H 5.75, found C 82.72, H 5.64.

2-((4-Methoxyphenyl)ethynyl)-1,3-phenylene diacetate (1g)

(in this case TEA was used as base instead piperidine). Brown solid, mp: 117- 119 °C. (85 %). *R_f* = 0.45 (Et₂O/Cyclohexane, 30/70, SiO₂). ¹H NMR (CDCl₃, 300 MHz): δ 2.36 (6H, s), 3.83 (3H, s), 6.88 (2H, d, *J* = 8.8 Hz), 7.04 (2H, d, *J* = 8.0 Hz), 7.35 (1H, t, *J* = 8.0 Hz), 7.40 (2H, d, *J* = 8.8 Hz). ¹³C NMR (75 MHz, CDCl₃): δ 20.9 (2CH₃), 55.4 (CH₃), 78.4 (C), 99.0 (C), 112.8 (C), 114.2 (2CH), 114.8 (C), 119.9 (2CH), 128.8 (CH), 133.1 (2CH), 152.2 (2C), 160.2 (C), 168.6 (2C). IR (cm⁻¹, neat): 1756, 1515, 1458, 1374, 1190, 1029, 882, 836, 734. Anal. Calcd for C₁₉H₁₆O₅ (324.33): C 70.36, H 4.97, found C 70.01, H 4.75.

4-((2,6-Dimethoxyphenyl)ethynyl)benzonitrile (1h)

White solid, White solid, mp: 120-122 °C. (88 %). *R_f* = 0.20 (Et₂O/Cyclohexane, 5/95, SiO₂). NMR (CDCl₃, 300 MHz): δ 3.92 (6H, s), 6.57 (2H, d, *J* = 8.4 Hz), 7.27 (1H, t, *J* = 8.4 Hz), 7.60 (2H, d, *J* = 8.6 Hz), 7.65 (2H, d, *J* = 8.6 Hz). ¹³C NMR (75 MHz, CDCl₃): δ 56.2 (2CH₃), 87.0 (C), 96.2 (C), 100.7 (C), 103.6 (2CH), 111.0 (C), 118.8 (C), 129.1 (C), 130.9 (CH), 131.9 (2CH), 132.2 (2CH), 161.7 (2C). IR (cm⁻¹, neat): 2215, 1585, 1475, 1257, 1110, 834, 774, 725. Anal. Calcd for C₁₇H₁₃NO₂ (263.29): C 77.55, H 4.98, found C 77.13, H 4.70.

4-((2,6-Dichlorophenyl)ethynyl)benzonitrile (1i)

White solid, mp: 144-146 °C. (90 %). *R_f* = 0.32 (Et₂O/Cyclohexane, 5/95, SiO₂). NMR (CDCl₃, 300 MHz): δ 7.22 (1H, t, *J* = 8.8 Hz), 7.38 (2H, d, *J* = 8.8 Hz), 7.66 (2H, d, *J* = 8.7 Hz), 7.69 (2H, d, *J* = 8.7 Hz). NMR (75 MHz, CDCl₃): δ 87.5 (C), 97.7 (C), 112.3 (C), 118.5 (C), 122.5 (C), 127.5 (C), 127.8 (2CH), 130.0 (CH), 132.2 (2CH), 132.4 (2CH), 137.6 (2C). IR (cm⁻¹, neat): 2229, 1550, 1504, 1425, 1192, 834, 778, 718. Anal. Calcd for C₁₅H₇Cl₂N (272.13): C 66.20, H 2.59, found C 65.91, H 2.50.

1,3-dichloro-2-(phenylethynyl)benzene (1j)

White solid, mp: 56-58 °C. (75 %). *R_f* = 0.60 (Et₂O/Cyclohexane, 2/98, SiO₂). NMR (CDCl₃, 300 MHz): δ 6.95 (1H, dd, *J* = 7.5 Hz, *J* = 1.2 Hz), 7.10-7.23 (5H, m), 7.35-7.45 (2H, m). ¹³C NMR (75 MHz, CDCl₃): δ 83.6 (C), 100.0 (C), 122.7 (C), 123.5 (C), 127.6 (2CH), 128.5 (2CH), 129.0 (CH), 129.1 (CH), 132.0 (2CH), 137.3 (2C). IR (cm⁻¹, neat): 2220, 1553, 1493, 1443, 1428, 1189, 1101, 788, 766, 749, 716. Anal. Calcd for C₁₄H₈Cl₂ (247.12): C 68.04, H 3.26, found C 67.84, H 3.31.

1,3-Dichloro-2-((4-methoxyphenyl)ethynyl)benzene (1k)

White solid, mp: 71-73 °C. (53 %). *R_f* = 0.34 (Et₂O/Cyclohexane, 5/95, SiO₂). ¹H NMR (CDCl₃, 300 MHz): δ 3.77 (3H, s), 6.83 (2H, d, *J* = 8.8 Hz), 7.10 (1H, t,

$J = 8.1$ Hz), 7.26 (2H, d, $J = 8.1$ Hz), 7.50 (2H, d, $J = 8.8$ Hz). ^{13}C NMR (75 MHz, CDCl_3): δ 55.4 (CH_3), 82.6 (C), 100.3 (C), 114.2 (2CH), 114.8 (C), 123.7 (C), 127.6 (2CH), 128.6 (CH), 133.5 (2CH), 137.0 (2C), 160.3 (C). IR (cm^{-1} , neat): 2195, 1604, 1509, 1429, 1248, 1024, 830, 716. Anal. Calcd for $\text{C}_{15}\text{H}_{10}\text{Cl}_2\text{O}$ (277.15): C 65.01, H 3.64, found C 64.88, H 3.54.

1,3-Dibromo-5-fluoro-2-(phenylethynyl)benzene (11)

Brown oil. (55 %). $R_f = 0.60$ ($\text{Et}_2\text{O}/\text{Cyclohexane}$, 5/95, SiO_2). NMR (CDCl_3 , 300 MHz): δ 7.20-7.33 (3H, m), 7.42-7.48 (4H, m). ^{13}C NMR (75 MHz, CDCl_3): δ 73.9 (C), 81.5 (C), 103.7 (d, $J_{\text{C-F}} = 3.7$ Hz, C), 119.1 (d, $J_{\text{C-F}} = 24.0$ Hz, 2CH), 121.7 (C), 129.2 (2CH), 131.3 (d, $J_{\text{C-F}} = 10.0$ Hz, 2C), 131.6 (CH), 132.5 (2CH), 161.9 (d, $J_{\text{C-F}} = 255.0$ Hz, C). Anal. Calcd for $\text{C}_{14}\text{H}_7\text{Br}_2\text{F}$ (354.01): C 47.50, H 1.99, found C 47.02, H 1.98.

Methyl 2-(4-(6-hydroxyhex-1-ynyl)phenyl)ethynyl-3,4,5-trimethoxybenzoate (10) was prepared from methyl-2-iodo-3,4,5-trimethoxybenzoate and 6-(4-ethynyl phenyl)hex-5-yn-1-ol (in this case heating to 80 °C was necessary). Yellow solid, mp: 118-120 °C. (77 %). $R_f = 0.43$ ($\text{Et}_2\text{O}/\text{Cyclohexane}$, 50/50, SiO_2). NMR (CDCl_3 , 300 MHz): δ 1.63 (4H, m), 2.37 (2H, t, $J = 6.4$ Hz), 3.59 (2H, t, $J = 6.5$ Hz), 3.79 (3H, s), 3.83 (3H, s), 3.86 (3H, s), 3.92 (3H, s), 7.24 (1H, s), 7.35 (4H, m). ^{13}C NMR (75 MHz, CDCl_3): δ 19.3 (CH_2), 25.0 (CH_2), 31.8 (CH_2), 52.2 (CH_3), 56.1 (CH_3), 61.1 (CH_3), 61.3 (CH_3), 62.1 (CH_2), 80.7 (C), 85.2 (C), 92.1 (C), 97.1 (C), 109.8 (C), 112.1 (C), 122.8 (C), 123.9 (C), 127.6 (C), 131.2 (2CH), 131.4 (2CH), 145.7 (C), 153.0 (C), 155.2 (C), 166.1 (CO). IR (cm^{-1} , neat): 3058, 2937, 1728, 1338, 1115. Anal. Calcd for $\text{C}_{25}\text{H}_{26}\text{O}_6$ (422.47): C 71.07, H 6.20, found C 69.95, H 6.32.

General procedure for the hydrostannation of alkynes (B).

Tributyltin hydride (11 mmol) was added dropwise at room temperature to a solution of $\text{PdCl}_2(\text{PPh}_3)_2$ (0.1 mmol) and alkyne **1** (10 mmol) in THF (15 mL). The dark brown reaction mixture was stirred for 30 minutes and tributyltin hydride (2 mmol) was added more on the crude mixture to complete the hydrostannation reaction. After stirring for 30 additional minutes, the solution was concentrated in vacuo. Purification by flash chromatography on silica gel gave the desired products.

Hydrostannation of 1b

(E)-Tributyl(1-(2,6-dimethoxyphenyl)-2-phenylvinyl)stannane (2b)

Colorless oil (86%). $R_f = 0.75$ ($\text{Et}_2\text{O}/\text{Cyclohexane}$, 1/9 TEA 1%, SiO_2). ^1H NMR (CDCl_3 , 300 MHz): δ 0.73-0.83 (15H, m), 1.20 (6H, sextet, $J = 7.2$ Hz), 1.32-1.44 (6H, m), 3.57 (6H, s), 6.43 (2H, d, $J = 8.3$ Hz), 6.64 (1H, s, $J_{\text{Sn-H}} = 67.0$ Hz), 6.91-7.11 (6H, m). ^{13}C NMR (75 MHz, CDCl_3): δ 10.6 (3 CH_2), 13.9 (3 CH_3), 27.5 (3 CH_2), 29.1 (3 CH_2), 55.7

(2 CH_3), 104.0 (2CH), 122.4 (C), 126.4 (CH), 126.5 (CH), 127.9 (2CH), 128.1 (2CH), 139.2 (C), 139.4 (CH), 141.6 (C), 155.4 (2C). IR (cm^{-1} , neat): 2954, 2925, 2870, 2852, 1579, 1494, 1467, 1431, 1375, 1282, 1245, 1171, 1110, 1074, 961, 921, 865, 778, 756, 713. Anal. Calcd for $\text{C}_{28}\text{H}_{42}\text{O}_2\text{Sn}$ (529.34): C 63.53, H 8.00, found C 63.41, H 8.05.

Hydrostannation of 1c

(E)-1-(2,6-Bis(benzyloxy)phenyl)-2-phenylvinyltributylstannane (2c)

Colorless oil (90%). $R_f = 0.56$ ($\text{Et}_2\text{O}/\text{Cyclohexane}$, 5/95 TEA 1%, SiO_2). ^1H NMR (CDCl_3 , 300 MHz): δ 0.54-0.91 (15H, m), 1.10 (6H, sextet, $J = 7.4$ Hz), 1.21-1.41 (6H, m), 4.82 (2H, d, $J = 12.4$ Hz), 4.86 (2H, d, $J = 12.4$ Hz), 6.43 (2H, d, $J = 8.3$ Hz), 6.70 (1H, s, $J_{\text{Sn-H}} = 68.0$ Hz), 6.85-7.25 (16H, m). NMR (75 MHz, CDCl_3): δ 10.7 (3 CH_2), 13.8 (3 CH_3), 27.5 (3 CH_2), 29.0 (3 CH_2), 70.1 (2 CH_2), 105.6 (2CH), 123.5 (C), 126.3 (CH), 126.4 (CH), 127.0 (4CH), 127.5 (2CH), 128.0 (2CH), 128.2 (2CH), 128.3 (4CH), 137.7 (2C), 139.3 (C), 139.5 (1CH), 142.0 (C), 154.5 (2C). IR (cm^{-1} , neat): 2954, 2921, 2870, 2852, 1580, 1496, 1449, 1418, 1377, 1246, 1229, 1201, 1177, 1155, 1096, 1074, 1029, 961, 922, 864, 843, 733, 693. Anal. Calcd for $\text{C}_{40}\text{H}_{50}\text{O}_2\text{Sn}$ (681.53): C 70.49, H 7.39, found C 70.10 H 7.50.

Hydrostannation of 1d

(E)-2-(2-Phenyl-1-(tributylstannyl)vinyl)-1,3-phenylene diacetate (2d)

Colorless oil (65%); $R_f = 0.60$ ($\text{Et}_2\text{O}/\text{Cyclohexane}$, 3/7 TEA 1%, SiO_2). ^1H NMR (CDCl_3 , 300 MHz): δ 0.63-1.10 (15H, m), 1.23 (6H, sextet, $J = 7.4$ Hz), 1.33-1.58 (6H, m), 2.02 (6H, s), 6.66 (1H, s, $J_{\text{Sn-H}} = 61.4$ Hz), 6.87 (2H, d, $J = 8.0$ Hz), 6.98-7.21 (6H, m). ^{13}C NMR (75 MHz, CDCl_3): δ 11.3 (3 CH_2), 13.8 (3 CH_3), 21.0 (2 CH_3), 27.6 (3 CH_2), 29.0 (3 CH_2), 120.3 (2CH), 126.2 (CH), 127.4 (CH), 128.2 (2CH), 128.3 (2CH), 131.8 (C), 137.6 (C), 139.3 (C), 142.0 (1CH), 146.9 (2C), 168.8 (2CO). IR (cm^{-1} , neat): 2956, 2921, 2851, 1767, 1493, 1455, 1366, 1184, 1156, 1074, 1025, 985, 962, 926, 881, 867. Anal. Calcd for $\text{C}_{30}\text{H}_{42}\text{O}_4\text{Sn}$ (585.36): C 61.56, H 7.23, found C 61.74, H 7.48.

Hydrostannation of 1e

(E)-Tributyl(1-(2,6-dimethoxyphenyl)-2-(4-methoxyphenyl)vinyl)stannane (2e)

Colorless oil (71%). $R_f = 0.14$ ($\text{Et}_2\text{O}/\text{Cyclohexane}$, 2/98 TEA 1%, SiO_2). ^1H NMR (CDCl_3 , 300 MHz): δ 0.66-0.92 (15H, m), 1.20 (6H, sextet, $J = 7.3$ Hz), 1.30-1.44 (6H, m), 3.57 (6H, s), 3.65 (3H, s), 6.44 (2H, d, $J = 8.3$ Hz), 6.52-6.67 (3H, m), 6.93 (2H, d, $J = 8.8$ Hz), 7.05 (1H, t, $J = 8.3$ Hz). ^{13}C NMR (75 MHz, CDCl_3): δ 10.6 (3 CH_2), 13.9 (3 CH_3), 27.5 (3 CH_2), 29.1 (3 CH_2), 55.3 (CH_3), 55.7 (2 CH_3), 104.1 (2CH), 113.3 (2CH), 126.4 (CH), 129.4 (2CH), 132.3 (C), 138.6 (CH), 138.8 (C), 155.5 (2C), 158.2

(C), 177.1 (C). IR (cm⁻¹, neat): 2994, 2954, 2927, 2870, 2835, 1604, 1582, 1508, 1466, 1431, 1375, 1292, 1244, 1175 1109, 1036, 960, 896, 874, 823, 805, 781, 760, 732. Anal. Calcd for C₂₉H₄₄O₃Sn (559.37): C 62.27, H 7.93, found C 62.00, H 8.18.

Hydrostannation of **1f**

(*E*)-(1-(2,6-Bis(benzyloxy)phenyl)-2-(4-methoxyphenyl)-vinyl)tributylstannane (**2f**)

Colorless oil (55%). R_f = 0.37 (Et₂O/Cyclohexane, 5/95 TEA 1%, SiO₂). ¹H NMR (CDCl₃, 300 MHz): δ 0.70-0.92 (15H, m), 1.18 (6H, sextet, *J* = 7.3 Hz), 1.29-1.49 (6H, m), 3.75 (3H, s), 4.94 (2H, d, *J* = 12.7 Hz), 4.98 (2H, d, *J* = 12.7 Hz), 6.53 (2H, d, *J* = 8.3 Hz), 6.67 (2H, d, *J* = 8.6 Hz), 6.73 (1H, s, *J*_{Sn-H} = 67.0 Hz), 6.97-7.10 (3H, m), 7.17-7.38 (10H, m). ¹³C NMR (75 MHz, CDCl₃): δ_c 10.6 (3CH₂), 13.8 (3CH₃), 27.5 (3CH₂), 29.0 (3CH₂), 55.2 (CH₃), 70.1 (2CH₂), 105.8 (2CH), 113.4 (2CH), 123.8 (C), 126.2 (CH), 127.0 (4CH), 127.4 (2CH), 128.3 (4CH), 129.4 (2CH), 132.5 (C), 137.8 (2C), 138.8 (CH), 139.3 (C), 154.7 (2C), 158.2 (C). IR (cm⁻¹, neat): 2953, 2929, 2869, 2852, 2836, 1604, 1582, 1508, 1464 1449, 1417, 1377, 1291, 1245, 1226, 1201, 1175, 1110, 1095, 1072, 1031, 959, 935, 901, 877, 862, 823, 784, 766. Anal. Calcd for C₄₁H₅₂O₃Sn (711.56): C 69.21, H 7.37, found C 69.36, H 7.20.

Hydrostannation of **1g**

(*E*)-2-(2-(4-Methoxyphenyl)-1-(tributylstannyl)vinyl)-1,3-phenylene diacetate (**2g**)

Colorless oil (70%). R_f = 0.52 (Et₂O/Cyclohexane, 30/70 TEA 1%, SiO₂). ¹H NMR (CDCl₃, 300 MHz): δ 0.64-1.00 (15H, m), 1.22 (6H, sextet, *J* = 7.3 Hz), 1.34-1.49 (6H, m), 2.02 (6H, s), 3.65 (3H, s), 6.58 (1H, s, *J*_{Sn-H} = 62.0 Hz), 6.61 (2H, d, *J* = 8.8 Hz), 6.88 (2H, d, *J* = 8.1 Hz), 6.96 (2H, d, *J* = 8.8 Hz), 7.13 (1H, t, *J* = 8.1 Hz). ¹³C NMR (75 MHz, CDCl₃): δ 11.3 (3CH₂), 13.8 (3CH₃), 21.0 (2CH₃), 27.6 (3CH₂), 29.0 (3CH₂), 55.2 (CH₃), 113.5 (2CH), 120.3 (2CH), 126.0 (CH), 129.7 (2CH), 130.6 (C), 132.1 (C), 136.2 (C), 141.3 (CH), 147.2 (2C), 158.9 (C), 168.9 (2CO). IR (cm⁻¹, neat): 2955, 2929, 1767, 1604, 1509, 1454 1419, 1367, 1293, 1250, 1191, 1177, 1157, 1113, 1074, 1026, 985, 959, 908, 878, 825, 802, 781. Anal. Calcd for C₃₁H₄₄O₅Sn (615.39): C 60.50, H 7.21, found C 60.24, H 7.18.

Hydrostannation of **1h**

(*E*)-4-(2-(2,6-dimethoxyphenyl)-2-(tributylstannyl)vinyl) benzonitrile (**2l**) (major α-isomer)

Colorless oil (86%). R_f = 0.59 (Et₂O/Cyclohexane, 30/70 TEA 1%, SiO₂). ¹H NMR (CDCl₃, 300 MHz): δ 0.73-1.01 (15H, m), 1.27 (6H, sextet, *J* = 7.4 Hz), 1.37-1.53 (6H, m), 3.61 (6H, s), 6.50 (2H, d, *J* = 8.4 Hz), 6.72 (1H, s, ³*J*_{Sn-H} = 66.0 Hz), 7.05-7.20 (3H, m), 7.37 (2H, d, *J* = 8.4 Hz). ¹³C NMR (75 MHz, CDCl₃): δ 10.7 (3CH₂), 13.9 (3CH₃), 27.5 (3CH₂), 29.0 (3CH₂), 55.6 (2CH₃), 103.9 (2CH), 109.4 (C), 119.5 (CN), 121.2 (C), 127.3 (CH), 128.4 (2CH), 131.8

(2CH), 137.6 (CH), 143.5 (C), 147.8 (C), 155.0 (2C). IR (cm⁻¹, neat): 2957, 2925, 2893, 2870, 2853, 2836, 2226, 1730, 1714, 1600, 1582, 1494, 1468, 1431, 1376, 1290, 1246, 1208, 1173, 1155, 1111, 1075, 1039, 960, 901, 879, 862, 840, 820, 781, 757. Anal. Calcd for C₂₉H₄₁NO₂Sn (554.35): C 62.83, H 7.45, found C 62.75, H 7.27.

Hydrostannation of **1i**

(*E*)-4-(2-(2,6-Dichlorophenyl)-2-(tributylstannyl)vinyl) benzonitrile (**2i**)

Colorless oil (88%). R_f = 0.50 (Et₂O/Cyclohexane, 5/95 TEA 1%, SiO₂). ¹H NMR (CDCl₃, 300 MHz): δ 0.79 (9H, t, *J* = 7.3 Hz), 0.86-1.00 (6H, m), 1.21 (6H, sextet, *J* = 7.3 Hz), 1.33-1.48 (6H, m), 6.73 (1H, s, *J*_{Sn-H} = 57.0 Hz), 6.92-7.08 (3H, m), 7.21 (2H, d, *J* = 8.0 Hz), 7.36 (2H, d, *J* = 8.4 Hz). ¹³C NMR (75 MHz, CDCl₃): δ 11.5 (3CH₂), 13.7 (3CH₃), 27.4 (3CH₂), 28.8 (3CH₂), 110.5 (C), 119.1 (CN), 127.3 (CH), 128.2 (2CH), 128.4 (2CH), 131.4 (2C), 132.2 (2CH), 138.5 (CH), 141.8 (C), 142.2 (C), 150.5 (C). IR (cm⁻¹, neat): 2955, 2930, 2871, 2851, 2227, 1602, 1553, 1502, 1462, 1426, 1405, 1377, 1339, 1253, 1187, 1148, 1088, 1071, 1017, 961, 903, 876, 824, 777, 729. Anal. Calcd for C₂₇H₃₅Cl₂NSn (563.19): C 57.58, H 6.26, found C 57.41, H 6.03.

Hydrostannation of **1j**

(*E*)-Tributyl (1-(2,6-dichlorophenyl)-2-phenylvinyl) stannane (**2j**)

Colorless oil (98%). R_f = 0.64 (Et₂O/Cyclohexane, 2/98 TEA 1%, SiO₂). ¹H NMR (CDCl₃, 300 MHz): δ 0.79 (9H, t, *J* = 7.3 Hz), 0.85-1.01 (6H, m), 1.21 (6H, sextet, *J* = 7.3 Hz), 1.32-1.47 (6H, m), 6.70 (1H, s, *J*_{Sn-H} = 60.8 Hz), 6.88-7.14 (6H, m), 7.21 (2H, d, *J* = 7.9 Hz). ¹³C NMR (75 MHz, CDCl₃): δ 11.3 (3CH₂), 13.8 (3CH₃), 27.5 (3CH₂), 28.9 (3CH₂), 126.8 (CH), 127.3 (CH), 127.9 (2CH), 128.0 (2CH), 128.3 (2CH), 131.8 (2C), 138.0 (C), 140.3 (1CH), 142.8 (C), 144.8 (C). IR (cm⁻¹, neat): 2955, 2923, 2870, 2851, 1553, 1493, 1463, 1425, 1376, 1254, 1191, 1148, 1088, 1073, 1047, 1028, 1001, 960, 921, 893, 874, 774. Anal. Calcd for C₂₆H₃₆Cl₂Sn (538.18): C 58.02, H 6.74, found C 58.37, H 6.77.

Hydrostannation of **1k**

(*E*)-Tributyl(1-(2,6-dichlorophenyl)-2-(4-methoxyphenyl)-vinyl)stannane (**2k**)

Colorless oil (98%). R_f = 0.43 (Et₂O/Cyclohexane, 5/95 TEA 1%, SiO₂). ¹H NMR (CDCl₃, 300 MHz): δ 0.80 (9H, t, *J* = 7.3 Hz), 0.84-0.95 (6H, m), 1.20 (6H, sextet, *J* = 7.3 Hz), 1.33-1.53 (6H, m), 6.60 (2H, d, *J* = 8.8 Hz), 3.66 (3H, s), 6.62 (1H, s, *J*_{Sn-H} = 62.10 Hz), 6.84 (2H, d, *J* = 8.8 Hz), 6.95 (1H, t, *J* = 8.3 Hz), 7.21 (2H, d, *J* = 8.0 Hz). ¹³C NMR (75 MHz, CDCl₃): δ 11.3 (3CH₂), 13.8 (3CH₃), 27.5 (3CH₂), 28.9 (3CH₂), 55.3 (1CH₃), 113.8 (2CH), 126.7 (CH), 128.0 (2CH), 129.4 (2CH), 131.0 (C), 132.1 (2C), 139.7 (CH), 142.0 (C), 142.9 (C), 158.8 (C). IR (cm⁻¹, neat): 2955, 2925, 2870, 2852, 1603, 1552, 1508, 1462,

1426, 1376, 1340, 1292, 1249, 1176, 1148, 1112, 1088, 1072, 1036, 960, 879, 823. Anal. Calcd for $C_{27}H_{38}Cl_2OSn$ (568.21): C 57.07, H 6.74, found C 57.22, H 6.38.

Hydrostannation of **1l**

(E)-Tributyl(1-(2,6-dibromo-4-fluorophenyl)-2-phenylvinyl) stannane (2l)

Colorless oil (48%). $R_f = 0.50$ (Et₂O/Cyclohexane, 2/98 TEA 1%, SiO₂). ¹H NMR (CDCl₃, 300 MHz): δ 0.54-0.86 (15H, m), 1.08-1.42 (12H, m), 6.29 (1H, s, $J_{Sn-H} = 66.0$ Hz), 7.05-7.10 (1H, m), 7.18 (2H, t, $J = 6.9$ Hz), 7.29 (2H, d, $J = 7.6$ Hz), 7.37 (2H, m). ¹³C NMR (75 MHz, CDCl₃): δ 11.0 (3CH₂), 13.7 (3CH₃), 27.5 (3CH₂), 29.0 (3CH₂), 103.7 (d, $J_{C-F} = 5.0$ Hz, C), 119.1 (d, $J_{C-F} = 24.0$ Hz, 2CH), 126.4 (C), 128.1 (2CH), 128.2 (2CH), 131.3 (d, $J_{C-F} = 10.0$ Hz, 2C), 131.6 (CH), 140.1 (1C), 154.2 (CH), 161.9 (d, $^1J_{C-F} = 255.0$ Hz, C). Anal. Calcd for $C_{26}H_{35}Br_2FSn$ (645.07): C 48.41, H 5.47, found C 48.60, H 5.33.

Hydrostannation of **1n**

(E)-3-Mesityl-3-(tributylstannyl)prop-2-en-1-ol (2n)

Colorless oil (81%). $R_f = 0.41$ (AcOEt/Cyclohexane, 5/95 TEA 1%, SiO₂). ¹H NMR (CDCl₃, 300 MHz): δ 0.78-0.86 (9H, m), 1.16-1.44 (19H, m), 2.05 (6H, s), 2.23 (3H, s), 3.87 (2H, s), 5.98 (1H, t, $J = 5.6$ Hz, $J_{Sn-H} = 63.0$ Hz), 6.78 (2H, s). ¹³C NMR (75 MHz, CDCl₃): δ 10.9 (3CH₂), 14.1 (3CH₃), 20.9 (2CH₃), 21.3 (CH₃), 27.8 (3CH₂), 29.2 (3CH₂), 61.8 (CH₂), 128.4 (2CH), 132.8 (C), 134.8 (C), 139.7 (C), 139.8 (2C), 148.4 (CH). IR (cm⁻¹, neat): 3340, 2950, 2930, 2840, 1460, 1370, 1010. Anal. Calcd for $C_{24}H_{42}OSn$ (465.30): C 61.95, H 9.10, found C 62.21, H 8.98.

Hydrostannation of **1o**

Methyl-2-((E)-2-(4-((E)-6-hydroxy-1-(tributyl stannyl)hex-1-enyl)phenyl)-1-(tributylstannyl)vinyl)-3,4,5 trimethoxybenzoate (2o)

Yellow oil (91 %). $R_f = 0.28$ (AcOEt/Cyclohexane, 30/70 TEA 1%, SiO₂). ¹H NMR (CDCl₃, 300 MHz): δ 0.35 (30H, m), 1.23 (14H, m), 1.43 (14H, m), 1.97 (2H, q, $J = 7.0$ Hz), 3.48 (2H, dd, $J = 5.5$ Hz), 3.57 (3H, s), 3.65 (3H, s), 3.89 (3H, s), 3.90 (3H, s), 5.66 (1H, t, $J = 7.0$ Hz, $^3J_{Sn-H} = 62.0$ Hz), 6.61 (1H, s, $J_{Sn-H} = 66.0$ Hz), 6.64 (2H, d, $J = 8.2$ Hz), 6.81 (2H, d, $J = 8.2$ Hz), 7.23 (1H, s). ¹³C NMR (75 MHz, CDCl₃): δ 10.9 (6CH₂), 13.6 (6CH₃), 25.7 (CH₂), 26.9 (CH₂), 27.2 (6CH₂), 28.9 (6 CH₂), 31.9 (CH₂), 51.7 (CH₃), 55.9 (CH₃), 60.6 (CH₃), 60.7 (CH₃), 62.4 (CH₂), 109.7 (CH), 122.5 (C), 126.7 (2CH), 127.9 (2CH), 134.7 (C), 135.4 (C), 137.2 (CH), 141.6 (CH), 143.4 (C), 144.8 (C), 145.3 (C), 146.1 (C), 148.9 (C), 150.8 (C), 167.7 (C). IR (cm⁻¹, neat): 2961, 2849, 1721, 1589, 1291, 1061. Anal. Calcd for $C_{49}H_{82}O_6Sn_2$ (1004.59): C 58.58, H 8.23, found C 58.39, H 8.50.

Hydrostannation of **1p**

Tributyl(1-(2,6-dimethoxyphenyl)vinyl)stannane (2p)

Colorless oil (92 %). $R_f = 0.70$ (AcOEt/Cyclohexane, 5/95 TEA 1%, SiO₂). ¹H NMR (300 MHz, CDCl₃) δ 0.93-0.74 (15H, m), 1.62-1.09 (12H, m), 3.75 (6H, s), 5.63 (1H, d, $J = 3.3$ Hz, $J_{H-Sn} = 64.3$ Hz), 5.89 (1H, d, $J = 3.3$ Hz, $J_{H-Sn} = 137.0$ Hz), 6.52 (2H, t, $J = 8.5$ Hz), 7.08 (1H, t, $J = 8.5$ Hz). ¹³C NMR (75 MHz, CDCl₃) δ 10.6 (3CH₂), 13.9 (3CH₃), 27.5 (3CH₂), 29.1 (3CH₂), 55.80 (2CH₃), 103.9 (2CH), 124.2 (C), 126.4 (CH), 129.0 (2C), 147.4 (C), 156.0 (C). IR (cm⁻¹, neat): 2957, 2928, 2870, 1585, 1468, 1433, 1247, 1115. Anal. Calcd for $C_{22}H_{38}O_2Sn$ (453.25): C 58.30, H 8.45, found C 58.34, H 8.42.

Hydrostannation of **1q**

Tributyl(1-(2,6-dichlorophenyl)vinyl)stannane (2q)

Colorless oil (98 %). $R_f = 0.8$ (Cyclohexane, TEA 1%, SiO₂). ¹H NMR (300 MHz, CDCl₃) δ 1.03-0.74 (15H, m), 1.52-1.15 (12H, m), 5.69 (1H, d, $J = 2.5$ Hz), 5.79 (1H, d, $J = 2.5$ Hz), 7.01 (1H, t, $J = 8.0$ Hz), 7.39-7.17 (2H, m). ¹³C NMR (75 MHz, CDCl₃) δ 11.3 (3CH₂), 13.8 (3CH₃), 27.4 (3CH₂), 28.9 (3CH₂), 126.8 (CH), 127.8 (2CH), 130.1 (2C), 132.2 (C), 152.2 (C). IR (cm⁻¹, neat): 2955, 2922, 1555, 1425, 1192, 1075, 930, 774, 743, 688. Anal. Calcd for $C_{20}H_{32}Cl_2Sn$ (462.08): C 51.98, H 6.98, found C 51.95, H 6.94.

Typical Procedure for Iodination of *Ortho-Ortho'* Vinylstannes (C).

To a flame-dried flask under a nitrogen atmosphere were added at 0°C vinyl stannane **2k** (1 equiv.), dry CH₂Cl₂ (2 mL per mmol of substrate), sublimed finely divided I₂ (1.05 equiv.) and the dark wine solution was vigorously stirred at room temperature until all of the substrate had been consumed (TLC). Saturated aqueous Na₂S₂O₃ was added to remove the excess of iodine followed by addition of a potassium fluoride aqueous solution. After stirring at room temperature for 1 h, the resulting white precipitate of tributyltin fluoride was removed by filtration and the filtrate was extracted with ether. The combined organic layers were washed with brine, dried over MgSO₄ and concentrated (the crude vinyl iodide could be used in the further step without purification).

(E)-1,3-Dichloro-2-(1-iodo-2-(4-methoxyphenyl)vinyl) benzene (3a)

Colorless oil (yield = 98% after filtration through silica gel); $R_f = 0.50$ (Et₂O/Cyclohexane, 5/95 TEA 1%, SiO₂); ¹H NMR (300 MHz, CDCl₃): δ 3.65 (3H, s), 6.61 (2H, d, $J = 8.8$ Hz), 6.75 (2H, d, $J = 8.8$ Hz), 7.15 (1H, t, $J = 8.8$ Hz), 7.28 (2H, d, $J = 8.5$ Hz), 7.39 (s, 1H). ¹³C NMR (75 MHz, CDCl₃) δ 55.3 (CH₃), 86.5 (C), 114.0 (2CH), 128.7 (2CH), 129.1 (C), 129.6 (2CH), 130.0 (CH), 134.2 (2C), 139.6 (C), 143.9 (CH), 159.5 (C). IR (cm⁻¹, neat): 3077, 2955, 2837, 1602, 1574, 1554, 1509, 1459, 1428, 1355, 1308, 1294, 1260, 1179, 1169, 1151, 1114, 1092, 1034, 951, 935, 891, 878, 816, 780, 739, 679.

Methyl 2-((E)-2-(4-((E)-6-hydroxy-1-iodohex-1-enyl)phenyl)-1-iodovinyl)-3,4,5-trimethoxybenzoate (3b)

Following the above general procedure (C), using vinylstannane **2o** (1.3 g, 1.29 mmol), DCM (40 mL) as solvent, I₂ solution (2.2 eq., 723 mg, 2.85 mmol) in DCM (40 mL). The reaction was stirred at -40 °C for 4 h in the dark.

Yellow oil (yield = 98 % after filtration through silica gel); R_f = 0.37 (AcOEt/Cyclohexane, 20/80 TEA 1%, SiO₂); ¹H NMR (300 MHz, CDCl₃): δ 1.21 (4H, m), 1.76 (2H, q, *J* = 7.4 Hz), 3.35 (2H, t, *J* = 5.7 Hz), 3.61 (3H, s), 3.67 (3H, s), 3.69 (3H, s), 3.78 (3H, s), 6.21 (1H, t, *J* = 7.4 Hz), 6.62 (2H, d, *J* = 8.6 Hz), 6.85 (2H, d, *J* = 8.7 Hz), 7.14 (1H, s), 7.29 (1H, s). ¹³C NMR (75 MHz, CDCl₃): δ 18.9 (CH₂), 32.6 (2CH₂), 46.1 (CH₂), 51.3 (CH₃), 55.6 (CH₃), 59.9 (CH₃), 60.1 (CH₃), 60.2 (CH₂), 91.6 (C), 94.3 (C), 108.7 (CH), 123.9 (2 CH), 127.4 (C), 128.5 (C), 131.2 (2 CH), 136.8 (CH), 140.5 (CH), 145.9 (C), 150.1 (C), 153.2 (2C), 170.9 (C=O). IR (cm⁻¹, neat): 3406, 2937, 2857, 1725, 1585, 1489, 1451, 1431, 1393, 1333, 1255, 1223, 1194, 1171, 1116, 1052, 755.

Typical Procedure for Negishi coupling between Ortho-Ortho' vinyl iodide and organozinc compounds (D).

To a solution of vinyl iodide **2**, PdCl₂(PPh₃)₂ (5 mol%) in THF was added at room temperature ArZnCl (2 equiv.) prepared by transmetallation from the corresponding Grignard reagent (2 equiv.) and anhydrous ZnCl₂ (2.1 equiv.). The reaction was stirred at room temperature and monitored by TLC until complete consumption of starting materials (2 to 4 h). The reaction was hydrolyzed at 0°C with aqueous HCl (1N), extracted with Et₂O, the organic extract was dried over MgSO₄ and the solvent was removed in vacuo.

(Z)-4,4'-(1-(2,6-Dichlorophenyl)ethene-1,2-diyl)bis(methoxybenzene) (4a)

colorless oil (yield = 73%); R_f = 0.29 (Et₂O/Cyclohexane, 5/95, SiO₂); ¹H NMR (300 MHz, CDCl₃): δ 3.66 (3H, s), 3.73 (3H, s), 6.63 (2H, d, *J* = 8.9 Hz), 6.79 (2H, d, *J* = 8.9 Hz), 6.84 (2H, d, *J* = 8.9 Hz), 6.99 (1H, s), 7.22-7.11 (3H, m), 7.31 (2H, d, *J* = 7.7 Hz). ¹³C NMR (75 MHz, CDCl₃): δ 55.3 (CH₃), 55.4 (CH₃), 113.8 (2CH), 114.1 (2CH), 127.2 (2CH), 128.6 (2CH), 128.6 (CH), 129.4 (CH), 129.7 (2CH), 129.8 (C), 132.8 (C), 133.9 (C), 135.7 (2C), 138.4 (C), 158.8 (C), 159.2 (C). IR (cm⁻¹, neat): 3001, 2955, 2932, 2900, 1606, 1573, 1555, 1511, 1462, 1441, 1427, 1366, 1302, 1288, 1256, 1241, 1175, 1153, 1113, 1090, 1031, 908, 850, 827, 783, 767, 754, 681. Anal. Calcd for C₂₂H₁₈Cl₂O₂ (385.28): C 68.58, H 4.71, found C 68.62, H 4.54.

Methyl 2-((Z)-2-(4-((E)-6-hydroxy-1-(4-methoxyphenyl)hex-1-enyl)phenyl)-1-(4-methoxyphenyl)vinyl)-3,4,5-trimethoxybenzoate (4b)

Following the above general procedure (D), using bromo (4-methoxyphenyl)zinc (6 eq.) in THF, PdCl₂(PPh₃)₂ (5 %)

and **3l** (1 eq.). The reaction was stirred at room temperature for 2 h in the dark.

Yellow oil (yield = 61 %); R_f = 0.10 (AcOEt/Cyclohexane, 30/70, SiO₂); ¹H NMR (400 MHz, CDCl₃): δ 1.44 (4H, m), 1.62 (2H, m), 2.01 (1H, brs, OH), 3.71 (2H, m), 3.76 (6H, s), 3.81 (3H, s), 3.91 (3H, s), 3.94 (3H, s), 3.97 (3H, s), 6.08 (1H, t, *J* = 7.8 Hz), 6.87-6.91 (12H, m), 7.12 (1H, s), 7.23 (1H, s). ¹³C NMR (100 MHz, CDCl₃): δ 25.9 (CH₂), 29.1 (CH₂), 31.9 (CH₂), 51.1 (CH₃), 59.9 (CH₃), 60.5 (CH₃), 60.7 (CH₃), 62.3 (CH₂), 109.4 (CH), 113.3 (2CH), 113.5 (2CH), 127.8 (2 CH), 127.5 (2 CH), 128.1 (2C), 129.4 (C), 135.3 (2CH), 135.5 (2CH), 135.8 (C), 136.4 (2C), 136.7 (C), 138.5 (C), 139.0 (CH), 140.9 (CH), 152.6 (C), 158.6 (2C), 158.8 (2C), 167.3 (C=O). IR (cm⁻¹, neat): 2940, 2250, 1726, 1510, 1335, 1115, 910, 730; Anal. Calcd for C₃₉H₄₂O₈ (638.75): C 73.33, H 6.63, found C 73.42, H 6.32.

General procedure for the hydrosilylation of alkynes (E).

In a sealed tube, PtO₂ (11.35 mg, 0.05 mmol) and alkyne (1 mmol) were placed under nitrogen atmosphere. Triethylsilane (0.24 mL, 1.5 mmol) was introduced via syringe and the mixture was stirred at 60°C in an oil bath for 1 h. in the absence of solvent. The residue was then purified by column chromatography over silica gel to yield the title adducts either as a single α-isomer **5** or as a mixture of inseparables **5a** and **5β**-isomers.

(E)-(1-(2,6-Dimethoxyphenyl)-2-phenylvinyl)triethylsilane (α-5a). colorless oil (yield = 90 % after filtration through silica gel); R_f = 0.70 (AcOEt/Cyclohexane, 20/80, SiO₂); **Major α isomer** : ¹H NMR (300 MHz, CDCl₃) δ 0.61 (6H, q, *J* = 6.1 Hz), 0.93 (9H, t, *J* = 6.2 Hz), 3.63 (6H, s), 6.52 (2H, d, *J* = 8.3 Hz), 6.85 (1H, s), 7.12-6.99 (5H, m), 7.16 (1H, t, *J* = 8.3 Hz). ¹³C NMR (75 MHz, CDCl₃) δ 3.7 (3CH₂), 7.4 (3CH₃), 55.6 (2 CH₃), 104.0 (2 CH), 120.2 (C), 126.8 (CH), 127.1 (CH), 127.9 (2 CH), 128.5 (2 CH), 136.2 (C), 138.9 (C), 139.6 (CH), 156.5 (2C). IR (cm⁻¹, neat): 2950, 2875, 1583, 1468, 1431, 1246, 1110, 1006, 907, 781, 762, 649. Anal. Calcd for C₂₂H₃₀O₂Si (354.56): C 74.53, H 8.53, found C 74.41, H 8.44.

(E)-(1-(2,6-Dimethoxyphenyl)-2-(4-methoxyphenyl)vinyl)triethylsilane (α-5b)

Colorless oil (yield = 97 % after filtration through silica gel); R_f = 0.65 (AcOEt/Cyclohexane, 20/80, SiO₂); **Major α isomer** : ¹H NMR (300 MHz, CDCl₃) δ 0.58 (6H, q, *J* = 7.8 Hz), 0.93 (9H, t, *J* = 7.8 Hz), 3.65 (6H, s), 3.72 (3H, s), 6.54 (2H, d, *J* = 8.3 Hz), 6.64 (2H, d, *J* = 8.8 Hz), 6.78 (1H, s), 6.99 (2H, d, *J* = 8.8 Hz), 7.16 (1H, t, *J* = 8.3 Hz). ¹³C NMR (75 MHz, CDCl₃) δ 3.7 (3CH₂), 7.4 (3CH₃), 55.2 (CH₃), 55.6 (2 CH₃), 104.1 (2CH), 113.4 (2CH), 120.4 (C), 127.0 (CH), 129.8 (2CH), 131.9 (C), 133.5 (C), 138.8 (CH), 156.6 (2C), 158.5 (C). IR (cm⁻¹, neat): 2950, 1508, 1468, 1432, 1246, 1176, 1111, 1036, 1007, 905, 762, 727, 696, 650. Anal. Calcd for C₂₃H₃₂O₃Si (384.58): C 71.83, H 8.39, found C 71.49, H 8.32.

(*E*)-(1-(2,6-Dichlorophenyl)-2-phenylvinyl)triethylsilane
(**α -5c**)

Colorless oil (yield = 98 % after filtration through silica gel); R_f = 0.40 (Cyclohexane, SiO_2); ^1H NMR (300 MHz, CDCl_3) δ 0.72 (6H, q, J = 6.1 Hz), 0.96 (9H, t, J = 6.1 Hz), 7.18–6.88 (6H, m), 7.30–7.26 (3H, m). ^{13}C NMR (75 MHz, CDCl_3) δ 4.4 (3 CH_2), 7.4 (3 CH_3), 127.6 (CH), 127.7 (CH), 128.2 (CH), 128.3 (2CH), 133.4 (2C), 137.7 (C), 140.7 (C), 141.5 (2CH), 148.2 (C). IR (cm^{-1} , neat): 2954, 2875, 1426, 1009, 965, 937, 777, 765, 749, 730, 717, 688. Anal. Calcd for $\text{C}_{20}\text{H}_{24}\text{Cl}_2\text{Si}$ (363.40): C 66.10, H 6.66, found C 66.05, H 6.45.

Acknowledgments

We thank the CNRS for support this research.

References

- (a) Peyrere, M.; Quintard, J.-P.; Rahm, A. *Tin in Organic Synthesis*; Butterworth: London, 1987. (b) Farina, V.; Krishnamurthy, V.; Scott, W. J. *Org. React.* **1997**, *50*, 1 and references therein. (c) Shirakawa, E.; Nakao, Y.; Tsuchimoto, T.; Hiyama, T. *Chem. Commun.* **2002**, 1962.
- (a) Tolstikov, G. A.; Miftakhov, M. S.; Danilova, N. A.; Vel'Der Y. L. *Synthesis* **1986**, 496. (b) Nativi, C.; Taddei, M. *J. Org. Chem.* **1988**, *53*, 820. (c) Miyake, H.; Yamamura, K. *Chem. Lett.* **1989**, 981. (d) Zhang, H. X.; Guibé, F.; Balavoine G. *J. Org. Chem.* **1990**, *55*, 1857. (e) Stille, J. K. *Angew. Chem., Ed. Engl.* **1986**, *25*, 508. (f) Chu, K. H.; Wang, K. K. *J. Org. Chem.* **1986**, *51*, 767. (g) Lautens, M.; Huboux, A. H. *Tetrahedron Lett.* **1990**, *31*, 3105. (h) Marshall, J. A.; Bourbeau, M. *P. Org. Lett.* **2002**, *4*, 3931.
- (a) Miyake, H.; Yamamura, K. *Chem. Lett.* **1989**, 981. (b) Zhang, H. X.; Guibé, F.; Balavoine, G. *J. Org. Chem.* **1990**, *55*, 1857. (c) Smith, N. D.; Mancuso, J.; Lautens M. *Chem. Rev.* **2000**, *100*, 3257. (d) Trost, B. M.; Ball, Z. T. *Synthesis* **2005**, 853.
- Betzer, J. F.; LeMenez, P.; Prunet, J.; Brion, J.-D.; Ardisson, J.; Pancrazi, A. *Synlett* **2002**, 1.
- (a) Greeves, N.; Torode, J. S. *Synlett* **1994**, 537. (b) Semmelhack, M. F.; Hooley, R. J. *Tetrahedron Lett.* **2003**, *44*, 5737. (c) Marshall, J. A.; Bourbeau, M. P. *Tetrahedron Lett.* **2003**, *44*, 1087. (d) Oikawa, H.; Yoneta, Y.; Ueno, T.; Oikawa, M.; Wakayama, W.; Ichihara, A. *Tetrahedron Lett.* **1997**, *38*, 7897.
- (a) Magriotis, P. A.; Brown, J. T.; Scott, M. E. *Tetrahedron Lett.* **1991**, *32*, 5047. (b) Huang, X.; Ma, Y. *Synthesis* **1997**, 417. (c) Buissonneaud, D.; Cintrat, J.-C. *Tetrahedron Lett.* **2006**, *47*, 3139. (d) Casson, S.; Kocienski, P. *Synthesis* **1993**, 1133. (e) Boden, C. D. J.; Pattenden, G.; Ye T. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2417. (f) Paley, R. S.; Weers, H. L.; Fernandez, P. *Tetrahedron Lett.* **1995**, *36*, 3605.
- (a) Alami, M.; Ferri, F. *Synlett* **1996**, 755. (b) Hamze, A.; Provot, O.; Brion, J.-D.; Alami, M. *J. Org. Chem.* **2007**, *72*, 3868.
- (a) Ferri, F.; Alami, M. *Tetrahedron Lett.* **1996**, *37*, 7971. (b) Bujard, M.; Ferri, F.; Alami M. *Tetrahedron Lett.* **1998**, *39*, 4243.
- (a) Liron, F.; Le Garrec, P.; Alami, M. *Synlett.* **1999**, 246. (b) Alami, M.; Liron, F.; Gervais, M.; Peyrat, J.-F.; Brion, J.-D. *Angew. Chem., Int. Ed.* **2002**, *41*, 1578. (c) Liron, F.; Gervais, M.; Peyrat, J.-F.; Alami, M.; Brion J.-D. *Tetrahedron Lett.* **2003**, *44*, 2789.
- Hamze, A.; Veau, D.; Provot, O., Brion, J.-D.; Alami, M. *J. Org. Chem.* **2009**, *74*, 1337.
- Hamze, A.; Provot, O.; Brion, J.-D.; Alami M. *Org. Lett.* **2005**, *7*, 5625.
- (a) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, 4467. (b) Alami, M.; Ferri, F.; Linstrumelle G. *Tetrahedron Lett.* **1993**, *34*, 6403.
- For diaryl derivatives, α isomers have been fully identified by NOESY experiments. *e.g.* for **2b**.

- a) Liron, F.; Gervais, M.; Peyrat, J.-F.; Alami, M.; Brion, J.-D. *Tetrahedron Lett.*, **2003**, *44*, 2789. b) Bujard, M.; Ferri, F.; Alami, M. *Tetrahedron Lett.*, **1998**, *39*, 4243.
- See for examples: (a) Tanpure, R. P.; Harkrider, A. R.; Strecker, T. E.; Hamel, E.; Trawick, M. L.; Pinney, K. G. *Bioorg. Med. Chem.* **2009**, *17*, 6993. (b) Harper, M. J. K.; Walpole, A. L. *Nature* **1966**, *212*, 87. (c) Rasolofonjatovo, E.; Provot, O.; Hamze, A.; Bignon, J.; Brion, J.-D.; Alami, M. *Eur. J. Med. Chem.* **2010**, *in press*.
- Hayashi, K.; Iyoda, J.; Shiihara I. *J. Organomet. Chem.* **1967**, *10*, 81.