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Palladium-Catalyzed Consecutive One-Pot Reaction of Acetylenes with Allyl Bromide and Organotin Compounds

Masanori KOSUGI,* Takashi SAKAYA, Shinji OGAWA, and Toshihiko MIGITA†
Department of Chemistry, Faculty of Engineering, Gunma University, Kiryu, Gunma 376
† School of High Technology for Human Welfare, Tokai University, Numazu, Shizuoka 410-03

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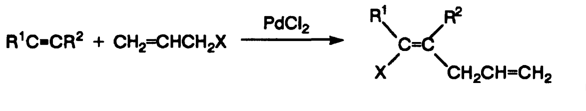
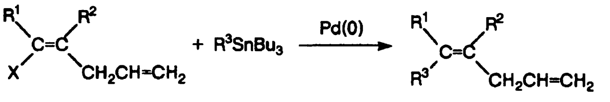
Allyl bromide adds to a terminal acetylene under the palladium complex to give 1-bromo-1,4-pentadiene which can further react with organotin compounds without further addition of palladium complex to give 1-substituted 1,4-pentadiene. These two reactions involving different catalytic species can be composed into the consecutive one-pot process.

In 1974 Kaneda et al. reported that acetylenes reacted with allylic halides in the presence of palladium dihalide to give 1-halo-1,4-dienes (Eq. 1).[1] The reaction was recently applied to the intramolecular cyclization.[2] Since the products are vinylic halides, they are expected to react with organotin compounds in the presence of palladium(0) complex (Eq. 2). Final results of these two reactions are equivalent to the cross-coupling of allylic halide with organotin compound involving insertion of acetylene. As an extention of our investigation about the cross-coupling of organic halide with organotin compound involving insertion of olefin in the presence of palladium complex,[3] the possibility of combination of the two reactions were investigated. This paper shows that these two reactions can be composed into the consecutive one-pot process.



(1)



(2)

Results and Discussion

A combination of the above two reactions seems to be quite noteworthy, because proposed catalytic mechanisms for both reactions are different from each other as shown in Scheme 1. The first reaction is believed to proceed through the halopalladation of dihalopalladium to acetylene, followed by the carbopalladation to allyl halide, then the elimination of dihalopalladium giving 1-halo-1,4-pentadienes. The reaction involves palladium(II) complex as a catalytic species. When allyl bromide was used, 1-bromo-1,4-pentadiene which might be a reactive substrate toward organotins, was obtained. Table 1 shows the results of the first reaction.

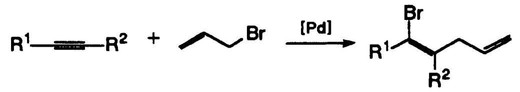


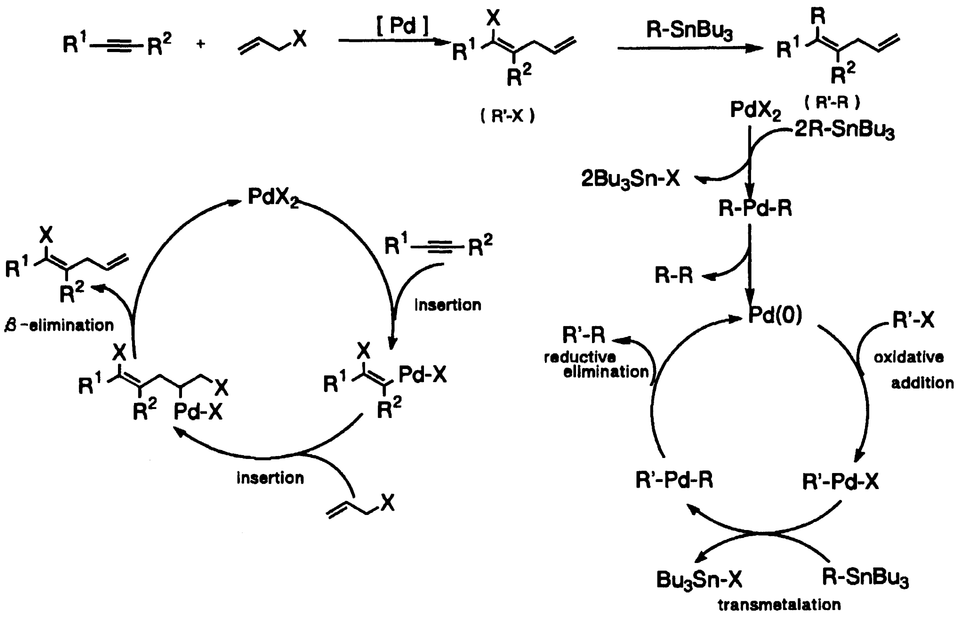
Table 1. Pd-Catalyzed Reaction of Acetylene with Allyl Bromide[a]

Entry	R^1	R^2	Isolated yield/%
1	*n*-Bu–	–H	63
2	Me$_3$Si–	–H	67
3	Ph–	–H	60
4	H–	–CO$_2$Me	72
5	EtOCH$_2$–	–H	49

a) 5 mol% of PdCl$_2$(MeCN)$_2$, r.t., 2 h.

As Kaneda et al. reported, the reaction proceeded smoothly at room temperature for 2 h to give the vinylic bromide in moderate yields by adding the acetylene to the solution of an excess of allyl bromide (more than 10 molar equivalents) including 5 mol% of dichlorobis(acetonitrile)palladium, which was a better catalyst than dichlorobis(benzonitrile)palladium for the sake of the easy product, 1,4-pentadiene separation. Use of a stoichiometric amount of allyl bromide toward the acetylene under the appropriate solvent gave the 1,4-pentadiene in rather low yield. In this reaction, polymerization of acetylene in the presence of palladium catalyst could not be completely eliminated.[4] One specific feature is a regiochemistry of the 1,4-pentadiene, that is, when the reaction of methyl propiolate with allyl bromide was carried out, methyl 2-allyl-3-bromopropenoate was obtained. On the other hand, 1-substituted 1-bromo-1,4-pentadienes were obtained, when being used other acetylenes, for example, hexyne, trimethylsilylacetylene, phenylacetylene, or 3-ethoxypropyne. The obtained 1,4-pentadiene was mainly *Z*-isomer, containing small amounts of *E*-isomer.

Addition of organotin compounds should reduce the dihalopalladium(II) to palladium(0) species, therefore, cross-coupling would be expected according to the mechanism shown in right-hand of Scheme 1. To search for the optimum reaction conditions of the cross-coupling, the reaction of the obtained 1,4-pentadiene with organotins in the presence of palladium(II) complex was separatedly investigated. In order to attain the one-pot process, the same dichlorobis(acetonitrile)-palladium catalyst must be used. Although the reactions of the 1,4-pentadienes with vinyl-, phenyl-, and phenylethynyltributyltin were examined in various solvents, yields of the expected products were only trace



Scheme 1.

amounts except for the reaction of the 1,4-pentadiene shown in Entry 4 of Table 1. Recently, it was reported that addition of tri-2-furylphosphine or triphenylarsine in place of triphenylphosphine,$^{5)}$ or of tetraethylammonium chloride$^{6)}$ accelerated the cross-coupling reaction of organic halides or triflates with organotins. So the effects of the ligand or the additive were also investigated. The best results at present were shown in Table 2.

Table 2 shows that steric effects of the substituent in R^1 seem to be still important, since the yields of the expected products were relatively low. A recent paper has also shown that the steric effect for the palladium-catalyzed cross-coupling with organotins was the serious problem.$^{7)}$ The effects of the addition of ligand, additive, or solvent show no explainable tendencies. Interestingly, addition of tetraethylammonium chloride gave tributyltin chloride as a main by-product, not tributyltin bromide. These effects were observed especially in the reaction of phenyltributyltin. However, in Entry 9 of Table 2 such an effect was not observed.

Based upon the results of Tables 1 and 2, consecutive one-pot reactions were carried out as follows; after the first reaction was carried out, excess of allyl bromide was recovered under the reduced pressure. Then, the solvent and tri-2-furylphosphine or tetraethylammonium chloride was added to the reaction mixture. The solution without further addition of palladium(II) complex was heated at 80 °C for 24 h. The product was isolated after the usual workup. Table 3 shows the results of the one-pot reaction.

Thus, one-pot consecutive reactions are thought to take place smoothly, judging from the yields from Tables 1 and 2. For example, Entry 8 of Table 3 shows 36% yield, while the expected one is 47%. Two metal-catalyzed reactions involving different catalytic species of Pd(II) and Pd(0) could be composed into the consecutive one-pot process.

Experimental

Instruments. ^{1}H NMR spectra were recorded on a Varian Gemini 200 spectrometer. GC-MS spectra were measured on a Shimadzu QP2000A instrument, and HRMS was on a JEOL JMS-AX505W instrument. GC analyses were performed on a Shimadzu GC-8A instrument using 2 m column packed with 5% SE-30 on Celite 545. LC analyses were carried out by using LC-08 instrument of Japan Analytical Industry Co., Ltd. IR spectra were recorded on a A-100 Infrared spectrometer of Japan Spectroscopic Co., Ltd.

Materials. Vinyltributyltin,$^{8)}$ phenyltributyltin,$^{9)}$ phenylethynyltributyltin,$^{10)}$ and dichlorobis(acetonitrile)palladium,$^{11)}$ were prepared from the methods described in the literatures. Allyl bromide, 1-hexyne, trimethylacetylene, phenylacetylene, propargyl alcohol, triphenylphosphine, hexamethylphosphioric triamide (HMPA), *N*-methyl-2-pyrrolidone (NMP), were available commercially by Wako Pure Chemical Industries, Ltd. or Tokyo Kasei Kogyo Co., Ltd. Tri-2-furylphosphine was prepared by the reaction of furan with butyllithium, followed by the reaction with trichlorophosphine, yields 50%, bp 110 °C/1.0 mmHg (lit,$^{12)}$ 95 °C/1.5 mmHg, 1mmHg=133.322 Pa).

Pd-Catalyzed Reaction of Allyl Bromide with Acetylenes. In three necked round-bottom flask, to a 100 mL of allyl bromide dissolved in 5 mmol of dichlorobis(acetonitrile)palladium was added a 100 mmol of acetylene dropwisely. After the addition was completed, the reaction mixture was stirred for 2 h at room temperature. Then evaporation of an excess of allyl bromide, followed by distillation under the reduced pressure gave the expected product, bromide. Results were shown in Table 1.

5-Bromo-1,4-nonadiene: ^{1}H NMR ($CDCl_3$) δ=0.97 (t, J=8 Hz, 3H), 1.3 (m, 2H), 1.6 (m, 2H), 2.44 (t, J=8 Hz, 2H), 2.9 (m, 2H), 5.0 (m, 2H), 5.5—5.9 (m, 2H); IR (NaCl) 1620 and 1640 cm^{-1} (C=C); GC-MS 204 (M^++2), 202 (M^+),

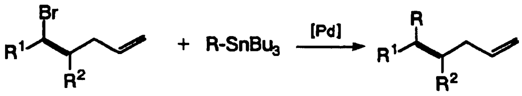


Table 2. Pd-Catalyzed Reaction of the 1,4-Pentadiene with Organotins[a)]

Entry	R^1	R^2	R-SnBu3	Ligand	Additive	Solvent	Yield/%
1	*n*-Bu-	-H	H_2C=CH-	P(2-furyl)3	—	HMPA	35
2			Ph-	—	Et_4NCl	HMPA	52
3			PhC≡C-	—	Et_4NCl	HMPA	0
4	Me_3Si-	-H	H_2C=CH-	P(2-furyl)3	—	PhMe	40
5			Ph-	—	Et_4NCl	HMPA	52
6			PhC≡C-	—	—	HMPA	26
7	Ph-	-H	Ph-	—	Et_4NCl	HMPA	55
8	H-	$-CO_2Me$	H_2C=CH-	P(2-furyl)3	—	NMP	99
9			Ph-	P(2-furyl)3	—	HMPA	65
10			PhC≡C-	P(2-furyl)3	—	PhMe	88
11	$EtOCH_2$-	-H	H_2C=CH-	P(2-furyl)3	—	PhMe	8
12			Ph-	—	Et_4NCl	HMPA	55

a) $PdCl_2(MeCN)_2$ 1 mol%, ligand 2 mol%, additive 1.2 equiv, at 80 °C for 24 h.

Table 3. Pd-Catalyzed One-pot Reaction of Acetylenes, Allyl Bromide, and Organotins

Entry	R^2	R^2	R-SnBu3	Ligand	Additive	Solvent	Yield/%
1	*n*-Bu-	-H	H_2C=CH-	P(2-furyl)3	—	HMPA	20
2			Ph-	—	Et_4NCl	HMPA	24
3	Me_3Si-	-H	H_2C=CH-	P(2-furyl)3	—	PhMe	16
4			Ph-	—	Et_4NCl	HMPA	23
5			PhC≡C-	—	—	HMPA	10
6	Ph-	-H	Ph-	—	Et_4NCl	HMPA	26
7	H-	$-CO_2Me$	H_2C=CH-	P(2-furyl)3	—	NMP	16[a)]
8			Ph-	P(2-furyl)3	—	HMPA	36
9			PhC≡C-	P(2-furyl)3	—	PhMe	53
10	$EtOCH_2$-	-H	Ph-	—	Et_4NCl	HMPA	21

a) The product seems to polymerize.

123, 81, 67 (100), 41; HRMS Found: *m/z* 202.0324. Calcd for $C_9H_{15}Br$: M, 202.0357.

1-Bromo(1,4-pentadienyl)trimethylsilane: ^{1}H NMR ($CDCl_3$) δ=0.20 (s, 9H), 3.0—3.1 (m, 2H), 5.0—5.2 (m, 2H), 5.7—5.9 (m, 2H), 6.25 (t, J=6 Hz, 1H); IR (NaCl) 1610 and 1640 (C=C), 1420, 1260, and 850 cm^{-1} (Si–C); GC-MS 219 (M^++2), 217 (M^+), 139, 137, 73 (100); HRMS Found: *m/z* 220.0024. Calcd for $C_8H_{15}SiBr$: (M+2), 220.0105.

1-Bromo(1,4-pentadienyl)benzene: ^{1}H NMR ($CDCl_3$) δ=3.1—3.2 (m, 2H), 5.0—5.2 (m, 2H), 5.8—6.0 (m, 1H), 6.23 (t, J=7 Hz, 1H), 7.3—7.6 (m, 5H); IR (NaCl) 1640 cm^{-1} (C=C); GC-MS 224 (M^++2), 222 (M^+), 143, 128 (100), 115.

Methyl 2-(2-Propenyl)-3-bromopropenoate: ^{1}H NMR ($CDCl_3$) δ=3.1 (m, 2H), 3.82 (s, 3H), 5.6—5.9 (m, 1H), 6.55 (s, 1H); IR (NaCl) 1720 (C=O), 1610 and 1640 (C=C), 1210 and 1120 cm^{-1} (C–O); GC-MS 206 (M^++2), 204 (M^+), 191, 189, 175, 173, 125; HRMS Found: *m/z* 203.9794. Calcd for $C_7H_9O_2Br$: M, 203.9786.

2-Bromo-2,5-hexadienyl Ethyl Ether: ^{1}H NMR ($CDCl_3$) δ=1.23 (t, J=7 Hz, 3H), 2.9—3.0 (m, 2H), 3.50 (q, J=7 Hz, 2H), 4.12 (s, 2H), 5.0—5.2 (m, 2H), 5.7—5.9 (m, 1H), 6.0—6.1 (m, 1H); IR (NaCl) 1650 cm^{-1} (C=C); GC-MS 206 (M^++2), 204 (M^+), 85, 79, 59 (100), 41.

Pd-Catalyzed Reaction of the 1,4-Pentadienes Obtained with Organotins. A mixture of the 1,4-pentadiene (1 mmol), organotin compound (1.1 mmol), dichlorobis(acetonitrile)palladium (0.01 mmol), solvent (1 mL), and tri-2-furylphosphine (0.02 mmol) or tetraethylammonium chloride (1 mmol) was sealed in vacuo, and immersed in a thermobath at 80 °C for 24 h. After the reaction mixture was treated with aqueous potassium fluoride, extracted with ether, and then dried with magnesium sulfate. The product was isolated with column chromatography. Results were shown in Table 2.

Pd-Catalyzed One-Pot Reaction. To a solution of allyl bromide (5 mL) and 5 mol% of dichlorobis(acetonitrile)palladium based on the acetylene, the acetylene (5 mmol) was added dropwisely and stirred at room temperature for 2 h. After an excess of allyl bromide was recovered under the reduced pressure, organotin compound (5 mmol), solvent (5 mL), and tri-2-furylphosphine (10 mol%) or tetraethylammonium chloride (6 mmol) were added to the reaction mixture, which was then heated at 80 °C for 24 h. The product was isolated by column chromatography after a usual workup. Results were shown in Table 3.

Products. **3-Butyl-1,3,6-heptatriene:** ^{1}H NMR ($CDCl_3$) δ=0.92 (t, J=7 Hz, 3H), 1.3—1.5 (m, 4H), 2.20 (t, J=7 Hz, 2H), 2.9—3.0 (m, 2H), 5.0—5.5 (m, 5H), 5.7—5.9 (m, 5H), 6.6—6.7 (m, 1H); IR (NaCl) 1610 and 1650 cm^{-1} (C=C); GC-MS 150 (M^+−1), 108, 93 (100), 79, 67, 41; HRMS Found: *m/z* 151.1473. Calcd for $C_{11}H_{19}$: M, 151.1487.

5-Phenyl-1,4-nonadiene: ^{1}H NMR ($CDCl_3$) δ=0.85 (t, J=7 Hz, 3H), 1.2—1.4 (m, 4H), 2.35 (t, J=7 Hz, 2H), 2.6—2.7 (m, 2H), 4.9—5.1 (m, 2H), 5.60 (t, J=8 Hz, 1H), 5.7—5.9 (m, 1H), 7.2—7.6 (m, 5H); IR (NaCl) 1600, 1620, and 1640 cm^{-1} (C=C); GC-MS 200 (M$^+$), 143 (100), 128, 115, 91; HRMS Found: m/z 200.1526. Calcd for $C_{15}H_{20}$: M, 200.1565.

3-Trimethylsilyl-1,3,6-heptatriene: ^{1}H NMR ($CDCl_3$) δ=0.15 (s, 9H), 3.0—3.1 (m, 2H), 5.0—5.4 (m, 4H), 5.7—5.9 (m, 2H), 6.6—6.7 (m, 1H); IR (NaCl) 1610 and 1640 (C=C), 1420, 1260, and 850 cm^{-1} (Si–C); GC-MS 166 (M$^+$), 73 (100), 59; HRMS Found: m/z 166.1212. Calcd for $C_{10}H_{18}Si$: M, 166.1178.

1-Phenyl(1,4-pentadienyl)trimethylsilane: ^{1}H NMR ($CDCl_3$) δ=0.05 (s, 9H), 2.6—2.7 (m, 2H), 4.9—5.0 (m, 2H), 5.7—5.9 (m, 1H), 5.97 (t, J=7 Hz, 1H), 6.9—7.3 (m, 5H); IR (NaCl) 1600, 1610, and 1640 (C=C), 1450, 1250, and 840 cm^{-1} (Si–C); GC-MS 217 (M$^+$+1), 73 (100), 59, 45; HRMS Found: m/z 216.1337. Calcd for $C_{14}H_{20}Si$: M, 216.1334.

1-Phenylethynyl(1,4-pentadienyl)trimethylsilane: ^{1}H NMR ($CDCl_3$) δ=0.21 (s, 9H), 3.2—3.3 (m, 2H), 5.0—5.2 (m, 2H), 5.8—6.0 (m, 1H), 6.15 (t, J=7 Hz, 1H), 7.3—7.5 (m, 5H); IR (NaCl) 1600 and 1640 (C=C), 1420, 1250, and 850 cm^{-1} (Si–C); GC-MS 241 (M$^+$+1), 91, 73 (100), 66; HRMS Found: m/z 240.1278. Calcd for $C_{16}H_{20}Si$: M, 240.1334.

1,1-Diphenyl-1,4-pentadiene: ^{1}H NMR ($CDCl_3$) δ=2.8—2.9 (m, 2H), 5.0—5.2 (m, 2H), 5.8—6.0 (m, 1H), 6.10 (t, J=7 Hz, 1H), 7.1—7.4 (m, 10H); IR (NaCl) 1600 and 1640 cm^{-1} (C=C); GC-MS 222 (M$^+$+2), 220 (M$^+$), 191, 178, 165, 142, 129 (100), 115, 91; HRMS Found: m/z 220.1243. Calcd for $C_{17}H_{16}$: M, 220.1252.

Methyl 2-(2-Propenyl)-2,4-pentadienoate: ^{1}H NMR ($CDCl_3$) δ=3.08 (d, J=6 Hz, 2H), 3.77 (s, 3H), 5.0—5.2 (m, 2H), 5.3—5.5 (m, 2H), 5.7—6.0 (m, 1H), 6.40 (d, J=11 Hz, 1H), 7.2—7.4 (m, 1H); IR (NaCl) 1720 (C=O), 1610 and 1640 (C=C), 1120 and 1210 cm^{-1} (C–O); GC-MS 152 (M$^+$), 91 (100), 77, 59, 41; HRMS Found: m/z 152.0820. Calcd for $C_9H_{12}O_2$: M, 152.0837.

Methyl 2-(2-Propenyl)-3-phenyl-2-propenoate: ^{1}H NMR ($CDCl_3$) δ=3.18 (d, J=6 Hz, 2H), 3.65 (s, 3H), 5.1—5.2 (m, 2H), 5.8—6.0 (m, 1H), 6.69 (s, 1H), 7.2—7.4 (m, 5H); IR (NaCl) 1720 (C=O), 1610 and 1640 (C=C), 1120 and 1210 cm^{-1} (C–O); GC-MS 203 (M$^+$+1), 143 (100), 128, 115; HRMS Found: m/z 202.0960. Calcd for $C_{13}H_{14}O_2$: M, 202.0994.

Methyl 2-(2-Propenyl)-5-phenyl-2-propen-4-ynoate: ^{1}H NMR ($CDCl_3$) δ=3.16 (d, J=6 Hz, 2H), 3.75 (s, 3H), 5.1—5.2 (m, 2H), 5.7—6.0 (m, 1H), 6.20 (s, 1H), 7.3—7.5 (m, 5H); IR (NaCl) 1720 (C=O), 1610 and 1640 (C=C), 1120 and 1210 cm^{-1} (C–O); GC-MS 226 (M$^+$), 167, 165 (100); HRMS Found: m/z 226.0986. Calcd for $C_{15}H_{14}O_2$: M, 226.0994.

1-Ethoxymethyl-1-phenyl-1,4-pentadiene: ^{1}H NMR ($CDCl_3$) δ=1.20 (t, J=7 Hz, 3H), 2.7—2.8 (m, 2H), 3.52 (q, J=7 Hz, 2H), 4.18 (s, 2H), 4.9—5.1 (m, 2H), 5.7—5.9 (m, 2H), 7.2—7.4 (m, 5H); IR (NaCl) 1600 and 1650 cm^{-1} (C=C); GC-MS 202 (M$^+$), 44 (100); HRMS Found: m/z 202.1287. Calcd for $C_{14}H_{18}O$: M, 202.1358.

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