Stereoselective Synthesis of (*E*)- and (*Z*)-Acetals of Pent-2-en-4-yn-1-al and Related Dienynes and Dienediynes

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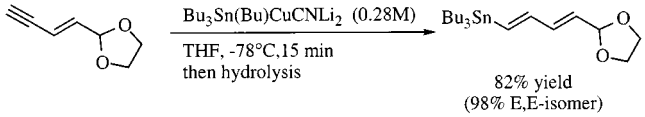
(3*E*)-5,5-Diethoxypent-3-en-1-yne was stereospecifically prepared by Sonogashira–Linstrumelle cross-coupling between (*E*)-3-iodoacrolein diethylacetal and (trimethylsilyl)-acetylene. The (*Z*) isomer was obtained by Stille cross-coupling between the corresponding (*Z*)-vinyltin and 1-bromo-2-(trimethylsilyl)acetylene. In the case of the (*E*) isomer, transacetalisation occurred without isomerization affording a large variety of (*E*)-enynals protected as acetals. It has also been shown to be possible to obtain the corresponding (*E*,*E*)-dienediyne through sp–sp homo-coupling under appropriate experimental conditions.

Introduction

Polyenic building blocks with fixed configurations appear to be of great importance for the synthesis of bioactive compounds such as arachidonic acid derivatives,[1] retinoids and nor-retinoids,[2] macrolide antibiotics[3] or pheromones.[4] Furthermore, such structures could be of considerable use in producing materials having possible applications because of potential nonlinear optical properties[5] or high conductivity.[6] Stereodefined dienyltin compounds are good candidates for this purpose because of their fairly good stability and ease of control of their stereochemistry, the more usual access to this type of precursors requiring the regio- and stereoselective stannylation of α,β-enynes.[7][8] While free-radical hydrostannation usually affords a mixture of isomers[8] and because palladium-catalyzed hydrostannation increases the rate of formation of branched dienyltins,[9][10] it has been recently demonstrated by Pancrazi[8][11] and ourselves[10] that the regioselectivity of the *syn*-stannylcupration of α,β-enynes can be controlled using appropriate experimental conditions. When the stannylcupration was achieved in the presence of proton sources, the kinetic vinyltin cuprate was trapped before retro-stannylcupration.[8][11] In the presence of a functional group, like an acetal group, however, we have been able to drive the reaction to the "thermodynamic adduct" because of intra- and intermolecular chelations,[10] as exemplified in Scheme 1.



Scheme 1. Stannylcupration of pent-2-en-4-yn-1-al dioxolanyl acetal

In order to obtain a dienyltin precursor having both a nucleophilic site (Sn−C bond) and an electrophilic site (acetal function), we need to have an efficient route to obtain stereodefined protected enynals. The literature contains numerous possibilities for reaching enynes by coupling between activated alkenes[12] or vinylmetal compounds[13][14] with alkynyl halides, or by coupling of alkynylmetal compounds[15] or alkynes[16] with vinyl halides, in our case, however, we have to take into account the availability of the desired compounds and the nature of the experimental conditions in order to avoid unwanted isomerizations.

The fact that 1-tributylstannyl-3,3-diethoxyprop-1-ene can be prepared in good yields as a clean (*E*) isomer **1a-*E***[17] or as a clean (*Z*) isomer **1a-*Z***[18] from commercially available 3,3-diethoxyprop-1-yne was first considered in order to obtain the vinylic moiety. Indeed, vinyltin acetals can be either directly used in Stille cross-coupling reactions with alkynyl halides[14] or as precursors of vinyl iodides, which can be subsequently used in Sonogashira−Linstrumelle cross-coupling reactions.[16] Due to the number of papers which report the use of this last approach, we first attempted to reach the desired compounds according to this route.

Synthesis of Protected Enynals by Sonogashira−Linstrumelle Cross-Coupling Reactions

Optimization of the Experimental Conditions

The most appropriate experimental conditions are usually dependent on the substrate and must be optimized in terms of relative rates of reagents, catalysts, bases or temperature.[16] Therefore, taking as "basic experimental conditions" those described by Lee[19] for obtaining α,β-enynes,

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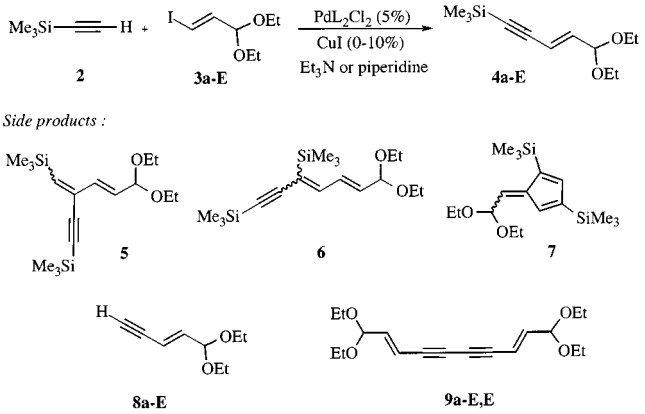
we studied the influence of the above-mentioned parameters on the yield of desired product and on the rate of by-products. The results obtained are reported in Table I (Entries 1−3). While the desired product **4a-*E*** was often obtained as the major compound (Scheme 2), considerable amounts of side products were also observed when the reaction was performed at room temperature. Using triethylamine as the base and $Pd(PPh_3)_2Cl_2$ as the catalyst at room temperature, the best results were obtained using a 1.5 alkyne/vinyl iodide ratio (Entry 2). In these experimental conditions, the desired compound **4a-*E*** was obtained in fairly good yield but with an important contamination by side product **5**.

Side product **5** can be seen as the result of the *syn* addition of the excess of **2** on **4a-*E***. The addition might occur through the alkynylcopper intermediate in agreement with the absence of **5** when the reaction was performed without cuprous iodide (Entry 3).[20] Another possibility might be the carbopalladation of 1,4-bis(trimethylsilyl)but-1,3-diyne by a vinylpalladium compound resulting from the oxidative addition of **3a-*E*** on PdL_2.[21]



Scheme 2. Cross-coupling of (*E*)-3,3-diethoxy-1-iodoprop-1-ene with (trimethylsilyl)acetylene

The formation of the side compounds obtained in the absence of cuprous iodide might be explained by several competitive reactions involving the first formed organopalladium intermediate which can generate **4a-*E***, **6** or **7** according to Scheme 3, while alkynylcopper intermediates drive the reaction to **4a-*E*** because of a direct cross-coupling reaction with the first-formed vinylpalladium compound. Note that fulvene-type compounds such as **7** have been previously described in these reactions,[19] but obtaining compounds like **6** simultaneously has not been reported. Under these experimental conditions, one should mention that **4a-*E*** and **6** were obtained by an *anti*-retrohydropalladation.[22] Obviously, obtaining **4a-*E*** according to Scheme 3 is one possibility among more conventional ones.[15][16]

Taking into account the difficulties encountered in avoiding the formation of side products using $PdCl_2(PPh_3)_2$ as catalyst and triethylamine as base, modifications were made, in agreement with Linstrumelle,[16e] with $PdCl_2(MeCN)_2$ used as the catalyst and piperidine as the base. Under these new experimental conditions, at room temperature, the vinyl iodide was consumed in about 30 min (against 12 h under previous experimental conditions) and contamination by **5** appeared to be less (Entry 4). However, an increase in the concentration of the reagents induced the formation of the desilylated compound **8a-*E*** and of the subsequent homocoupling product **9a-*EE*** (Entry 5). On the other hand, the increased reactivity allowed the achievement of the reaction at 0°C and the clean obtaining of **4a-*E*** (75% isolated yield) after 2 h (Entry 6).

Scope and Limitations of the Method

The above-mentioned results demonstrate that the Sonogashira−Linstrumelle cross-coupling can be efficient in obtaining cleanly (3*E*)-5,5-diethoxy-1-(trimethylsilyl)pent-3-en-1-yne (**4a-*E***) and, subsequently, (3*E*)-5,5-diethoxypent-3-en-1-yne (**8a-*E***) upon treatment with tetrabutylammonium fluoride[23] according to Scheme 4.

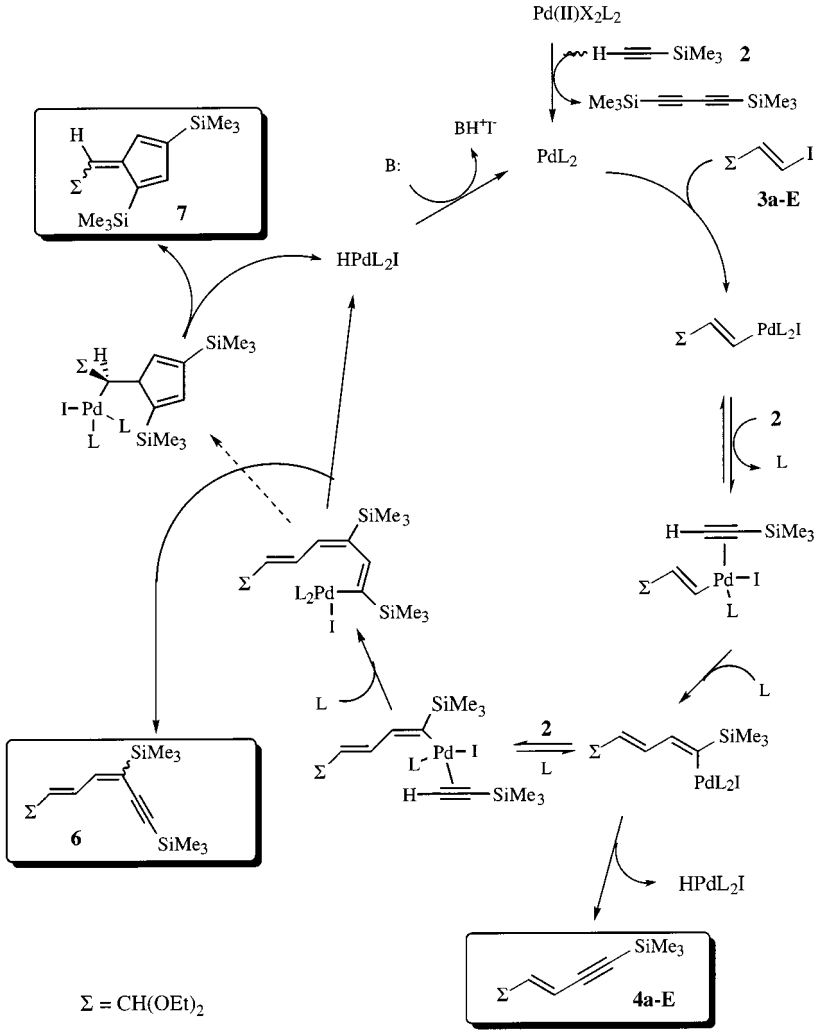
The desilylation reaction occurs without isomerization of the *E* double bond in this case and transacetalisation of **8a-*E*** with diols can also be achieved under mild experimental conditions without isomerization to afford the corresponding cyclic acetals in good yields (Scheme 5).

However, while the above-mentioned method appears to be satisfactory in obtaining numerous (*E*)-protected α,β-enynals, problems arise when similar reactions were attempted in order to obtain the **8-*Z*** isomers. The first problem was the poor configurational stability of the vinyl iodide **3a-*Z*** which is usually obtained as a mixture of (*E*) and (*Z*) isomers when the iododestannylation of **1a-*Z*** was performed at 0°C, prohibiting a clean stereochemical control for the

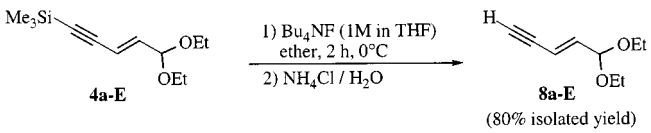
Table 1. Optimization of the synthesis of **4a-E** by Sonogashira−Linstrumelle cross-coupling reaction

Entry	**2**/**3aE**	**3aE** [mol L^{-1}]	Pd catalyst	CuI [%]	base	*T* [°C], time [h]	Product **4aE** (yield in%)[a]	By-products (yield in%)
1	2.5	0.156	$Pd(PPh_3)_2Cl_2$	5	Et_3N	20, 12	60	**5** (30)
2	1.5	0.26	$Pd(PPh_3)_2Cl_2$	5	Et_3N	20, 12	(70)	**5** (30)
3	2	0.195	$Pd(PPh_3)_2Cl_2$	0	Et_3N	20, 12	(50)	**6** (25) + **7** (25)
4	2	0.195	$Pd(MeCN)_2Cl_2$	10	piperidine	20, 0.5	62	**5** (15)
5	2.5	0.325	$Pd(MeCN)_2Cl_2$	10	piperidine	20, 0.25	17	**8aE** (25) + **9aEE** (8)
6	2.5	0.195	$Pd(MeCN)_2Cl_2$	10	piperidine	0, 2	75	−

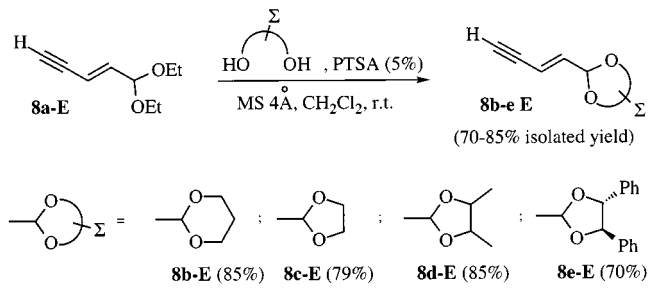
[a] Reported values are isolated yields or conversion rates (values in parentheses).



Scheme 3. Sonogashira cross-coupling of **3a-E** with (trimethylsilyl)acetylene and possible explanation for the formation of the products in the absence of CuI



Scheme 4. Desilylation of **4a-*E***

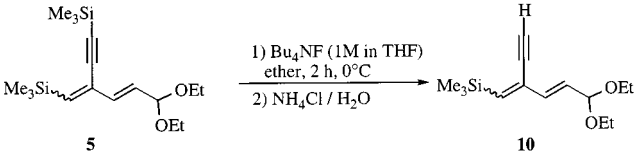


Scheme 5. Transacetalisation of **8a-*E***

Sonogashira–Linstrumelle cross-coupling (at 0 °C) to reach **8a-*Z***. Furthermore, while **1a-*Z*** is fairly stable under neutral conditions, the transacetalisation of this isomer also occurs with some isomerization, prohibiting attempts to reach cleanly the (*Z*)-protected enynal according to this route.

Selective Preparation of Dienynes and Dienediynes

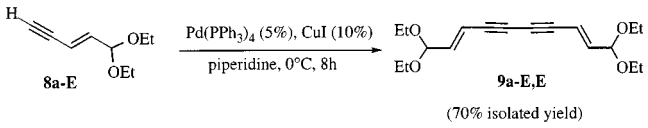
Compound **5** was selectively desilylated by tetrabutylammonium fluoride at the sp-carbon atom affording the monosilylated dienyne **10** (Scheme 6).



Scheme 6. Desilylation of **5**

More interesting is the possible homocoupling of the α,β-enyne **8a-*E*** to afford the dienediyne **9a-*EE***. Although known in principle, the homocoupling of alkynes is described in only a limited number of publications.[24] Under experimental conditions close to those used in Sonogashira

cross-coupling, results of this type have been obtained for arylacetylenes[25] and very recently for aryl- and alkylacetylenes.[26] In our case (homocoupling of protected enynals) nothing had been described previously. Nevertheless, using $Pd(PPh_3)_4$ and CuI as catalysts, in the presence of piperidine, a good yield of the homocoupling product was obtained after 8 h at 0°C (Scheme 7).

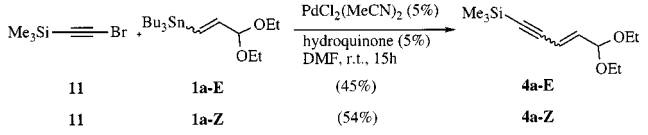


Scheme 7. Homocoupling of **8a-*E***

This product, which can be easily deprotected to afford the corresponding deca-2,8-diene-4,6-diyne-1,10-dial on wet silica, constitutes an interesting precursor in order to obtain polyunsaturated materials.

Synthesis of Protected Enynals by Stille Cross-Coupling Reaction

The problems encountered with isomerization of compounds of the type **1-*Z*** in transacetalisation reactions and the poor configurational stability of the vinyl iodide **3a-*Z*** prohibits the use of Sonogashira-type reactions to reach the (*Z*)-protected enynals. Considering the good isomeric stability of **1a-*Z*** under neutral conditions, the more appropriate route to circumvent these difficulties was the use of a Stille cross-coupling between this vinyltin compound and 1-bromo-2-(trimethylsilyl)acetylene (**11**) using experimental conditions for cross-couplings of this type previously described by our group.[14b] The reaction was performed on both isomers of 1-tributylstannyl-3,3-diethoxyprop-1-ene and afforded the expected silylated enynes without significant isomerization of the double bond (Scheme 8).



Scheme 8. Preparation of **4a-*E*** and **4a-*Z*** by Stille cross-coupling reaction

Desilylation of the compounds obtained with tetrabutylammonium fluoride, as previously described, afforded the desired terminal enynes **8a-*E*** (80% yield) and **8a-*Z*** (70% yield) with complete retention of the stereochemistry at the double bond. Therefore, starting from the appropriate acetals of prop-2-yn-1-al, this method should proceed to every type of acetal of pent-2-en-4-yn-1-al with complete control of the *E* or *Z* stereochemistry of the double bond.

Conclusion

Acetals of pent-2-en-4-yn-1-al have been obtained selectively as (*E*) or (*Z*) isomers without isomerization of the double bond using appropriate experimental conditions.

The (*E*) isomer was efficiently prepared by Sonogashira−Linstrumelle cross-coupling between (trimethylsilyl)acetylene and (*E*)-β-iodoacrolein diethylacetal or by Stille cross-coupling between (*E*)-β-(tributylstannyl)acrolein diethylacetal and 1-bromo-2-(trimethylsilyl)acetylene. The desilylation reaction was performed with tetrabutylammonium fluoride. In this case, a large variety of (*E*)-protected enynals can be subsequently obtained by transacetalisation of the diethylacetal with diols. For the less stable (*Z*) isomer, Stille cross-coupling must be used in order to avoid isomerization of the double bond. Finally, the optimization of an homocoupling side reaction has been exploited in order to reach functional (*E*,*E*)-dienediynes. Accordingly, bis(diethylacetal) of deca-2,8-diene-4,6-diyne-1,10-dial was obtained in good yield as (*E*,*E*) isomer in a clean fashion.

The polyunsaturated compounds obtained are useful building blocks by themselves and also offer interesting possibilities after regio- and stereoselective stannylcupration reaction. Work is in progress in order to evaluate their effective potential in organic synthesis both as precursors of new materials or as precursors of molecules of biological interest

Experimental Section

General and Starting Materials: ^{1}H- and ^{13}C-NMR spectra were recorded with Bruker AC 200 or Bruker AC 400 spectrometers. Chemical shifts are given as δ values related to tetramethylsilane and coupling constants in Hz (solvent = $CDCl_3$). − Mass spectra were obtained in EI mode (70 eV) with a Hewlett-Packard apparatus (Engine 5989A) in direct introduction mode or in GC-MS mode. Organotin fragments are given for ^{120}Sn. − IR spectra were recorded with a Bruker IFS apparatus. − (Trimethylsilyl)acetylene is a commercially available compound (Aldrich) which was converted into 1-bromo-2-(trimethylsilyl)acetylene upon treatment with *n*-butyllithium (diethyl ether, −78°C) and quenching with bromine. β-(Tributylstannyl)acrolein diethylacetal was obtained cleanly as a pure (*E*) isomer **1a-*E*** by stannylcupration of 3,3-diethoxypropyne by Lipshutz reagent according to a previously described procedure.[17] Similarly, its (*Z*) isomer **1a-*Z*** was obtained by titanation of 1-(tributylstannyl)-3,3-diethoxyprop-1-yne as already described.[18] When corresponding iodides were desired, they were obtained by iododestannylation of **1a-*E*** or **1a-*Z***,[17][18] however, while vinyl iodide **3a-*E*** can be obtained easily as a pure compound from **1a-*E***, the preparation of **3a-*Z*** from **1a-*Z***, even possible at low temperature, is much more tedious since partial isomerization occurs at 0°C (temperature required for further coupling).

(*E*)-3,3-Diethoxy-1-(tributylstannyl)prop-1-ene (1a-*E*): ^{1}H NMR: δ = 0.80−0.95 (m, 15 H), 1.22 (t, $^3J_{2H}$ = 7.1, 6 H), 1.22−1.60 (m, 12 H), 3.47 (qd, $^2J_{1H}$ = 9.5, $^3J_{3H}$ = 7.1, 2 × 1 H), 3.62 (qd, $^2J_{1H}$ = 9.5, $^3J_{3H}$ = 7.1, 2 × 1H), 4.78 (dd,$^3J_{1H}$ = 4.8, $^4J_{1H}$ = 1.1, $^4J_{SnH}$ = 7.9, 1 H), 5.94 (dd, $^3J_{1H}$ = 19.3, $^3J_{1H}$ = 4.8, $^3J_{SnH}$ = 60/63, 1 H), 6.33 (dd, $^3J_{1H}$ = 19.3, $^4J_{1H}$ = 1.1, $^2J_{SnH}$ = 68/71, 1 H). − ^{13}C NMR: δ = 9.3 (3 C, $^1J_{SnC}$ = 328/344), 13.5 (3 C), 15.1 (2 C), 27.5 (3 C, $^3J_{SnC}$ = 54), 29.1 (3 C, $^2J_{SnC}$ = 21), 60.4 (2 C), 102.7 ($^3J_{SnC}$ = 72), 132.0 ($^1J_{SnC}$ = 362/377), 145.7 ($^2J_{SnC}$ = 43). − ^{119}Sn NMR: δ = −46.4. − MS; *m*/*z* (%): organotin fragments: 363 (17), 319 (8), 307 (2), 291 (2), 235 (5), 179 (9), 177 (13), 165 (9), 121 (8); organic fragments: 129 (100), 103 (6), 101 (6), 85 (27), 75 (7), 73 (7), 57 (15), 55 (5),47 (9). − IR: $\tilde{\nu}$ = 2957−2865 cm^{-1}, 1653, 1615, 1465, 1377, 1343, 1185, 1126, 1064, 1000, 970, 876, 692, 668.

(*Z*)-3,3-Diethoxy-1-(tributylstannyl)prop-1-ene (1a-*Z*): ^{1}H NMR: δ = 0.88 and 0.91 (2t, ^3J = 7.1, 15 H), 1.22 (t, $^3J_{2H}$ = 7.1, 6 H), 1.23−1.58 (m, 12 H), 3.50 (qd, $^3J_{2H}$ = 7.1, $^2J_{1H}$ = 9.5, 2 × 1H), 3.65 (qd, $^3J_{2H}$ = 7.1, $^2J_{1H}$ = 9.5, 2 × 1 H), 4.83 (dd, $^3J_{1H}$ = 5, $^4J_{1H}$ = 1.1, $^4J_{SnH}$ = 8.5, 1 H), 6.20 (dd, $^3J_{1H}$ = 13.4, $^4J_{1H}$ = 1.1, $^2J_{SnH}$ = 60/63, 1 H), 6.51 (dd, $^3J_{1H}$ = 13.4, $^3J_{1H}$ = 5, $^3J_{SnH}$ = 129/135, 1 H). − ^{13}C NMR: δ = 10.9 (3 C, $^1J_{SnC}$ = 333/349), 13.7 (3 C), 15.3 (2 C), 27.3 (3 C, $^3J_{SnC}$ = 56/59), 29.1 (3 C, $^2J_{SnC}$ = 21), 60.5 (2 C), 102.3 ($^3J_{SnC}$ = 31), 134.2 ($^1J_{SnC}$ = 351/368), 144.7 ($^2J_{SnC}$ = 6.5). − ^{119}Sn NMR: δ = −61.2. − MS; *m*/*z* (%): organotin fragments: 363 (17), 317 (32), 235 (1), 179 (5), 177 (7), 121 (7); organic fragments: 129 (100), 103 (1), 101 (13), 85 (19), 75 (2), 73 (12), 57 (15), 47 (6), 29 (9). − IR: ṽ = 2956 cm^{-1}, 2926, 2872, 1610, 1465, 1376, 1118, 1053, 1002, 875, 670.

(*E*)-3,3-Diethoxy-1-iodoprop-1-ene (3a-*E*): ^{1}H NMR: δ = 1.22 (t, $^3J_{2H}$ = 7.1, 6 H), 3.50 (qd, $^3J_{3H}$ = 7.1, $^2J_{1H}$ = 9.8, 2 × 1 H), 3.62 (qd, $^3J_{2H}$ = 7.1, $^2J_{1H}$ = 9.8, 2 × 1 H), 4.85 (dd, $^3J_{1H}$ = 2.2, $^4J_{1H}$ = 0.9, 1 H), 6.56 (dd, $^3J_{1H}$ = 16.5, $^4J_{1H}$ = 0.9, 1 H), 6.57 (dd, $^3J_{1H}$ = 16.5,$^3J_{1H}$ = 2.2, 1 H) . − ^{13}C NMR: δ = 15.2 (2 C), 61.1 (2 C), 81.4, 101.2, 143.4. − MS; *m*/*z* (%): 211 (75) [M$^{\cdot+}$ − 45], 183 (100), 155 (11), 145 (37), 129 (58), 127 (5), 103 (25), 101 (29), 85 (13), 75 (25), 73 (33), 55 (30), 47 (37). − IR: ṽ = 3076 cm^{-1}, 2974, 2928, 2877, 1610, 1481, 1444, 1391, 1332, 1128, 1051, 1005, 943.

(*Z*)-3,3-Diethoxy-1-iodoprop-1-ene (3a-*Z*, Mixture with 3a-*E*): ^{1}H NMR: δ = 1.24 (t, $^3J_{2H}$ = 7.1, 6 H), 3.58 (qd, $^3J_{3H}$ = 7.1, $^2J_{1H}$ = 9.3, 2 × 1 H), 3.70 (qd, $^3J_{2H}$ = 7.1, $^2J_{1H}$ = 9.3, 2 × 1 H), 5.10 (dd, $^3J_{1H}$ = 6.3, $^4J_{1H}$ = 0.9, 1 H), 6.39 (dd, $^3J_{1H}$ = 7.9,$^3J_{1H}$ = 6.3, 1 H), 6.54 (dd, $^3J_{1H}$ = 7.9,$^4J_{1H}$ = 0.9, 1 H). − ^{13}C NMR: δ = 15.5 (2 C), 61.9 (2 C), 84.3, 103.4, 138.4. − GC MS; *m*/*z* (%): 255 (1) [M$^{\cdot+}$ −H], 227 (2), 211 (74), 183 (100), 155 (6), 129 (47), 127 (5), 103 (6), 101 (19), 75 (9), 73 (20), 55 (17), 47 (20), 29 (38), 27 (24).

Cross-Coupling of 3a-*E* with (Trimethylsilyl)acetylene. − Typical Experimental Procedure (for Entry 6, Table 1): In a Schlenk tube were placed 0.109 mmol (0.029 g) of $PdCl_2(MeCN)_2$ and 0.218 mmol (0.042 g) of cuprous iodide in piperidine (10 mL). The reaction mixture was degassed before addition of vinyl iodide **3a-*E*** (2.18 mmol, 0.558 g) and further addition of trimethylsilylacetylene (5.45 mmol, 0.543 g) at 0°C. At the end of the reaction (monitored by TLC), 20 mL of water and 20 mL of hexane were added to the reaction mixture before usual treatments (extraction, drying, removal of solvents). The desired compound **4a-*E*** was obtained as a crude product which can be purified or directly used in desilylation reaction when the reaction has been conducted under the experimental conditions described above. − For other attempts at optimization, the amount of palladium catalyst $PdCl_2L_2$ was maintained at 0.109 mmol and the amount of vinyl iodide **3a-*E*** at 2.18 mmol, the solvent being the amine. The other parameters were modified according to Table 1. After determination of the more appropriate conditions, this coupling has been proved to be possible at higher scales.

(*E*)-5,5-Diethoxy-1-(trimethylsilyl)pent-3-en-1-yne (4a-*E*): ^{1}H NMR: δ = 0.19 (s, 9 H), 1.21 (t, $^3J_{2H}$ = 7.1, 6 H), 3.48 (qd, $^3J_{3H}$ = 7.1, $^2J_{1H}$ = 9.35, 2 × 1 H), 3.63 (qd, $^3J_{3H}$ = 7.1, $^2J_{1H}$ = 9.35, 2 × 1H), 4.93 (dd, $^3J_{1H}$ = 4.3, $^4J_{1H}$ = 1.2, 1 H), 5.86 (dd, $^3J_{1H}$ = 16.2, $^4J_{1H}$ = 1.2, 1 H), 6.12 (dd, $^3J_{1H}$ = 16.2, $^3J_{1H}$ = 4.3, 1 H). − ^{13}C NMR: δ = 0.1 (3 C), 15.2 (2 C), 61.0 (2 C), 96.6, 99.9, 102.6, 113.2, 140.7. − MS; *m*/*z* (%): 226 (6) [M$^{\cdot+}$], 211 (10), 197 (27), 182 (16), 181 (92), 153 (19), 139 (15), 137 (30), 125 (29), 117 (12), 113 (10), 111 (12), 109 (16), 103 (21), 97 (11), 83 (30), 79 (10), 77 (10), 75 (64), 73 (100), 47 (10), 45 (13), 41 (12), 29 (29). − IR: ṽ = 2976−2876 cm^{-1}, 2170, 2130, 1630, 1251, 1137, 1053, 1000, 950, 844, 760. − $C_{12}H_{22}O_2Si$ (226.39): calcd. C 63.73, H 9.73; found C 63.46, H 9.68.

6,6-Diethoxy-1-(trimethylsilyl)-3-[(trimethylsilyl)methylene]hex-4-en-1-yne (5): ^{1}H NMR: δ = 0.18 (s, 9 H), 0.23 (s, 9 H), 1.25 (t, $^3J_{2H}$ = 7.1, 6 H), 3.54 (qd, $^3J_{3H}$ = 7.1, $^2J_{1H}$ = 9.4, 2 × 1 H), 3.69 (qd, $^3J_{3H}$ = 7.1, $^2J_{1H}$ = 9.4, 2 × 1 H), 5.05 (br. d, $^3J_{1H}$ = 4.6, 1 H), 6.16 (dd, $^3J_{1H}$ = 15.3, $^3J_{1H}$ = 4.6, 1 H), 6.33 (s, 1 H), 6.59 (br. d, $^3J_{1H}$ = 15.3, 1 H). − MS; *m*/*z* (%): 324 (1) [M$^{\cdot+}$], 295 (4), 279 (7), 251 (4), 207 (6), 206 (7), 177 (18), 147 (16), 133 (10), 129 (34), 103 (36), 83 (11), 75 (43), 73 (100), 59 (15), 47 (16), 45 (20), 29 (34).

7,7-Diethoxy-1,3-bis(trimethylsilyl)hepta-3,5-dien-1-yne (6): A single isomer obtained as a mixture with **7**. − ^{1}H NMR: δ = 0.14 (s, 9 H), 0.24 (s, 9 H), 1.23 (t, $^3J_{2H}$ = 6.9, 6 H), 3.4−3.8 (m, 4 H), 5.0 (dd, $^3J_{1H}$ = 5.2, $^4J_{1H}$ = 1.1, 1 H), 5.83 (m, $^3J_{1H}$ = 15.4, $^3J_{1H}$ = 5.2, $^4J_{1H}$ = 0.6, 1 H), 6.57 (dd, $^3J_{1H}$ = 10.7, $^4J_{1H}$ = 0.6, 1 H), 6.96 (m, $^3J_{1H}$ = 15.4, $^3J_{1H}$ = 10.7, $^4J_{1H}$ = 1.1, 1 H). − MS; *m*/*z* (%): 324 (2) [M$^{\cdot+}$], 295 (10), 279 (10), 251 (5), 191 (5), 147 (14), 133 (12), 103 (20), 75 (20), 73 (100), 45 (15), 29 (15).

6-Diethoxymethyl-1,3-bis(trimethylsilyl)fulvene (7): A single isomer obtained as a mixture with **6**. − ^{1}H NMR: δ = 0.14 (s, 9 H), 0.24 (s, 9 H), 1.24 (t, $^3J_{2H}$ = 6.9, 6 H), 3.4−3.8 (m, 4 H), 5.50 (d, $^3J_{1H}$ = 6.8, 1 H), 6.30 (br. d, $^3J_{1H}$ = 6.8, 1 H), 6.79 (br. s, 1 H), 6.86 (br. s, 1 H). − MS; *m*/*z* (%): 324 (2) [M$^{\cdot+}$], 295 (7), 280 (10), 251 (7), 192 (4), 163 (14), 147 (10), 133 (9), 103 (9), 75 (20), 73 (100), 45 (14), 29 (15).

Desilylation of 4a-*E* and 5: In a 100-mL three-necked reactor were placed 3.65 mmol (0.826 g) of crude **4a-*E*** in diethyl ether (20 mL). After cooling at 0°C, 4 mL of Bu_4NF solution (1 M in THF) were added and the reaction mixture was stirred for 2 h at 0°C before adding 15 mL of a saturated aqueous ammonium chloride solution. After filtration and ether extraction, the organic phase was washed with an aqueous solution of sodium chloride before drying with magnesium sulfate. After removal of the solvents, **8a-*E*** (0.67 g, 70% yield from **1a-*E***) was obtained as a pure product by liquid chromatography on silica gel 60 (hexane/triethylamine, 98:2). Similar treatment was applied to **5** in order to obtain **10**.

(*E*)-5,5-Diethoxypent-3-en-1-yne (8a-*E*): ^{1}H NMR: δ = 1.22 (t, $^3J_{2H}$ = 7.0, 6 H), 2.96 (br. d, $^4J_{1H}$ = 2.2, 1 H), 3.50 (qd, $^3J_{3H}$ = 7, $^2J_{1H}$ = 9.5, 2 × 1 H), 3.64 (qd, $^3J_{3H}$ = 7, $^2J_{1H}$ = 9.5, 2 × 1 H), 4.95 (dd, $^3J_{1H}$ = 4.4, $^4J_{1H}$ = 1.4, 1 H), 5.84 (ddd, $^3J_{1H}$ = 16.1, $^4J_{1H}$ = 1.4, $^4J_{1H}$ = 2.2, 1 H), 6.18 (ddd, $^3J_{1H}$ = 16.1, $^3J_{1H}$ = 4.4, $^5J_{1H}$ = 0.5, 1 H). − ^{13}C NMR: δ = 15.3 (2 C), 61.2 (2 C), 79.3, 81.2, 99.8, 112.3, 141.7. − MS; *m*/*z* (%): 154 (1) [M$^{\cdot+}$], 125 (5), 110 (15), 109 (100), 98 (9), 97 (11), 82 (12), 81 (87), 79 (6), 70 (8), 53 (46), 52 (12), 51 (11), 47 (9), 43 (5), 29 (24), 27 (17). − IR: ṽ = 3300 cm$^{-1,}$ 2978, 2920, 2876, 2105, 1640, 1339, 1138, 1056, 1000, 950, 610. − $C_9H_{14}O_2$ (154.21): calcd. C 70.15, H 9.09; found C 69.66, H 9.10. − Upon treatment with wet silica, pent-2-en-4-yn-1-al was obtained as a crude product: − ^{1}H NMR: δ = 3.73 (d, $^4J_{1H}$ = 1.7, 1 H), 6.55 (dd, $^3J_{1H}$ = 16.0, $^3J_{1H}$ = 5.2, 1 H), 6.58 (br. d, $^3J_{1H}$ = 16.0, 1 H), 9.59 (dd, $^3J_{1H}$ = 5.2, $^4J_{1H}$ = 2.2, 1 H).

6,6-Diethoxy-3-[(trimethylsilyl)methylene]hex-4-en-1-yne (10): ^{1}H NMR: δ = 0.17 (s, 9 H), 1.22 (t, $^3J_{2H}$ = 7.1, 6 H), 3.02 (s, 1 H), 3.51 (qd, $^3J_{3H}$ = 7.1, $^2J_{1H}$ = 9.4, 2 × 1 H), 3.66 (qd, $^3J_{3H}$ = 7.1, $^2J_{1H}$ = 9.4, 2 × 1 H), 5.03 (dd, $^3J_{1H}$ = 4.5, $^4J_{1H}$ = 1, 1 H), 6.17 (dd, $^3J_{1H}$ = 15.4, $^3J_{1H}$ = 4.5, 1 H), 6.32 (s, 1 H), 6.58 (br. d, $^3J_{1H}$ = 15.4, 1 H). − ^{13}C NMR: δ = 1.1 (3 C), 16.3, 16.4, 62.0, 62.2, 79.1, 83.8, 101.6, 132.1, 133.2, 135.1, 145.4. − MS; *m*/*z* (%): 252 (3) [M$^{\cdot+}$], 223 (5), 207 (18), 179 (14), 163 (16), 135 (11), 129 (25), 106 (12), 105 (35), 103 (35), 91 (11), 89 (37), 85 (10), 83 (28), 77 (16), 75 (100), 73 (90), 59 (25), 55 (11), 47 (26), 45 (33), 43 (28), 31 (11),

29 (81), 27 (24). − IR: $\tilde{\nu}$ = 3315 cm^{-1}, 2976, 2962−2850, 2250, 1550, 1340, 1251, 1134, 1053, 1000, 950, 905, 864, 735, 610.

Transacetalisation of 8a-*E*: In a 100-mL flask, 10 g of molecular sieves (4 Å) was activated by warming under vacuum. After cooling under dry argon, dry dichloromethane (50 mL), *p*-toluenesulfonic acid (18 mg, 0.0105 mmol) and the diol (2.3 mmol) were successively added. The reaction mixture was stirred for 30 min at room temperature before addition of **8a-*E*** (0.3 g, 1.95 mmol). The reaction was monitored by TLC before neutralization with triethylamine. After filtration through neutral aluminium oxide (CH_2Cl_2) and removal of the solvents, the (*E*)-enynals were directly isolated and characterized.

(1′*E*)-2-(But-1′-en-3′-yn-1′-yl)-1,3-dioxane (8b-*E*): ^{1}H NMR: δ = 1.38 (br. d, $^2J_{1H}$ = 13.4, 1 H), 2.12 (dtt, $^2J_{1H}$ = 13.4, $^3J_{2H}$ = 12.3, $^3J_{2H}$ = 5.0, 1 H), 2.95 (d, $^4J_{1H}$ = 2.1, 1 H), 3.83 (br. dt, $^2J_{1H}$ = 11.8, $^3J_{1H}$ = 12.3, $^3J_{1H}$ = 2.4, 2 × 1 H), 4.15 (ddd, $^2J_{1H}$ = 11.8, $^3J_{1H}$ = 5.0, $^3J_{1H}$ = 1.2, 2 × 1 H), 5.00 (dd, $^3J_{1H}$ = 3.9, $^4J_{1H}$ = 1.0, 1 H), 5.86 (ddd, $^3J_{1H}$ = 16.1, $^4J_{1H}$ = 2.1, $^4J_{1H}$ = 1.0, 1 H), 6.13 (dd, $^3J_{1H}$ = 16.1, $^3J_{1H}$ = 3.9, 1 H).

(1′*E*)-2-(But-1′-en-3′-yn-1′-yl)-1,3-dioxolane (8c-*E*): ^{1}H NMR: δ = 2.98 (d, $^4J_{1H}$ = 2.0, 1 H), 3.85−4.05 (m, 4 H), 5.32 (dd, $^3J_{1H}$ = 5.1, $^4J_{1H}$ = 0.5, 1 H), 5.86 (ddd, $^3J_{1H}$ = 16.0, $^4J_{1H}$ = 2.0, $^4J_{1H}$ = 0.5, 1 H), 6.14 (dd, $^3J_{1H}$ = 16.0, $^3J_{1H}$ = 5.1, 1 H). − ^{13}C NMR: δ = 65.0 (2 C), 79.9, 80.7, 102.2, 113.2, 140.0. − MS; *m/z* (%): 124 (38) [M^+], 123 (28), 96 (10), 80 (21), 79 (38), 73 (23), 68 (78), 66 (25), 65 (39), 64 (13), 63 (54), 62 (15), 53 (16), 52 (100), 51 (55), 50 (40), 45 (34), 39 (19), 38 (25), 29 (29). − IR: $\tilde{\nu}$ = 3291 cm^{-1}, 2957, 2891, 2107, 1641, 1389, 1148, 1078, 1022, 960, 668. − $C_7H_8O_1$ (124.14): calcd. C 67.71, H 6.50; found C 67.93, H 6.53.

dl-(1′*E*)-2-(But-1′-en-3′-yn-1′-yl)-4,5-dimethyl-1,3-dioxolane (8d-*E*): ^{1}H NMR: δ = 1.25 (d, $^3J_{1H}$ = 6.0, 3 H), 1.29 (d, $^3J_{1H}$ = 5.8, 3 H), 2.85 (d, $^4J_{1H}$ = 2.3, 1 H), 3.56−3.72 (m, 2 H), 5.41 (d, $^3J_{1H}$ = 5.3, 1 H), 5.84 (dd, $^3J_{1H}$ = 16.0, $^4J_{1H}$ = 2.3, 1 H), 6.16 (dd, $^3J_{1H}$ = 16.0, $^3J_{1H}$ = 5.3, 1 H). − ^{13}C NMR: δ = 16.87, 16.94, 78.4, 79.8, 80.1, 81.0, 101.3, 113.0, 141.2. − MS; *m/z* (%): 152 (42) [$M^{\cdot+}$], 107 (19), 101 (6), 81 (23), 80 (70), 79 (98), 73 (23), 64 (15), 63 (39), 55 (46), 53 (25), 52 (100), 51 (26), 43 (57), 41 (15), 29 (22), 27 (23). − IR: $\tilde{\nu}$ = 3289 cm^{-1}, 2964, 2933−2860, 2105, 1622, 1381, 1261, 1180, 1100, 1021, 962, 800, 662.

(4*R*,5*R*,1′*E*)-2-(But-1′-en-3′-yn-1′-yl)-4,5-diphenyl-1,3-dioxolane (8e-*E*): ^{1}H NMR: δ = 3.03 (d, $^4J_{1H}$ = 2.2, 1 H), 4.76 (d, $^3J_{1H}$ = 8.0, 1 H), 4.81 (d, $^3J_{1H}$ = 8.0, 1 H), 5.88 (dd, $^3J_{1H}$ = 5.3, $^4J_{1H}$ = 0.5, 1 H), 6.03 (ddd, $^3J_{1H}$ = 16.0, $^4J_{1H}$ = 2.2, $^4J_{1H}$ = 0.5, 1 H), 6.41 (dd, $^3J_{1H}$ = 16.0, $^3J_{1H}$ = 5.3, 1 H), 7.2−7.4 (m, 10 H). − ^{13}C NMR: δ = 80.2, 80.8, 84.9, 86.7, 103.1, 113.5, 126.5 (2 C), 126.8 (2 C), 128.4 (2 C), 128.6 (4 C), 136.2, 137.2, 140.3. − MS; *m/z* (%): 197 (1), 170 (28), 169 (54), 142 (29), 141 (100), 115 (21), 105 (9), 90 (9), 89 (17), 79 (10), 77 (16), 63 (15), 55 (22), 51 (12), 39 (5). − IR: $\tilde{\nu}$ = 3287 cm^{-1}, 3089−3040, 2890, 2105, 1641, 1605, 1498, 1455, 1395, 1286, 1144, 1088, 1022, 955, 760, 700, 650, 534. − $C_{19}H_{16}O_2$ (276.33): calcd. C 82.58, H 5.84; found C 82.85, H 5.93.

Synthesis of Dienediyne 9a-*E*,*E*: In a Schlenk tube were successively placed 0.048 mmol (0.055 g) of $Pd(PPh_3)_4$ and 0.097 mmol (0.0185 g) of cuprous iodide in piperidine (7.5 mL). The reaction mixture was cooled to 0°C and degassed before addition of **8a-*E*** (0.3 g, 1.95 mmol). The reaction mixture was stirred at 0°C until disappearance of **8a-*E*** (TLC monitoring). At the end of the reaction, water (20 mL) and hexane (20 mL) were successively added before extraction of the organic products with ether. After usual treatments and liquid chromatography on silica gel (hexane/ether/triethylamine, 78:20:2), the desired dienediyne **9a-*E*,*E*** was obtained in 70% yield (210 mg).

(2*E*,8*E*)-1,1,10,10-Tetraethoxydeca-2,8-diene-4,6-diyne (9a-*EE*): ^{1}H NMR: δ = 1.21 (t, $^3J_{2H}$ = 7.1, 12 H), 3.49 (qd, $^3J_{3H}$ = 7.1, $^2J_{1H}$ = 9.5, 4 × 1 H), 3.63 (qd, $^3J_{3H}$ = 7.1, $^2J_{1H}$ = 9.5, 4 × 1 H), 4.97 (dd, $^3J_{1H}$ = 4.3, $^4J_{1H}$ = 1.1, 2 × 1 H), 5.94 (dd, $^3J_{1H}$ = 15.7, $^4J_{1H}$ = 1.1, 2 × 1 H), 6.23 (dd, $^3J_{1H}$ = 15.7, $^3J_{1H}$ = 4.3, 2 × 1 H). − ^{13}C NMR: δ = 15.1 (4 C), 61.1 (4 C), 75.5 (2 C), 79.3 (2 C), 99.5 (2 C), 111.9 (2 C), 143.1 (2 C). − MS; *m/z* (%): 306 (8) [$M^{\cdot+}$], 277 (10), 261 (45), 232 (15), 221 (12), 203 (12), 176 (8), 175 (20), 159 (17), 147 (16), 131 (35), 119 (11), 116 (15), 105 (11), 103 (25), 102 (13), 91 (23), 77 (49), 76 (11), 75 (19), 51 (12), 47 (14), 29 (100). − IR: $\tilde{\nu}$ = 2976−2850 cm^{-1}, 2204, 1625, 1371, 1337, 1250, 1123, 1055, 1000, 950, 845. − $C_{18}H_{26}O_4$ (306.40): calcd. C 70.56, H 8.55; found C 70.85, H 8.58 − Upon treatment with wet silica, deca-2,8-diene-4,6-diyne-1,10-dial was obtained as a crude product which could be used without further purification. − ^{1}H NMR: δ = 6.61 (dd, $^3J_{1H}$ = 16.0, $^3J_{1H}$ = 6.2, 2 × 1 H), 6.99 (dd, $^3J_{1H}$ = 16.0, $^4J_{1H}$ = 1.1, 2 × 1 H), 9.63 (dd, $^3J_{1H}$ = 6.2, $^4J_{1H}$ = 1.1, 2 × 1 H). − IR: $\tilde{\nu}$ = 3012−2850 cm^{-1}, 2132, 1677, 1625, 1598, 1290, 1118, 968, 578.

Synthesis of 4a-*Z* and 4a-*E* by Stille Cross-Coupling: In a Schlenk tube were successively added 10 mL of DMF, 2 mmol (0.84 g) of **1a-*Z***, 2.2 mmol (0.390 g) of 1-bromo-2-(trimethylsilyl)acetylene (**11**) and 0.1 mmol (0.011 g) of hydroquinone before addition of $PdCl_2(MeCN)_2$ (0.1 mmol, 0.027 g). The reaction mixture was stirred at room temperature and the advancement of the reaction was monitored by TLC until disappearance of **1a-*Z***. At the end of the reaction (about 15 h), the reaction mixture was diluted in ethyl acetate (10 mL) and vigorously stirred with a saturated aqueous solution of sodium fluoride (10 mL) in order to precipitate tributylstannyl fluoride. After filtration, extraction and drying of the organic phase with magnesium sulfate, the enyne **4a-*Z*** was obtained as a nearly chemically pure product (54%, isolated yield) which was characterized by physicochemical methods before desilylation as previously described to afford **8a-*Z*** in 60% yield after liquid chromatography (cf. desilylation reactions). The same procedure was similarly applied in order to obtain **4a-*E*** and subsequently **8a-*E***.

(*Z*)-5,5-Diethoxy-1-(trimethylsilyl)pent-3-en-1-yne (4a-*Z*): ^{1}H NMR: δ = 0.20 (s, 9 H), 1.24 (t, $^3J_{1H}$ = 7.0, 6 H), 3.58 (dq, $^3J_{3H}$ = 7.0, $^2J_{1H}$ = 9.5, 2 × 1 H), 3.71 (dq, $^3J_{3H}$ = 7.0, $^2J_{1H}$ = 9.5, 2 × 1 H), 5.35 (dd, $^3J_{1H}$ = 7.5, $^4J_{1H}$ = 0.6, 1 H), 5.69 (dd, $^3J_{1H}$ = 11.2, $^4J_{1H}$ = 0.6, 1 H), 5.95 (dd, $^3J_{1H}$ = 11.2, $^3J_{1H}$ = 7.5, 1 H). − ^{13}C NMR: δ = −0.1 (3 C), 15.4 (2 C), 62.1 (2 C), 66.0, 99.3, 100.6, 112.4, 140.3. − MS; *m/z* (%): 226 (4) [$M^{\cdot+}$], 197 (25), 182 (14), 181 (67), 153 (25), 139 (13), 137 (23), 125 (28), 103 (21), 83 (31), 79 (21), 75 (74), 73 (100), 47 (13), 45 (14), 43 (16), 29 (26). − IR: $\tilde{\nu}$ = 3065 cm^{-1}, 3032, 2956, 2924, 2872, 1653, 1599, 1496, 1465, 1378, 1330, 1160, 1100, 973, 832, 814, 764, 700, 664, 581, 548.

(*Z*)-5,5-Diethoxypent-3-en-1-yne (8a-*Z*): ^{1}H NMR: δ = 1.24 (t, $^3J_{2H}$ = 7.0, 6 H), 3.15 (dd, $^4J_{1H}$ = 2.4, $^5J_{1H}$ = 0.8, 1 H), 3.57 (dq, $^3J_{3H}$ = 7.0, $^2J_{1H}$ = 9.5, 2 × 1 H), 3.70 (dq, $^3J_{3H}$ = 7.0, $^2J_{1H}$ = 9.5, 2 H), 5.37 (br. d, $^3J_{1H}$ = 7.5, 1 H), 5.68 (br. dd, $^4J_{1H}$ = 2.4, $^3J_{1H}$ = 11.2, 1 H), 6.20 (br. dd, $^3J_{1H}$ = 11.2, $^3J_{1H}$ = 7.5, 1 H). − ^{13}C NMR: δ = 15.4 (2 C), 62.0 (2 C), 79.3, 83.2, 99.2, 111.4, 141.4. − IR: $\tilde{\nu}$ = 3299 cm^{-1}, 3266, 2977, 2932, 2874, 2100, 1630, 1386, 1319, 1118, 1056, 1002, 840, 758, 640.

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[21] In the first case, **5** is expected to have the (*E*) geometry, in agreement with the usual *syn* addition of organocopper reagents on triple bonds, while in the second case, **5** is expected to have the (*Z*) geometry after a *syn* carbopalladation.

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