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Palladium-Catalyzed Regioselective Coupling of Propargylic Substrates with Terminal Alkynes. Application to the Synthesis of 1,2-Dien-4-ynes

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Abstract—The palladium-catalyzed reaction of propargyl halides, tosylates and acetates with terminal alkynes is reported. The best yields are obtained from propargyl chlorides and l-alkynes (i) in the presence of 2 equiv. of amine (triethylamine, diisopropylamine) in benzene, toluene or ethylacetate (ii) or in pure diisopropylamine. Propargyl acetates undergo the cross coupling reaction with moderate to high yields after modification of the general procedure.

Palladium(0) complexes are versatile catalysts for cross coupling reactions and play an important role in organic synthesis.[1] In our laboratory, we had studied the preparation of allenynes[2] by reaction of allenic halides with terminal alkynes in the presence of catalytic amounts of tetrakis[triphenylphosphine]palladium and copper(I) iodide in diethylamine at room temperature. A synthesis of allenynes[3,4] was also described by Tsuji from 2-alkynyl carbonates and terminal acetylenes.[5,6] Our interest in the development of synthetic methods based on palladium catalysis[7–10] stimulated us to examine the reactivity of propargylic halides, tosylates and acetates[11] with terminal alkynes in the presence of palladium-complexes. Usually propargylic halides undergo 1,1 or 1,3 substitution reaction[12–16] when treated with organometallic compounds.

We thus found a mild and convenient method[17] for the preparation of a large variety of substituted allenynes (1,1-disubstituted, 1,3-disubstituted, tri- and tetrasubstituted allenynes).

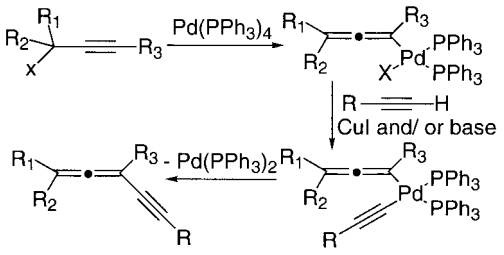
We have shown that this new procedure tolerates sensitive functional groups and is highly regioselective: pure allenynes were obtained without formation of 1,4-diyne isomers. The reaction most likely proceeded via an organopalladium complex which arose by oxidative addition of propargyl compound to the catalyst (Scheme 1) reaction with the acetylide and subsequent reductive elimination to give the allenyne.

This paper deals with a systematic study of the effects of reaction conditions which was carried out in order to optimize and generalize this procedure.

We first decided to examine the reactivity of propargyl halides under the standard reaction conditions reported for the synthesis of enynes from alkenyl halides with alkynes.[7–10] Under these conditions, the reaction of 1-chloro-2-octyne with trimethyl silylacetylene gave allenyne *2* in moderate yield (Scheme 2).

The standard reaction chosen for the study is shown in Scheme 3. Reaction conditions and yields are reported in Table 1.

The cross coupling reaction of 1-chloro-2-octyne **1a** with 1-heptyne was very sensitive to the nature of the amine (2 equiv.) when performed in the presence of $Pd(PPh_3)_4$-CuI as catalysts and benzene as solvent (entries 1–7). The best results were obtained with diethylamine (60%), diisopropylamine (88%) and triethylamine (79%). With pyridine (2 equiv.) or quinoline (2 equiv.), no allenyne was formed and the starting materials were recovered after 6 h at 20°C.



Scheme 1.

Keywords: palladium-catalyzed; allene; propargyl halides.

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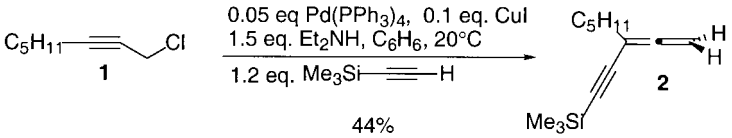
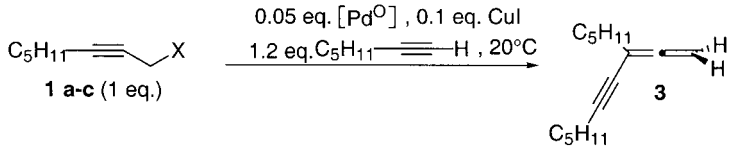


Scheme 2.



Scheme 3.

Table 1. Influence of the palladium catalyst, amine and solvent on the regioselective cross coupling reaction of 1-heptyne with primary propargyl halides **1a–c**

Entry	Starting material	X	Catalyst[a]	Amine (2 equiv.)	Solvent	Time (h)[b]	Isolated yield (%)[c]
1	**1a**	Cl	$Pd(PPh_3)_4$	*n*-Butylamine	C_6H_6	7	5[d]
2	**1a**	Cl	$Pd(PPh_3)_4$	Diethylamine	C_6H_6	6	60
3	**1a**	Cl	$Pd(PPh_3)_4$	Diisopropylamine	C_6H_6	3	88
4	**1a**	Cl	$Pd(PPh_3)_4$	Piperidine	C_6H_6	8	12[d]
5	**1a**	Cl	$Pd(PPh_3)_4$	Tri *n*-propylamine	C_6H_6	10	21[d]
6	**1a**	Cl	$Pd(PPh_3)_4$	*N*,*N*-Diisopropyl ethylamine	C_6H_6	24	14[d]
7	**1a**	Cl	$Pd(PPh_3)_4$	Triethylamine	C_6H_6	3	79
8	**1a**	Cl	$Pd(PPh_3)_4$	Triethylamine	THF	7	31
9	**1a**	Cl	$Pd(PPh_3)_4$	Triethylamine	Et_2O	7	31
10	**1a**	Cl	$Pd(PPh_3)_4$	Triethylamine	$CH_3C_6H_5$	3	79
11	**1a**	Cl	$Pd(PPh_3)_4$	Triethylamine	CH_3CO_2Et	3	79
12	**1a**	Cl	$Pd(PPh_3)_4$	–	Diisopropylamine	1.5	88
13	**1a**	Cl	$Pd(PPh_3)_4$	–	Triethylamine	4	79
14	**1a**	Cl	$Pd(PPh_3)_2Cl_2$	–	Diisopropylamine	2	85.5
15	**1a**	Cl	$PdCl_2+2PPh_3$	–	Diisopropylamine	1	92 (0)[e]
16	**1a**	Cl	$Pd(C_6H_5CN)_2Cl_2+2PPh_3$	–	Diisopropylamine	1	88 (0)[e]
17	**1a**	Cl	$Pd(OAc)_2+2PPh_3$	–	Diisopropylamine	1	92 (0)[e]
18	**1b**	Br	$Pd(PPh_3)_4$	Triethylamine	C_6H_6	3.5	15
19	**1b**	Br	$Pd(PPh_3)_4$	–	Diisopropylamine	1	51
20	**1c**	OTs	$Pd(PPh_3)_4$	Triethylamine	C_6H_6	3	25 (31)[f]
21	**1c**	OTs	$Pd(PPh_3)_4$	–	Diisopropylamine	2.5	69 (71)[f]

[a] All reactions were performed with 0.1 equiv. of CuI catalyst.
[b] Reaction times were monitored by GC.
[c] **3** is a colourless liquid.
[d] Propargyl halide was not completely consumed after the reaction time indicated.
[e] Reaction performed in the absence of PPh_3.
[f] In the presence of LiCl (2 equiv.).

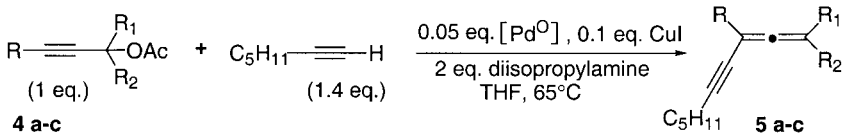
Although the role of the amine is yet unclear, its participation in the formation of acetylide-copper[12,13,18,19] is usually retained.

Inspection of Table 1 shows the great influence of the solvent when the reaction was performed with 2 equiv. of triethylamine (entries 7–11). Acetonitrile, dichloromethane, and *N*,*N*-dimethylformamide gave poor results (5–8%). Benzene could be replaced by toluene or ethyl acetate (entries 10–11). We also found that the preparation of allenyne compounds from primary propargyl halides (or tosylates) and 1-heptyne could be achieved in amine as a solvent such as diisopropylamine or triethylamine (entries 12–13, 19, 21). Acceleration of the reaction was apparent by using diisopropylamine (entries 3, 12).

The role of palladium(0) and copper(I) was evidenced in diisopropylamine as solvent. It was found that no reaction takes place without palladium or without palladium-copper salt catalysts. However, when the palladium(0) catalyst was used alone, a small amount of cross coupling product was observed (14% isolated yield). Other types of palladium complexes were also tested. We found that $PdCl_2$, $Pd(0Ac)_2$ or $Pd(C_6H_5CN)Cl_2$ in the absence of triphenylphosphine did not catalyze the coupling reaction (entries 15–17). An almost quantitative coupling was then obtained by the addition of 2 equiv. of triphenylphosphine as ligand for one equivalent of palladium. The possibility to prepare in situ an efficient Pd(0) catalyst is interesting since success in such catalyzed reactions depends on the quality of the palladium(0) complex: thus, $Pd(PPh_3)_4$ had to be stored under argon whereas the catalyst precursors $PdCl_2$ or $Pd(0Ac)_2$ could be stored without any particular care.

The nature of the leaving group was also very important. Propargyl chlorides gave better results than propargyl

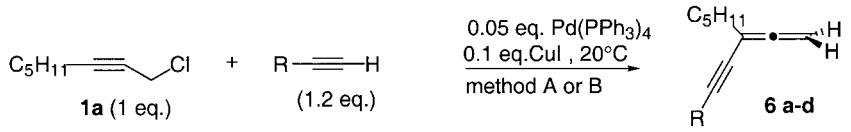
Table 2. Regioselective synthesis of allenynes from propargyl acetates and 1-heptyne in refluxing THF



Entry	Acetates>				Conditions	Product N^0	Time (h)	Isolated yield[a] (%)
	R	R^1	R^2	N^0				
1	C_5H_{11}	H	H	4a	$ZnCl_2$ (3 equiv.)	5a	7	52 (63)[b]
2	C_4H_9	Et	H	4b	$ZnCl_2$ (3 equiv.)	5b	4	74
3	C_4H_9	CH_3	CH_3	4c	LiCl (2 equiv.)	5c	6	42
4	C_4H_9	CH_3	CH_3	4c	$ZnCl_2$ (3 equiv.)	5c	3	74.5 (68)[b]

[a] All products are oils.
[b] Reaction performed in the absence of CuI.

Table 3. Regioselective synthesis of functionalized 1,1-disubstituted allenynes from 1-chloro-2-octyne and terminal alkynes



Entry	R	Method[a]	Time (h)	Product N^0	Isolated yield[b] (%)
1	Me_3Si	A	3	6a	60.5
2	Me_3Si	B	0.5	6a	84
3	$(CH_2)_3CO_2Me$	A	3	6b	69
4	$(CH_2)_3CO_2Me$	B	2	6b	69
5	$(CH_2)_2OH$	A	4.5	6c	53
6	$(CH_2)_2OH$	B	1	6c	80.5
7	CH_2OH	A	3.5	6d	29
8	CH_2OH	B	1.5	6d	73.5

[a] Method A: reaction performed in benzene with triethylamine (2 equiv.); method B: reaction performed in diisopropylamine.
[b] All products are oils.

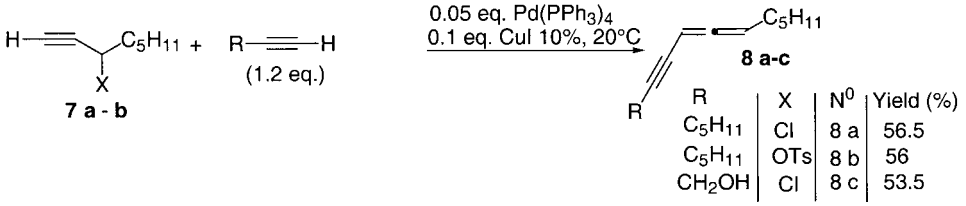
tosylates or bromides (entries 12, 19, 21). In addition, comparison of experiments carried out in pure diisopropylamine with those in benzene-2 equiv. triethylamine indicated that the reaction proceeded faster and with higher yields in pure diisopropylamine (entries 7, 12, 18–21).

Propargyl acetates were unreactive; however, they could be activated by the addition of zinc chloride or lithium chloride as mentioned in the literature[20,21] (Table 2).

The best results were obtained with $ZnCl_2$ in refluxing THF. Secondary and tertiary propargyl acetates gave good yields of coupling products, primary propargyl acetates were less reactive. Interestingly, we observed that the reaction could proceed without the presence of copper iodide. Presumably zinc acetylide was formed in situ and then underwent cross coupling reaction.

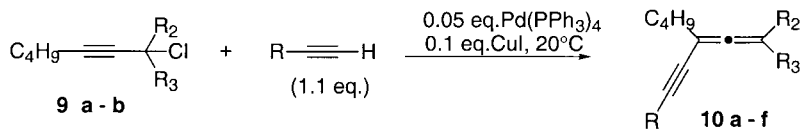
Table 3 illustrates the generality of the procedure for the synthesis of 1,1-disubstituted allenes from 1-chloro-2-octyne and functionalized terminal acetylenes. Satisfactory results were obtained with both methods A (benzene-2 equiv. of triethylamine) and B (diisopropylamine as solvent). The use of method B for the preparation of allenynols gave shorter reaction times and higher yields (entries 5–8).

Method B gave 1,3-disubstituted allenes (Scheme 4) in moderate yields (25%, R=C_5H_{11}; X=Cl). Another product, *N*,*N*-diisopropyl-3-amino-1-octyne, was formed in 56% yield by the reaction of diisopropylamine with the propargyl halide. The yields of the coupling product was considerably improved by slowly adding propargyl halide in benzene to a mixture of terminal alkyne, $Pd(PPh_3)_4$ 5%-CuI 10% in diisopropylamine (Scheme 4). Our results are comparable



Scheme 4. Regioselective synthesis of 1,3-disubstituted allenes from 3-chloro-1-octyne.

Table 4. Regioselective syntheses of tri- and tetrasubstituted allenes



Entry	Propargyl chlorides			R	Conditions[a]	Time (h)	Product N[0]	Yield[b] (%)
	R^2	R^3	N[0]					
1	H	Et	9a	C_5H_{11}	Method B	1	10a	91
2	H	Et	9a	C_5H_{11}	Method A	2	10a	91.5
	H	Et	9a	C_5H_{11}	Et_3N 2 equiv. in AcOEt	1.5	10a	92
3	H	Et	9a	$(CH_2)_3CO_2Me$	Method A	2	10b	85
4	H	Et	9a	$(CH_2)_2OH$	Method A	3	10c	86
5	CH_3	CH_3	9b	C_5H_{11}	Method B	1	10d	90
6	CH_3	CH_3	9b	C_5H_{11}	Method A	1.5	10d	93
	CH_3	CH_3	9b	C_5H_{11}	Et_3N 2 equiv. in AcOEt	1	10d	86
7	CH_3	CH_3	9b	$(CH_2)_3CO_2Me$	Method A	2.5	10e	87
8	CH_3	CH_3	9b	$(CH_2)_2OH$	Method A	2	10f	93.5

[a] Method A: reaction performed in benzene with triethylamine (2 equiv.); method B: reaction performed in diisopropylamine.
[b] Isolated yields, all products are oils.

with those of J. Goré and R. Baudouy[22] for the synthesis of *n*-tetradeca-4,5-dien-2-yn-1-ol, an intermediate in the synthesis of an insect pheromone.

The coupling reaction of secondary and tertiary propargyl chlorides with terminal alkynes gave good yields of tri- and tetrasubstituted allenes. The two methods are valuable for the preparation of branched allenes. High yields were obtained by using method A (Table 4). It is worth noting that allenynols can be prepared by the two methods.

In summary, the procedure described herein provides an interesting approach for the preparation of a large variety of substituted allenes. The reaction proceeds cleanly under mild conditions, tolerates sensitive functional groups and is highly regioselective. From the results of this investigation, it appears that different experimental conditions can be proposed for the cross coupling. Generally the reaction can be carried out in benzene, ethylacetate, and toluene, with 2 equiv. of amine (diethylamine, triethylamine, diisopropylamine), or in pure amine (triethylamine, diisopropylamine). We have shown that $PdCl_2$ and $Pd(OAc)_2$ can be used with triphenylphosphine instead of $Pd(PPh_3)_4$. The nature of the propargyl halide is important. Chlorides are the most appropriate but acetates can also be used.

Experimental

General

^1H and ^{13}C spectra were recorded on a Bruker VM 250 or AM 400 instrument ($CDCl_3$, δ (ppm), J (Hz)). Mass spectra were determined on a Nermag R 10/10 instrument in a NH_3 chemical ionisation mode. IR spectra were measured on a Perkin Elmer 599 spectrophotometer (neat, cm^{-1}). Purity of products was determined by gas chromatographic analyses performed on a Girdel equipped with capillary column (SGE 50 QC2/BP5 0.25). Products were purified by distillation or by column chromatography (silica gel 60 230–400 mesh). All glassware was oven-dried at 140°C and all reactions were conducted under argon atmosphere. Boiling points are uncorrected. Tetrahydrofuran was distilled from sodium and benzophenone. Benzene and toluene were distilled over CaH_2. Ethyl acetate was used without further purification. Diethylamine, *n*-butylamine, and *N*,*N*-diisopropylamine, piperidine, tri-*n*-propylamine, *N*,*N*-diisopropylethylamine were distilled over potassium hydroxide. 2-octyn-1-ol,[23] non-4-yn-3-ol,[23] 2-methyl-oct-3-yn-2-ol[23] and 1-bromo-2-octyne[24] were prepared by known procedures. $PdCl_2$ and $Pd(OAc)_2$ are commercial products. $Pd(PPh_3)_4$,[25] $Pd(C_6H_5CN)_2Cl_2$,[26] and $Pd(PPh_3)_2Cl_2$[27] were prepared by known procedures. Lithium and zinc chloride were dried at 200°C in high vacuum.

General procedure for the syntheses of allenynes from propargyl halides

Method A. Under an argon atmosphere, to a degassed solution of propargyl halide (2.75 mmol) in 3 ml of benzene, tetrakis[triphenylphosphine]palladium (0.05 equiv.) was rapidly added at room temperature. After stirring for 5 min, a solution of alkyne (1.1–1.2 equiv.) in 2 ml of benzene, copper iodide (0.1 equiv.) and triethylamine (2 equiv.) was added successively. After the time indicated in Table 3 or 4, the reaction mixture was diluted with 1:1 ether/pentane (20 ml), then the organic phase was washed twice with saturated aqueous ammonium chloride solution (10 ml), dried over magnesium sulfate and evaporated. The crude product was purified by flash chromatography.

Method B. Under an argon atmosphere, to a degassed solution of propargyl halide (2.75 mmol) in 3 ml of diisopropylamine, tetrakis[triphenylphosphine]palladium (0.05 equiv.) was rapidly added at room temperature. After stirring for 5 min, a solution of alkyne (1.1–1.2 equiv.) in 2 ml of diisopropylamine and copper iodide (0.1 equiv.) was added successively. After the reaction time indicated in Table 3 or 4, the reaction mixture was diluted with 1:1 ether/pentane (20 ml), then the organic phase was washed twice with saturated aqueous ammonium chloride solution (10 ml),

dried over magnesium sulfate and evaporated. The crude product was purified by flash chromatography.

General procedure for the preparation of allenynes 5 from propargyl acetates 4

Under an argon atmosphere, tetrakis[triphenylphosphine]-palladium (0.05 equiv.) was added rapidly to a solution of propargyl acetate (1 mmol) in 1 ml of tetrahydrofuran at 20°C. Then a solution of $ZnCl_2$ (3 equiv.) in 2 ml of tetrahydrofuran was added and the mixture was stirred for 5 min at 20°C. After the addition of diisopropylamine (2 equiv.) and copper iodide (0.1 equiv.), the reaction mixture was heated to refluxing tetrahydrofuran and a solution of alkyne (1.4 equiv.) was added slowly (addition time: 1 h). After the reaction time indicated in the Table 2, reaction mixture was cooled with an ice bath, diluted in diethylether (20 ml) and washed twice with an aqueous ammonium chloride solution (10 ml). The organic layer was dried over magnesium sulfate and evaporated. The crude product was purified by flash chromatography.

Procedure for the preparation of 1,3-disubstituted allenes

Synthesis of 8a. To a mixture of tetrakis[triphenylphosphine]palladium (0.08 g; 0.069 mmol) and copper iodide (0.026 g; 0.136 mmol) in 4 ml of diisopropylamine, at room temperature, under an argon atmosphere, was added a solution of 1-heptyne (0.16 g; 1.656 mmol) in 3 ml of diisopropylamine and very slowly (addition time 40 min) 3-chloro-1-octyne **7a** (0.20 g; 1.384 mmol) in solution in 4.5 ml of benzene. The reaction was stirred 20 min after the end of the addition and then diluted in 20 ml of diethylether, washed twice with saturated aqueous ammonium chloride solution (10 ml), dried over magnesium sulfate and evaporated. Purification by column chromatography (eluent: pentane) afforded 0.16 g (56.5%) of **8a**.

1-Chloro-2-octyne 1a. This was obtained from 2-octyn-1-ol according to the method described for the synthesis of 1-chloro-2-heptyne.[28] To a solution of alcohol (3.15 g; 25 mmol) and pyridine (0.29 g; 3.71 mmol) in 7 ml of diethylether cooled at −20°C, was added thionylchloride (3.75 g; 30 mmol) while keeping the temperature below −20°C. The mixture was stirred for 12 h at room temperature (20°C). The mixture was then cautiously poured into a sodium hydrogen carbonate solution (2 g/30 ml water) and extracted with diethylether (2×20 ml). These extracts were combined, dried ($MgSO_4$) and evaporated. Reduced pressure fractional distillation afforded 3 g (84%) of **1a**, bp 45°C/3 mm Hg. IR (neat) cm^{-1}: 2960, 2920, 2860, 2230, 1470, 1260, 1150; ^1H NMR: δ 4.15 (t, 2H, J=2.5 Hz), 2.23 (tt, 2H, J=6.9 Hz, J=2.5 Hz), 1.52 (quin, 2H, J=7.2 Hz), 1.41–1.27 (m, 4H), 0.9 (t, 3H, J=7.5 Hz); ^{13}C NMR: δ 87.5, 74.8, 31.1, 30.9, 28.0, 22.0, 18.6, 13.7; Anal. Calcd for $C_8H_{13}Cl$: C, 66.43; H, 9.06. Found: C, 66.62; H, 9.10.

1-Tosyloxy-2-octyne 1c. To a solution of *p*-toluenesulfonylchloride (5.24 g; 27.50 mmol) and 2-octyn-2-ol (3.15 g; 25 mmol) in 40 ml of diethylether cooled at −10°C, was added freshly fine powdered potassium hydroxide (10.40 g; 185 mmol) portionwise while keeping temperature below −10°C. The mixture was stirred at −5°C for 1 h and then poured into ice water (50 ml). After vigorous shaking, the layers were separated and the aqueous layer was extracted twice with small portions of diethylether. The combined organic layers were washed with brine and dried over $MgSO_4$. After the solvent was removed on a rotary evaporator, 7 g (100%) of the title compound **1c** was obtained without further purification. IR (neat) cm^{-1}: 2950, 2920, 2870, 2860, 2300, 2230, 1600, 1480, 1450, 1370, 1190, 1175; ^1H NMR: δ 7.80 (d, 2H, J=8.3 Hz), 7.33 (d, 2H, J=8.3 Hz), 4.68 (t, 2H, J=2.2 Hz), 2.45 (s, 3H), 2.05 (tt, 2H, J=7.0 Hz, J=2.2 Hz), 1.40–1.20 (m, 6H), 0.85 (t, 3H, J=6.6 Hz); ^{13}C NMR: δ 144.7, 133.1, 129.5, 127.8, 90.3, 71.6, 58.6, 30.6, 27.5, 21.8, 21.3, 18.3, 13.6; MS: *m*/*z* (%) 298 (100%, M+18); 281 (M+1).

1-Acetoxy-2-octyne 4a. To a solution of 2-octyn-1-ol (1.26 g; 10 mmol) in 1.7 ml of pyridine, acetic anhydride (2.04 g; 20 mmol) was added at −10°C. The temperature was allowed to rise to 0°C and the mixture was stirred for 12 h at 0°C. The reaction was quenched with water, extracted with diethylether, and dried over $MgSO_4$. After removal of the solvent, reduced pressure fractional distillation afforded 1.54 g (91.5%) of **4a**. Bp 103°C/15 mm Hg. IR (neat) cm^{-1}: 2960, 2920, 2860, 2220, 1745, 1380, 1220, 1030; ^1H NMR: δ 4.66 (t, 2H, J=2.2 Hz), 2.22 (tt, 2H, J=7.1 Hz, J=2.2 Hz), 2.09 (s, 3H), 1.46–1.58 (m, 2H), 1.27–1.41 (m, 4H), 0.9 (t, 3H, J=7.1 Hz); ^{13}C NMR: δ 170.0, 87.3, 73.7, 52.5, 30.8, 27.9, 21.9, 20.5, 18.5, 13.6; MS: *m*/*z* (%) 186 (100%, M+18); Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.58. Found: C, 71.28; H, 9.75.

3-Acetoxy-4-nonyne 4b. Following the same procedure described above for the synthesis of **4a**, non-4-yn-3-ol (1.40 g; 10 mmol) was transformed into **4b** (1.66 g; 91.5%) bp 92°C/15 mm Hg. IR (neat) cm^{-1}: 2960, 2920, 2860, 2220, 1740, 1460, 1370, 1230, 1020; ^1H NMR: δ 5.31 (tt, 1H, J=6.5 Hz, J=2.0 Hz), 2.22 (td, 2H, J=6.9 Hz, J=2.0 Hz), 2.08 (s, 3H), 1.75 (quin, 2H, J=7.1 Hz), 1.30–1.58 (m, 4H), 1.00 (t, 3H, J=7.4 Hz), 0.91 (t, 3H, J=7.1 Hz); ^{13}C NMR: δ 170.2, 86.2, 77.2, 65.7, 30.5, 28.3, 21.9, 21.1, 18.3, 13.6, 9.3; MS: *m*/*z* (%) 200 (M+18), 183 (M+1); %); Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.63; H, 10.11.

2-Acetoxy-2-methyl-3-octyne 4c. Based on a procedure described by A. Hassner,[29] to a mixture of 2-methyl-3-octyn-2-ol (1 g; 7.00 mmol), triethylamine (1.73 g; 17.09 mmol) and 4-dimethylaminopyridine (52 mg; 0.43 mmol), acetic anhydride (1.74 g; 17.09 mmol) was added dropwise. The mixture was stirred for 14 h at room temperature, hydrolyzed with saturated ammonium chloride solution, extracted with diethylether and dried over $MgSO_4$. Reduced pressure fractional distillation afforded 1.11 g (85.5%) of **4c**. Bp 77°C/15 mm Hg. IR (neat) cm^{-1}: 2980, 2960, 2920, 2220, 1740, 1460, 1360, 1240, 1010; ^1H NMR: δ 2.20 (t, 2H, J=6.9 Hz), 2.01 (s, 3H), 1.64 (s, 6H), 1.50–1.58 (m, 4H), 0.9 (t, 3H, J=7.1 Hz); ^{13}C NMR: δ 169.4, 84.6, 81.3, 72.6, 30.6, 29.3, 22.1, 21.6, 18.3, 13.6; MS: *m*/*z* (%) 200 (M+18), 183 (M+1); 140 (100%); Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.42; H, 9.84.

3-Chloro-1-octyne 7a. This was obtained according to the method described for the synthesis of 3-chloro-1-butene.[30] A solution of triphenylphosphine (8.52 g; 32.50 mmol) and 1-octyn-3-ol (3.15 g; 25.00 mmol) in 12 ml of tetrachloromethane was stirred for 3 days at 20°C. The crude suspension was filtered through a short silica gel column and the precipitate was rinsed with diethylether. The organic layers were collected and the solvent removed. Purification by column chromatography (eluent: pentane/ethylacetate: 98:2) afforded 2.52 g (70%) of **7a**. IR (neat) cm^{-1}: 3300, 2960, 2920, 2860, 1460, 1380; ^1H NMR: δ 4.51 (td, 1H, J=6.7 Hz, J=2.3 Hz), 2.60 (d, 1H, J=2.3 Hz), 1.86–2.02 (m, 2H), 1.44–1.63 (m, 2H), 1.20–1.43 (m, 4H), 0.91 (t, 3H, J=6.8 Hz); ^{13}C NMR: δ 82.1, 74.2, 47.9, 39.0, 31.0, 25.8, 22.5, 14.0.

3-Tosyloxy-1-octyne 7b. Following the same procedure described above for the synthesis of **1c**, 1-octyn-3-ol (3.15 g; 24.96 mmol) was transformed into **7b** (6.98 g; 100%). IR (neat) cm^{-1}: 3300, 2960, 2920, 2860, 2120, 1600, 1360, 1170; ^1H NMR: δ 8.38 (d, 2H, J=8.4 Hz), 7.34 (d, 2H, J=8.2 Hz), 5.06 (td, 1H, J=6.5 Hz, J=2.0 Hz), 2.46 (s, 3H), 2.40 (d, 1H, J=2.3 Hz), 1.82 (m, 2H), 1.35–1.47 (m, 2H), 1.27–1.35 (m, 4H), 0.87 (t, 3H, J=6.8 Hz); ^{13}C NMR: δ 144.8, 133.8, 129.6, 128.0, 79.0, 76.1, 71.1, 35.5, 30.9, 24.1, 22.3, 21.6, 13.8; MS: *m*/*z* (%) 298 (100%, M+18).

3-Chloro-4-nonyne 9a. Following the same procedure described above for the synthesis of 3-chloro-1-octyne **7a**, non-4-yn-3-ol (2.00 g; 0.28 mmol) was transformed into **9a** (1.47 g; 64%), bp 47°C/6 mm Hg. IR (neat) cm^{-1}: 2960, 2920, 2860, 2240, 1460; ^1H NMR: δ 4.53 (tt, 1H, J=6.3 Hz, J=2.1 Hz), 2.24 (td, 2H, J=6.9 Hz, J=2.1 Hz), 1.87–2.00 (m, 2H), 1.31–1.60 (m, 4H), 1.08 (t, 3H, J=7.3 Hz), 0.91 (t, 3H, J=7.1 Hz); ^{13}C NMR: δ 78.3, 87.1, 50.8, 32.8, 30.5, 21.8, 18.3, 13.4, 10.4; MS: *m*/*z* (%) 176 (M+18), 158 (M); 81 (100%).

2-Chloro-2-methyl-3-octyne 9b. Based on a procedure described by Hennion and Boisselle[31] which was modified by replacing the mass of CuCl by the same mass of $CuCl_2$. To a mixture of $CaCl_2$ (1.11 g; 10 mmol), $CuCl_2$ (0.8 g) and copper powder (10 mg; 0.16 mmol) in concentrated hydrochloric acid (8.60 ml; 103 mmol), 2-methyl-3-octyn-2-ol (2.78 g; 19.86 mmol) was added dropwise at 0°C. After stirring for 1 h at 20°C the mixture was diluted in diethylether. The layers were separated and the organic layer washed twice with distilled water and dried over potassium carbonate. Distillation under reduced pressure afforded 2.75 g (87%) of **9b** with the presence of 8% of chloroallene isomer as determinated by GC, bp 35°C/2 mm Hg. IR (neat) cm^{-1}: 2960, 2920, 2860, 2225, 1460, 1380; ^1H NMR: δ 2.22 (t, 2H, J=7.0 Hz), 1.83 (s, 6H), 1.32–1.58 (m, 4H), 0.91 (t, 3H, J=7.1 Hz); ^{13}C NMR: 84.5, 83.1, 58.5, 34.9 (2C), 30.2, 21.6, 18.1, 13.3; MS: *m*/*z* (%) 161 (^{37}Cl, M+1), 159 (^{35}Cl,M+1); 123 (100%).

1-Trimethylsilyl-3-pentyl-penta-3,4-dien-1-yne 2. IR (neat) cm^{-1}: 2960, 2920, 2860, 2140, 1940, 1460, 1250, 850, 760; ^1H NMR: δ 4.93 (t, 2H, J=2.9 Hz), 2.10 (tt, 2H, J=7.4 Hz, J=2.9 Hz), 1.42–1.59 (m, 2H), 1.21–1.39 (m, 4H), 0.89 (t, 3H, J=6.8 Hz), 0.18 (s, 9H); ^{13}C NMR: δ 214.0, 100.2, 96.5, 89.9, 76.8, 33.1, 31.0, 27.2, 22.4, 14.0, −0.03; MS: *m*/*z* (%) 224 (100%, M+18), 207 (M+1); Anal. Calcd for $C_{13}H_{22}Si$: C, 75.65; H, 10.74. Found: C, 75.60; H, 10.69.

3-Pentyl-deca-1,2-dien-4-yne 3. IR (neat) cm^{-1}: 2960, 2920, 2860, 2220, 1940, 1460, 1380, 850; ^1H NMR: δ 4.91 (m, 2H), 2.34 (tt, 2H, J=7.1 Hz, J=1.1 Hz), 2.11 (tt, 2H, J=7.5 Hz, J=3 Hz), 1.45–1.70 (m, 4H), 1.20–1.45 (m, 8H), 0.83–1.00 (m, 6H); ^{13}C NMR: δ 213.4, 92.6, 89.9, 76.0, 75.2, 33.6, 31.1 (2C), 28.5, 27.3, 22.4, 22.2, 19.5, 14.0, 13.9; MS: *m*/*z* (%) 222 (M+18), 205 (M+1, 100%).

5-Butyl-dodeca-3,4-dien-6-yne 5b. IR (neat) cm^{-1}: 2960, 2920, 2860, 1945, 1940, 1460, 1380, 860; ^1H NMR: δ 5.28–5.38 (m, 1H), 2.30 (td, 2H, J=7.1 Hz, J=0.9 Hz), 1.95–2.14 (m, 4H), 1.21–1.63 (m, 10H), 1.02 (t, 3H, J=7.4 Hz), 0.84–0.95 (m, 6H); ^{13}C NMR: 208.1, 94.0, 91.1, 90.9, 76.5, 34.1, 31.1, 30.1, 28.6, 22.2, 22.1, 22.0, 19.6, 14.0, 13.9, 13.3; MS: *m*/*z* (%) 236 (M+18), 219 (M+1, 100%); Anal. Calcd for $C_{16}H_{26}$: C, 88.00; H, 12.00. Found: C, 88.12; H, 11.98.

4-Butyl-1-methyl-undeca-2,3-dien-5-yne 5c. IR (neat) cm^{-1}: 2940, 2920, 2840, 1460, 1360; ^1H NMR: δ 2.29 (t, 2H, J=7.1 Hz), 2.05 (t, 2H, J=7.1 Hz), 1.71 (s, 6H), 1.23–1.62 (m, 10H), 0.9 (t, 6H, J=7.1 Hz); ^{13}C NMR: δ 205.6, 96.0, 89.7, 87.5, 76.8, 34.1, 30.9, 29.7, 28.3, 21.9, 21.6, 20.1, 19.2, 13.6, 13.5; MS: *m*/*z* (%) 236 (M+18), 219 (M+1, 100%); Anal. Calcd for $C_{16}H_{26}$: C, 88.00; H, 12.00. Found: C, 88.06; H, 12.02.

Methyl-7-pentyl-nona-7,8-dien-5-ynoate 6b. IR (neat) cm^{-1}: 2950, 2920, 2850, 1940, 1740, 1430, 1150, 850; ^1H NMR: δ 4.89 (m, 2H), 3.68 (s, 3H), 2.44 (m, 4H), 2.08 (tt, 2H, J=7.4 Hz, J=3.0 Hz), 1.86 (quin, 2H, J=7.2 Hz), 1.58–1.40 (m, 2H), 1.33 (m, 4H), 0.90 (t, 3H, J=6.8 Hz); ^{13}C NMR: 213.3, 173.3, 90.8, 89.5, 76.0, 69.0, 51.2, 33.3, 32.6, 30.9, 27.1, 23.7, 22.2, 18.8, 13.8; MS: *m*/*z* (%) 252 (100%, M+18), 235 (M+1).

5-Pentyl-hepta-5,6-dien-3-yn-1-ol 6c. IR (neat) cm^{-1}: 3340, 2960, 2920, 2860, 1935, 1460, 1040, 850; ^1H NMR: δ 4.90 (m, 2H), 3.74 (t, 2H, J=6.2 Hz), 2.60 (tt, 2H, J=6.2 Hz, J=1.2 Hz), 2.09 (tt, 2H, J=7.4 Hz, J=2.9 Hz), 1.80 (s, 1H), 1.44–1.57 (m, 2H), 1.24–1.40 (m, 4H), 0.89 (t, 3H, J=6.8 Hz); ^{13}C NMR: δ 213.4, 89.4, 88.4, 77.1, 76.4, 60.9, 33.2, 30.9, 27.2, 23.7, 22.3, 13.9; MS: *m*/*z* (%) 196 (M+18), 179 (100%, M+1); Anal. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.17. Found: C, 80.87; H, 10.13.

4-Pentyl-hexa-4,5-dien-2-yn-1-ol 6d. IR (neat) cm^{-1}: 3330, 2940, 2920, 2840, 2200, 1930, 1020, 850; ^1H NMR: δ 4.93 (m, 2H), 4.39 (t, 2H, J=0.9 Hz), 2.10 (tt, 2H, J=7.4 Hz, J=2.9 Hz), 1.63 (s, 1H), 1.43–1.58 (m, 2H), 1.24–1.38 (m, 4H), 0.90 (t, 3H, J=6.8 Hz); ^{13}C NMR: δ 213.0, 89.4, 89.1, 80.8, 76.7, 51.4, 33.0, 31.0, 27.3, 22.4, 14.0; MS: *m*/*z* (%) 182 (M+18, 100%), 165 (M+1); Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.81. Found: C, 80.31; H, 9.52.

Pentadeca-8,9-dien-6-yne 8a. IR (neat) cm^{-1}: 2960, 2920, 2860, 1950, 1460, 1380, 870; ^1H NMR: δ 5.38 (m, 2H), 2.30

(m, 2H), 2.05 (m, 2H), 1.20–1.65 (m, 12H), 0.90 (t, 6H, J=6.8 Hz); ^{13}C NMR: δ 211.9, 92.8, 90.8, 75.7, 73.3, 31.2, 31.0, 28.4 (2C), 28.2, 22.4, 22.2, 19.5, 14.0, 13.9; MS: *m/z* (%) 222 (M+18), 205 (M+1).

Undeca-4,5-dien-2-yn-1-ol 8c. IR (neat) cm^{-1}: 3340, 2960, 2920, 2860, 2210, 1940, 1460, 1380, 1010, 870; ^{1}H NMR: δ 5.40 (m, 2H), 4.38 (m, 2H), 2.06 (m, 2H), 1.69 (s, 1H), 1.20–1.53 (m, 6H), 0.90 (t, 3H, J=6.9 Hz); ^{13}C NMR: δ 211.9, 93.5, 87.6, 79.1, 74.9, 51.5, 31.2, 28.4, 28.0, 22.4, 14.0; MS: *m/z* (%) 182 (M+18), 164 (M), 107 (100%); Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.81. Found: C, 80.37; H, 9.86.

Methyl-7-butyl-undeca-7,8-dien-5-ynoate 10b. IR (neat) cm^{-1}: 2960, 2920, 2860, 1945, 1740, 1430; ^{1}H NMR: δ 5.34 (m, 1H), 3.68 (s, 3H), 2.45 (t, 2H, J=7.4 Hz), 2.39 (td, 2H, J=7.4, 1.1 Hz), 1.97–2.12 (m, 4H), 1.85 (quin, 2H, J=7.1 Hz), 1.26–1.54 (m, 4H), 1.02 (t, 3H, J=7.4 Hz) 0.90 (t, 3H, J=7.1 Hz); ^{13}C NMR: δ 208.0, 173.4, 94.0, 90.5, 89.3, 77.3, 51.3, 33.8, 32.6, 29.9, 23.9, 21.9, 21.8, 18.9, 13.7, 13.1; MS: *m/z* (%) 266 (M+18), 249 (M+1, 100%); Anal. Calcd for $C_{16}H_{24}O_2$: C, 77.37; H, 9.74. Found: C, 77.30; H, 9.76.

5-Butyl-nona-5,6-dien-3-yn-1-ol 10c. IR (neat) cm^{-1}: 3340, 2950, 2920, 2860, 1940, 1460, 1040; ^{1}H NMR: δ 5.30–5.42 (m, 1H), 3.73 (t, 2H, J=6.2 Hz), 2.60 (td, 2H, J=6.2 Hz, J=1.1 Hz), 1.98–2.15 (m, 4H), 1.75 (m, 1H), 1.26–1.55 (m, 4H), 1.02 (t, 3H, J=7.4 Hz) 0.91 (t, 3H, J=7.1 Hz); ^{13}C NMR: δ 208.3, 94.4, 90.5, 87.2, 78.3, 61.1, 33.9, 30.0, 23.7, 22.1, 22.0, 13.9, 13.3; MS: *m/z* (%) 210 (M+18), 193 (M+1, 100%); Anal. Calcd for $C_{13}H_{20}O$: C, 81.20; H, 10.48. Found: C, 81.15; H, 10.45.

Methyl-7-butyl-9-deca-7,8-dien-5-ynoate 10e. IR (neat) cm^{-1}: 2960, 2940, 2860, 1740, 1440, 1360, 1160, 1220; ^{1}H NMR: δ 3.68 (s, 3H), 2.45 (t, 2H, J=7.5 Hz), 2.38 (t, 2H, J=6.9 Hz), 2.04 (t, 2H, J=7.1 Hz), 1.85 (quin, 2H, J=7.3 Hz), 1.71 (s, 6H), 1.26–1.50 (m, 4H), 0.90 (t, 3H, J=7.1 Hz); ^{13}C NMR: δ 205.8, 175.8, 96.2, 88.1, 87.3, 77.8, 51.1, 34.0, 32.6, 29.7, 23.8, 21.6, 20.2, 18.8, 13.6; MS: *m/z* (%) 266 (M+18), 249 (M+1, 100%); Anal. Calcd for $C_{16}H_{24}O_2$: C, 77.37; H, 9.74. Found: C, 77.02; H, 9.48.

5-Butyl-7-methyl-octa-5,6-dien-3-yn-1-ol 10f. IR (neat) cm^{-1}: 3330, 2950, 2920, 2860, 1950, 1440, 1370, 1040, 840; ^{1}H NMR: δ 3.73 (t, 2H, J=6.3 Hz), 2.59 (t, 2H, J=6.3 Hz), 2.05 (t, 2H, J=7.2 Hz), 1.91 (s, 1H), 1.71 (s, 6H), 1.39 (m, 4H), 0.90 (t, 3H, J=7.1 Hz); ^{13}C NMR: δ 206.0, 96.7, 87.2, 85.8, 78.9, 61.0, 34.0, 29.8, 23.7, 21.8, 20.2, 13.7; MS: *m/z* (%) 210 (M+18), 193 (M+1, 100%).

References

1. Tamao, K. In *Comprehensive Organic Synthesis*, Trost, B. M., Fleming, I., Eds.; Pergamon: New York, 1991; 3, pp 435–480.
2. Jeffery-Luong, T.; Linstrumelle, G. *Synthesis* **1983**, *1*, 32–34.
3. For a review in allene chemistry see Bruneau, C.; Dixneuf, P. H. In *Comprehensive Organic Functional Group Transformations*; Katritzky, A. R., Meth-Cohn, O., Rees, C. W., Eds.; Pergamon: New York; 1995; Vol. 2, pp 953–996.
4. For coupling with acetylen and diacetylen see Markl, G.; Attenberger, P.; Kellner, J. *Tetrahedron Lett.* **1988**, *29*, 3651–3654.
5. Mandai, M.; Nakata, T.; Murayama, H.; Yamaoki, H.; Ogawa, M.; Kawada, M.; Tsuji, J. *Tetrahedron Lett.* **1990**, *31*, 7179–7180.
6. Mandai, M.; Murayama, H.; Nakata, T.; Yamaoki, H.; Ogawa, M.; Kawada, M.; Tsuji, J. *J. Organomet. Chem.* **1991**, *417*, 305–311.
7. Alami, M.; Linstrumelle, G. *Tetrahedron Lett.* **1991**, *32*, 6109–6112.
8. Alami, M.; Ferri, F.; Linstrumelle, G. *Tetrahedron Lett.* **1993**, *40*, 6403–6406.
9. Crousse, B.; Alami, M.; Linstrumelle, G. *Tetrahedron Lett.* **1995**, *36*, 4245–4248.
10. Crousse, B.; Alami, M.; Linstrumelle, G. *Tetrahedron Lett.* **1997**, *38*, 5297–5300.
11. For a review in Palladium-catalyzed coupling of propargyl compounds see Tsuji, J.; Mandai, T. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; 1998, pp 455–489.
12. Sevin, A.; Chodkiewicz, W.; Cadiot, P. *Tetrahedron Lett.* **1965**, *24*, 1953–1959.
13. Sevin, A.; Chodkiewicz, W.; Cadiot, P. *Bull. Soc. Fr. Chim.* **1974**, *5/6*, 913–917.
14. Baudouy, R.; Goré, J. *Bull. Soc. Fr. Chim.* **1975**, *9/10*, 2153–2158.
15. Vermeer, P.; Meijer, J.; Brandsma, L. *Recl. Trav. Chim.* **1975**, *94*, 112–114.
16. Ruitenberg, K.; Kleijn, H.; Elsevier, C. J.; Meijer, J.; Vermeer, P. *Tetrahedron Lett.* **1981**, *22*, 1451–1452.
17. Preliminary report: Gueugnot, S.; Linstrumelle, G. *Tetrahedron Lett.* **1993**, *34*, 3853–3856.
18. Baker, C. S. L.; Landor, P. D.; Landor, S. R. *Proc. Chem. Soc.* **1963**, 340.
19. Baker, C. S. L.; Landor, P. D.; Landor, S. R. *J. Chem. Soc.* **1965**, 4659–4664.
20. Elsevier, C. J.; Kleijn, H.; Ruitenberg, K.; Vermeer, P. *J. Chem. Soc., Chem. Commun.* **1983**, 1529–1530.
21. Elsevier, C. J.; Kleijn, H.; Boersma, J.; Vermeer, P. *Organometallics* **1986**, *5*, 716–720.
22. Baudouy, R.; Goré, J. *Synthesis* **1974**, 573–574.
23. Brandsma, L.; Verkruijsse, H. D. *Preparative Acetylenic Chemistry*, Elsevier: Amsterdam, 1988.
24. Gueugnot, S.; Alami, M.; Linstrumelle, G.; Mambu, L.; Petit, Y.; Larchevêque, M. *Tetrahedron* **1996**, *52*, 6635–6646.
25. Coulson, D. R. *Inorg. Synth.* **1972**, *13*, 121–124.
26. Kharasch, M. S.; Seyler, R. C.; Mayo, F. R. *J. Am. Chem. Soc.* **1938**, *60*, 882–884.
27. King, A. O.; Negishi, E. I. *J. Org. Chem.* **1978**, *43*, 358–360.
28. Brandsma, L.; Verkruijsse, H. D. *Preparative Acetylenic Chemistry*, Elsevier: Amsterdam, 1971.
29. Hassner, A.; Krepski, L. R.; Alexanian, V. *Tetrahedron* **1978**, *34*, 2069–2076.
30. Snyder, E. J. *J. Org. Chem.* **1972**, *37*, 1466.
31. Hennion, G. F.; Boisselle, A. P. *J. Org. Chem.* **1961**, *26*, 725–727.