A Convenient Synthesis of Symmetrically Functionalized 1,3-Dienes by Palladium(II)-Catalyzed Homocoupling of 1-Alkenylstannanes

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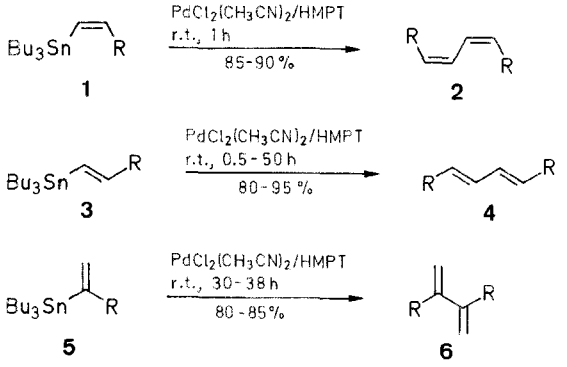
A convenient stereospecific method based on Pd(II)-catalyzed homocoupling of 1-alkenylstannanes is reported to synthesize symmetrically functionalized 1,3-dienes.

Effective stereospecific methods for the preparation of symmetric 1,3-dienes with organometallic reagents of lithium, silver, magnesium, aluminum and copper are well-known.[1] However, the described approaches are not suitable for the synthesis of functionalized 1,3-dienes. The latter were prepared from vinylmercury compounds effected by palladium(II) chloride/lithium chloride in hexamethylphosphoric triamide (HMPT).[2] The synthesis of symmetric 1,3-dienes of simple structure has been recently reported to proceed via oxidative homocoupling of 1-vinylstannanes in the presence of palladium(II) acetate.[3]

We have earlier reported a possible route to functionalized isomeric 1-vinylstannanes through regio- and stereoselective hydrostannylation of 3-hydroxy-4-aryloxy-1-butynes.[4] (*E*)-1-Alkenylstannanes thus prepared have been applied to the cuprate synthesis of ω-aryloxyprostaglandins.[5,6] The present paper presented describes a novel way of using these reagents to obtain functionalized symmetric 1,3-dienes.



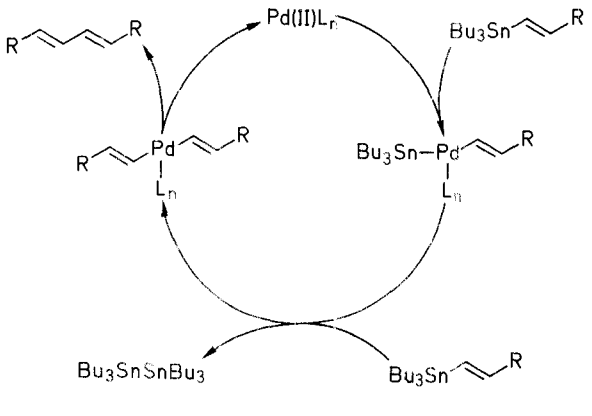
1–6	R
a	$CH_3CH_2CH_2CH_2CH_2CH(OH)$
b	$CH(OH)CH_2OPh$

3, 4	R
c	COC_5H_{11}-*n*
d	$CH_2(CH_3)C(OR')CH_2OPh$[a]
e	OTHP

[a] **3d**: R' = $SiMe_3$; **4d**: R' = H.

Alkenylstannanes **1,3** and **5** have been found to couple at room temperature in HMPT in the presence of catalytic amount of bis(acetonitrile)dichloropalladium(II) and to result in symmetric dienes **2, 4** and **6**, respectively, in 80–95% yields.

The result summarized in Table 1 demonstrate the stereochemistry of double bond to effect appreciably the reactivity of alkenylstannanes under study. Thus, comparable yields (80–90%) of (*Z,Z*)-, (*E,E*)- and α,α-dienes **2a, 4a** and **6a** have been obtained within, 1, 2, and 30 hours, respectively (for **2b, 4a, 6a**), (*Z*)-alkenylstannanes being the most active. (*E*)-Alkenyl stannanes have been studied to illustrate the dependence of homocoupling rate on the electronic and steric structure of substituent at a double bond.



The choice of solvent is of special importance for the catalytic process described. When HMPT was replaced by less polar solvents such as tetrahydrofuran and benzene, no traces of target product could be observed even after 48 hours.

Table 1. 1,3-Dienes **2, 4, 6** Prepared

Product	Reaction Time (h)[a]	Yield[b] (%)	Molecular Formula[c]	R_f[d]	K'[e] (Eluent[f])	Ratio of Diastereoisomers[g]
2a	1	90	$C_{16}H_{30}O_2$ (254.4)	0.24	–	–
2b	1	85	$C_{20}H_{22}O_2$ (294.4)	0.24	–	2 : 1 (A)
4a	2	80	$C_{16}H_{30}O_2$ (254.4)	0.23	2.23; 2.24 (A)	2 : 3 (A)
4b	2.5	80	$C_{20}H_{22}O_4$ (326.4)	0.23	2.87; 3.12 (B)	2 : 3 (A)
4c	0.25	85	$C_{16}H_{26}O_2$ (250.4)	0.62	–	–
4d	50	95	$C_{24}H_{30}O_4$ (382.5)	0.2	1.94; 2.12 (B)	1 : 2 (B)
4e	0.5	80	$C_{16}H_{26}O_4$ (282.4)	0.71	–	–
6a	30	85	$C_{16}H_{30}O_2$ (254.4)	0.27	–	3 : 2 (A)
6b	38	80	$C_{20}H_{22}O_4$ (326.4)	0.26	1.75; 2.1 (A)	3 : 2 (A, B)

[a] Time required for complete conversion of 1-alkenylstannane.
[b] For pure products isolated by chromatography.
[c] Satisfactory microanalyses obtained: C ±0.18, H ±0.1.
[d] Silufol UV-254 (CSSR), *n*-hexane/EtOAc, 1 : 1.
[e] K'-capacity factor Du-Pont-8800, Zorbax Sil (5 μc), UV-detector.
[f] *n*-Hexane/EtOAc, 70 : 30 (A) and *n*-hexane/*i*-PrOH, 95 : 5 (B) as eluents.
[g] Determined by HPLC (A) and ^{1}H-NMR (B).

Table 2. Spectral Data of Dienes **2**, **4**, **6**[a]

Product	^{1}H-NMR ($CDCl_3$/TMS)[b] δ, J(Hz)	^{13}C-NMR ($CDCl_3$/TMS)[c] δ
2a	0.88 (t, 6H, J = 6.6, H-1, H-16); 1.14–1.9 (m, 16H, H-2–H-5, H-12–H-15); 1.98 (br s, 2H, OH); 4.38–4.7 (m, 2H, H-6, H-11); 5.35–5.62 (m, 2H, H-7, H-10); 6.2–6.5 (m, 2H, H-8, H-9)	14.4 (q, C-1, C-16); 22.63 (t, C-2, C-15); 24.9 (t, C-4, C-13); 31.75 (t, C-3, C-14); 37.43 (t, C-5, C-12); 67.55 (d, C-6, C-11); 124.64 (d, C-8, C-9); 135.69 (d, C-7, C-10)
2b	3.96 (d, 2H, J = 5.4, H-1, H-8); 3.97 (d, 2H, J = 6.1, H-1, H-8); 4.33 (d, 2H, J = 4.2, OH); 5.04 (m, 2H, H-2, H-7); 5.63 (td, 2H, J = −1.9, 7.8, 8.2, H-3, H-6); 6.55 (m, 2H, H-4, H-5); 6.9–7.35 (m, 5H$_{arom}$)	66.79 (d, C-2, C-7); 71.56 (t, C-1, C-8); 126.66 (d, C-4, C-5); 131.8 (d, C-3, C-6); 114.6, 121.19, 129.47, 158.3 (d, d, d, s, C$_{arom}$)
4a	0.89 (t, 6H, J = 6.5, H-1, H-16); 1.08–1.85 (m, 16H, H-2–H-5, H-12–H-15); 2.12 (br s, 2H, OH); 4.1 (q, 2H, J = 7, H-6, H-11); 5.5–5.85 (m, 2H, H-7, H-10); 6.05–6.35 (m, 2H, H-8, H-9)	14.04 (q, C-1, C-16); 22.63 (t, C-2, C-15); 25.1 (t, C-4, C-13); 31.79 (t, C-3, C-14); 37.25 (t, C-5, C-12); 72.56 (d, C-6, C-11); 129.64 (d, C-8, C-9); 136.42 (d, C-7, C-10)
4b	3.83 (dd, 2H, J = 6.6, 9.6, H-1, H-8); 3.93 (dd, 2H, J = 4.6, 9.6, H-1, H-8); 4.29 (d, 2H, J = 4.7, OH); 4.45 (m, 2H, H-2, H-7); 5.8 (m, 2H, H-3, H-6); 6.83 (m, 2H, H-4, H-5); 6.75–7.33 (m, 5H$_{arom}$)	70.69 (d, C-2, C-7); 73.17 (t, C-1, C-8); 131.2 (d, C-4, C-5); 134.11 (d, C-3, C-6); 115.3, 121.19, 129.99, 160.11 (d, d, d, s, C$_{arom}$)
4c	0.88 (t, 6H, J = 6.7, H-1, H-16); 1.33 (m, 8H, H-2, H-3, H-14, H-15); 1.62 (m, 4H, H-4, H-13); 2.65 (t, 4H, J = 7.2, H-5, H-12); 6.6 (m, 2H, H-7, H-10); 7.3 (m, 2H, H-8, H-9)	
4d	2.04 (s, 6H, CH_3); 2.41 (d, 4H, J = 7.3, H-3, H-8); 2.54 (br s, 2H, OH); 4.05 (d, 2H, J = 7.05, H-1, H-10); 3.97 (d, 2H, J = 6.4, H-1, H-10); 4.17 (d, 2H, J = 7.05, H-1, H-10); 4.08 (d, 2H, J = 6.4, H-1, H-10); 5.63 (m, 2H, H-4, H-7); 6.07 (m, 2H, H-5, H-6); 6.81–7.34 (m, 5H$_{arom}$)	23.84 (q, CH_3); 42.12 (t, C-3, C-8); 71.9 (s, C-2, C-9); 74.17 (t, C-1, C-10); 127.27 (d, C-4, C-7); 133.72 (d, C-5, C-6); 114.8, 121.18, 129.59, 159.4 (d, d, d, s, C$_{arom}$)
4e	1.6 (m, 12H, CH_2); 3.2–3.8 (m, 4H, CH_2O); 3.8–4.3 (m, 4H, H-1, H-6); 5.35–5.9 (m, 4H, H-2, H-5); 6.08, 6.45 (m, 4H, H-3, H-4)	19.42 (t), 25.44 (t), 30.6 (t), 62.11 (t); 97.74 (d); 67.1 (t, C-1, C-6); 131.85 (d, C-2, C-5); 129.73 (d, C-3, C-4)
6a	0.9 (t, 6H, J = 6.5, H-1, H-16); 1.02–1.7 (m, 12H, H-2–H-4, H-13–H-15); 2.0–2.7 (m, 4H, H-5, H-12); 3.35 (br s, 2H, OH); 4.54, 4.72 (m, 2H, H-6, H-11); 4.88–5.07 (m, 4H, H-8, H-10)	14.03 (q, C-1, C-16); 22.59 (t, C-2, C-15); 25.41 (t, C-4, C-13); 31.7 (t, C-3, C-14); 35.42, 36.08 (t, C-5, C-12); 74.17, 73.25 (d, C-6, C-11); 114.37, 112.91 (t, C-8, C-10); 150.46, 150.89 (s, C-7, C-9)
6b	3.9 (dd, 2H, J = −9.8, 5.4, H-1, H-8); 4.06 (dd, 2H, J = −9.8, 6.1, H-1, H-8); 4.35, 4.56 (m, 2H, H-2, H-7); 5.89 (d, 2H, J = 10.4, H-4, H-7); 6.11, 6.16 (dd, J = 2.1, 2.4, 10.4, H-4, H-7)	72.36 (t, C-1, C-8); 72.45, 71.58 (d, C-2, C-7); 114.88, 113.8 (t, C-4, C-6); 148.26, 148.02 (s, C-3, C-5); 115.42, 121.39, 130.18, 159.88, 159.8 (d, d, d, s, C$_{arom}$)

[a] A pair of chemical shifts in place of one for a single proton or carbon in compounds **2d**, **6a** and **b** in ^{1}H- and ^{13}C-NMR spectra, respectively, denotes diastereoisomeric pairs.

[b] Recorded at 100 MHz on a BS-567 NMR spectrometer.

[c] Recorded at 22.5 MHz on a Jeol FX 90q NMR spectrometer.

[d] Measured in acetone-d_6.

It occurs evidently due to high dissolution and ionization ability of HMPT towards organotin compounds.[7] Another function of HMPT consists probably in retaining the palladium catalyst in its active state. Phosphine complexes of palladium(0), e.g. tetrakistriphenylphosphine palladium, reveal no catalytic effect in the reaction described. The hypothetical reaction mechanism for homocoupling of vinylstannanes involves double transmetalation followed by reductive elimination.

According to ^{1}H- and ^{13}C-NMR spectral data (Table 2), homocoupling of 1-vinylstannanes **1**, **3**, **5** proceeds exclusively with retention of the configuration of the double bond in the initial vinylstannane. The ratios of diastereomeric pairs of dienic diols **2**, **4**, **6** have been successfully estimated. One of the diastereoisomers has been found to prevail always (Table 1). Those diastereoisomers can be differentiated in ^{13}C- and ^{1}H-NMR spectra with 2,3-disubstituted butadienes **6a, b** only (Table 2).

In summary, the method presented here to synthesize symmetric 1,3-dienes has been considered useful owing to its stereospecifity, high yields, and experimental simplicity. The availability of starting vinylstannanes and the tolerance of their functional groups for the reaction under study make it quite advantageous for the preparation of symmetrically functionalized 1,3-dienes.

1-Alkenylstannanes **1**, **3** and **5** were prepared by the standard procedure.[4] Alkenylstannane **3c** was prepared from the corresponding alcohol by oxidation with chromic acid.[8]

1,3-Dienes 2, 4 and 6; General Procedure:

A solution of the appropriate vinylstannane **1**, **3** or **5** (1 mmol) in anhydrous HMPT (4 mL) containing 5 mol% of bis(acetonitrile)palladium dichloride is kept at room temperature in an argon atmosphere until the complete conversion of initial vinylstannane as monitored by TLC. The reaction mixture is then diluted with ether (30 mL), washed with 5% HCl (2 × 5 mL), brine (2 × 5 mL), dried ($MgSO_4$), and evaporated. Dienes **2**, **4** and **6** are isolated subsequently to evaporation by column chromatography of the residue on silica gel (*n*-hexane/EtOAc, 1:1).

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