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Unusual Regioselectivity of Pd(0)-Catalyzed Coupling Reaction of Electron-Deficient Alkenyl Halides with Allenic/Propargylic Zinc Reagents. Highly Selective Synthesis of 6-Phenylhex-5-yn-2(or 3)-enoates/Enitrile and 4-Phenyl-6-substituted-hexa-2,4,5-trienoates

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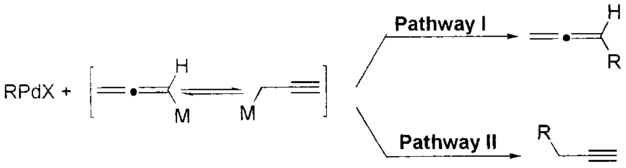
The Pd(0)-catalyzed coupling reaction of electron-deficient alkenyl halides with the organozinc formed by the subsequent treatment of 1-phenylalk-1-yne with *n*-BuLi and $ZnBr_2$ with or without a catalytic amount of $HgCl_2$ was studied. Both the allene-formation- and the alkyne-formation-type coupling reactions were observed with high regio- and stereoselectivity: the reaction of 1-phenylprop-1-yne afforded 6-phenylhex-5-yn-2(or 3)-enoates and -enitriles, while the reaction of 1-phenylhex-1-yne formed 4-phenyl-6-substituted-hexa-2,4,5-trienoates. A plausible explanation for the regioselectivity was discussed. The double bonds in 6-phenylhex-5-yn-2-enoates were prone to migrate to the position conjugated with the carbon−carbon triple bonds to form 6-phenylhex-5-yn-3-enoates at higher temperature. The migration did not occur in absence of an excess amount of allenic/propargylic zinc reagent or at low temperature.

Introduction

Formation of C−C bonds is one of the major objectives in organic synthesis. Cross-coupling reaction between an organometallic reagent and R′X (R′= alkenyl, aryl) with a transition-metal catalyst is very attractive because of the easy availability of both reactants.[1] For the coupling reaction between an organic halide and an allenic/propargylic metallic reagent there are, in principle, two outcomes: (1) the formation of allenes (pathway I) and (2) the formation of alkynes (pathway II) (Scheme 1).

Recently, we developed the $HgCl_2$-catalyzed monolithiation reaction of 1-arylalk-1-ynes. A catalytic amount of $HgCl_2$ was found to be crucial to avoid the polylithiation reaction.[2] The subsequent reaction of the lithium reagent formed in situ with benzylic[3] and allylic[4] halides was studied. Moreover, on the basis of this monolithiation reaction, a Pd(0)-catalyzed coupling reaction of aromatic halides with allenic/propargylic zinc reagents, which were formed in situ via transmetalation reaction, was developed for the efficient and selective synthesis of 1,1-diaryl-1,2-dienes (pathway I, Scheme 1).[5] It is interesting to observe that $ZnBr_2$ has similar effect on the monometalation reaction of 1-arylalk-1-ynes. In this paper, we disclose our most recent results on the coupling reaction of the organozinc reagents with alkenyl halides, which show both pathway I- and pathway II-type regiochemistry with high selectivity, depending on the structure of organic halides and 1-arylalk-1-ynes.

Scheme 1



Results and Discussion

As is reported in ref 5, the treatment of 1-phenylprop-1-yne with *n*-BuLi in the presence of 1.5 mol % $HgCl_2$ in THF at −78 °C followed by the addition of 1.5 molar equiv of $ZnBr_2$ (defined as procedure A), (*E*)-1-iodohexene, and 5 mol % $Pd(PPh_3)_4$ did not afford any coupling product. Neither did (*E*)-1-iodostyrene. However, when α-bromostyrene was used, it afforded 2,3-diphenyl-1,3,4-triene **3a** in 29% yield. Presumably, α-bromostyrene was not active enough, so α-iodostyrene was used, but the yield of the coupling product **3a** was only increased to 33% (Scheme 2). Here, it is important to note that the coupling reaction afforded the pathway-I type allenic triene product **3a**, not 2,5-diphenylalk-4-yn-1-ene **3b**, which is consistent with the results of aromatic halides.

From the above experiment, it is obvious that the substituent as well as its location in alkenyl halides affected the reaction greatly. To our surprise, the corresponding reaction of ethyl (*Z*)-3-iodopropenoate afforded a pathway-II type product, i.e., ethyl 6-phenylhex-5-yn-2(*Z*)-enoate ((*Z*)-**4a**), exclusively. A similar result was obtained with ethyl (*Z*)-3-bromopropenoate, but no reaction was observed with ethyl (*Z*)-3-chloropropenoate (Scheme 3). The configuration of the C=C bond remained intact.

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[1] Trost, B. M., Fleming, I., Eds. *Comprehensive Organic Synthesis*; Pergaman Press: Oxford, 1991; Vol. 3.

[2] (a) De Jong, R. L. P.; Brandsma, L. J. *J. Organomet. Chem.* **1986**, *312*, 277. (b) De Jong, R. L. P.; Brandsma, L. J. *Ibid.* **1982**, *238*, C17. (c) Becker, J. Y.; Klein, J. *J. Organomet. Chem.* **1978**, *157*, 1. (d) Becker, J. Y. *J. Organomet. Chem.* **1976**, *118*, 247.

[3] Ma, S.; Wang, L. *J. Org. Chem.* **1998**, *63*, 3497.

[4] Ma, S.; Wang, L. *Chin. J. Chem.* **1999**, *17*, 531.

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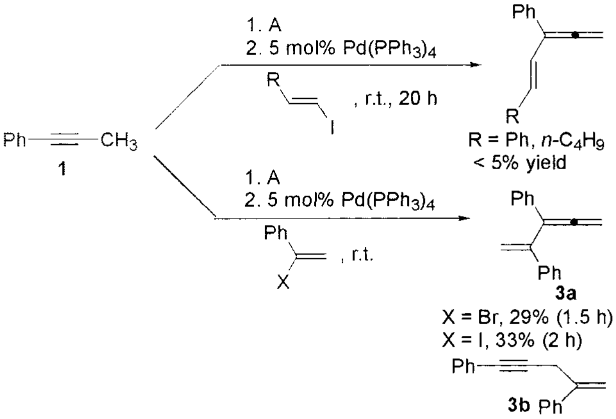
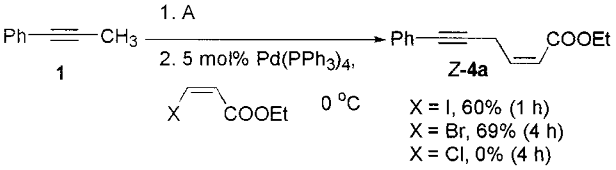
10.1021/jo991243g CCC: $19.00

Scheme 2

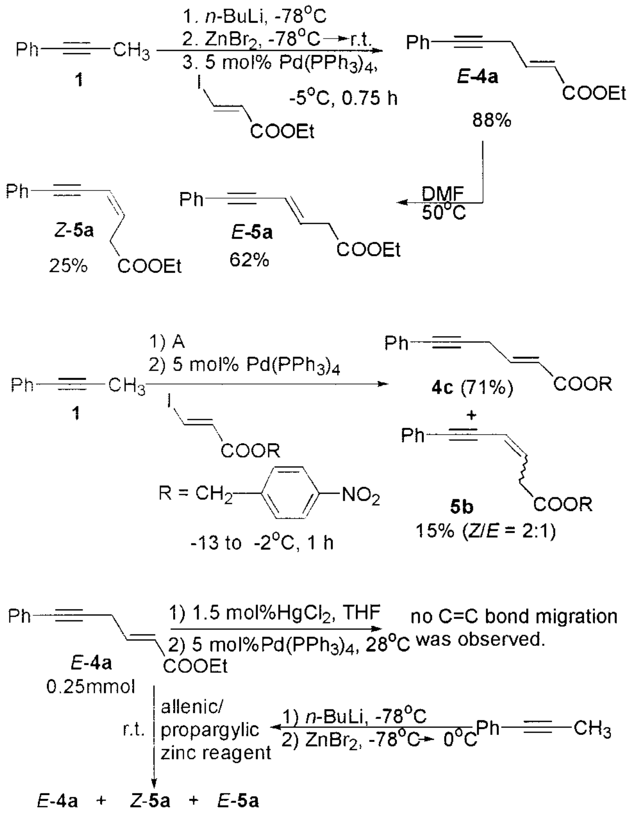


A = 1) 1.5 mol% $HgCl_2$; 2) n-BuLi, -78°C; 3) $ZnBr_2$, -78°C→r.t.

Scheme 3



Scheme 4[a]



zinc reagent[a]	temperature	time	NMR yield(%)		
(mmol)	(°C)	(h)	E-4a	Z-5a	E-5a
0.17	22	8.5	69	12	5
0.25	-15→-10	1	84	0	0
0.25	22	4	20	45	22
0.35	22	4	5	44	25

[a] Expressed in terms of the amount of 3-phenylprop-1-yne added.

When its steric isomer, i.e., ethyl (*E*)-3-iodopropenoate, was used, the coupling reaction at −5 °C afforded (*E*)-**4a** as the sole product in 88% yield (Scheme 4). However, the corresponding reaction under conditions A afforded three products, ethyl 6-phenylhex-5-yn-3(*Z*)-enoate ((*Z*)-**5a**), ethyl 6-phenylhex-5-yn-3(*E*)-enoate ((*E*)-**5a**), and ethyl 6-phenylhex-5-yn-2(*E*)-enoate ((*E*)-**4a**), in a ratio of 35:21:44 in 58% combined yield at 20 °C. Ratios depend on the temperature for the coupling reaction (Scheme 4).

The structures of (*Z*)-**4a**, (*E*)-**4a**, (*Z*)-**5a**, and (*E*)-**5a** were determined by HMBC (heteronuclear multiple-bond connectivity) spectra of (*Z*)-**4a** and (*Z*)-**5a**. The configuration of the carbon−carbon double bond was determined by the coupling constants of the olefinic protons.

To further confirm the structures of these products, *p*-nitrobenzyl (*E*)-3-iodopropenoate was prepared, and the corresponding reaction with or without $HgCl_2$ afforded three corresponding products **4c**, (*Z*)-**5b**, and (*E*)-**5b** (Scheme 4).

By recrystallization, pure *p*-nitrobenzyl 6-phenylhex-5-yn-3(*E*)-enoate (*E*)-**5b** was obtained in the form of single crystals. Thus, its structure was further confirmed by X-ray single-crystal diffraction study (see the Supporting Information for the ORTEP presentation). Moreover, the migration of the carbon−carbon double bond in (*Z*)-**4a** could also be furnished to afford (*Z*)-**5a** and (*E*)-**5a** in DMF at 50 °C completely (Scheme 4). Thus, it is obvious that **5a** was formed via the migration of carbon−carbon double bond in **4a**.

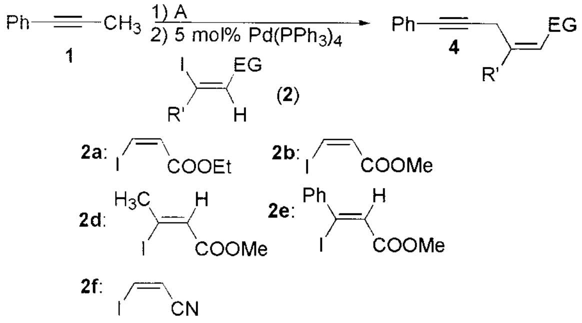
When (*E*)-**4a** was subsequently treated with 1.5 mol % $HgCl_2$ and 5 mol % $Pd(PPh_3)_4$, the C=C bond migration reaction was not observed, ruling out the possibility of $HgCl_2$- and/or $Pd(PPh_3)_4$-catalyzed migration of the C=C bond in (*E*)-**4a**. However, in the presence of an excess amount of the in-situ generated allenic/propargynic zinc reagents, (*E*)-**4a** isomerized to a mixture of (*E*)-**4a**, (*Z*)-**5a**, and (*E*)-**5a** at 21 °C. The C=C bond migration reaction at −15 → −10 °C did not occur. Thus, the excess amount of the zinc reagent and the temperature of the coupling reaction are responsible for the migration of the C=C double bond in **4a**-type products (Scheme 4).

(*Z*)-3-Iodopropenitrile could react similarly with the organozinc reagent formed by the subsequent treatment of 1-phenylprop-1-yne with n-BuLi and $ZnBr_2$ in the presence of $HgCl_2$ under the catalysis of $Pd(PPh_3)_4$ to afford 6-phenylhex-5-yn-2(*Z*)- enitrile (**4f**). While methyl α-bromopropenoate was used instead of ethyl (*Z*)-3-iodopropenoate, the reaction was complicated. Some representative examples with or without $HgCl_2$ are summarized in Table 1; in most cases the results with $HgCl_2$ are somewhat better.

On the other hand, it is interesting to observe that, by starting from 1-phenylhex-1-yne, both ethyl (*Z*)-3-iodopropenoate and ethyl (*E*)-3-iodopropenoate afforded the allenic product ethyl 4-phenylnona-2(*E*),4,5-trieneoate (*E*)-**7a** in 73% and 86% yields, respectively (Table 2).

The configuration of carbon−carbon double bond in **7a** was determined to be *E* since the coupling constant of the olefinic protons is 15.8 Hz. In contrast, when methyl (*Z*)-3-iodobutenoate was used, the configuration of the carbon−carbon double bond in product **7d** was confirmed to be **Z** by the 2D $^1H-^1H$ NOESY experiment of (*Z*)-**7d** (Figure 1). Thus, it is believed that in this case the configuration of the C−C double bond is retained during

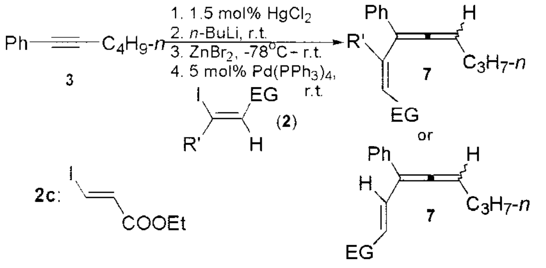
Table 1. Pd(0)-Catalyzed Coupling Reaction of Electron-Deficient Alkenyl Halides with the Organozinc Reagents Formed by the Subsequent Treatment of 1-Phenylprop-1-yne with *n*-BuLi and $ZnBr_2$ with or without the Addition of $HgCl_2$



entry	2	*T* (°C)	time (h)	product	yield[a] (%)
1	**2a**	0	1	(*Z*)-**4a**	60
2[b]	**2a**	0	1.5	(*Z*)-**4a**	66
3[c]	**2a**	0	2.5	(*Z*)-**4a**	62
4	**2b**	−3 → 0	1	(*Z*)-**4b**	62
5[b]	**2b**	−3 → 0	1.5	(*Z*)-**4b**	54
6	**2e**	50	2.5	(*Z*)-**4e**	49
7[b]	**2e**	50	0.5	(*Z*)-**4e**	39
8	**2f**	−15 → 0	1.2	(*Z*)-**4f**	90
9[b]	**2f**	−15 → 0	1	(*Z*)-**4f**	87

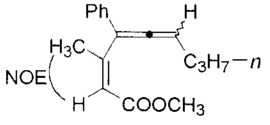
[a] Isolated yield. [b] In absence of $HgCl_2$. [c] 5 mol % $PdCl_2(PPh_3)_2$ was used as the catalyst.

Table 2. Pd(0)-Catalyzed Coupling Reaction of Electron-Deficient Alkenyl Halides with the Organozinc Reagents Formed by the Subsequent Treatment of 1-Phenylhex-1-yne with *n*-BuLi and $ZnBr_2$ with or without the Addition of $HgCl_2$



entry	2[a]	time (h)	product	yield[b] (%)
1	**2a**	2.25	(*E*)-**7a**	73
2[c]	**2a**	2.5	(*E*)-**7a**	30
3	**2b**	2	(*E*)-**7b**	85
4[c]	**2b**	3	(*E*)-**7b**	58
5	**2c**	2.5	(*E*)-**7a**	86
6[c]	**2c**	2	(*E*)-**7a**	78
7	**2d**	2.5	(*Z*)-**7d**	77
8[d]	**2e**	23	(*Z*)-**7e**	47
9[c,d]	**2e**	18	(*Z*)-**7e**	40

[a] See Table 1 for the structures of **2a**,**b** and **2d**,**e**. [b] Isolated yield. [c] In absence of $HgCl_2$. [d] 50% of **2e** was recovered.

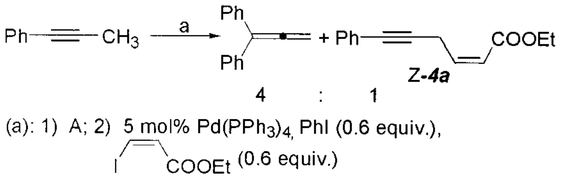


***Z*-7d**

Figure 1.

the reaction. Some representative examples with or without the addition of $HgCl_2$ are summarized in Table 2; here again, the yields in the presence of $HgCl_2$ are usually higher.[5]

Scheme 5



We did some further experiments to probe the mechanism of this reaction. In the absence of $Pd(PPh_3)_4$, the reaction of ethyl (*Z*)-3-iodopropenoate with the organozinc formed in situ by the subsequent treatment of 1-phenylprop-1-yne with *n*-BuLi and $ZnBr_2$ did not occur, ruling out the possibility of uncatalyzed Michael addition of the organozinc reagent to the conjugated C=C bond[6] followed by elimination of X^- to afford the alkynic products.

While the mixture of phenyl iodide (0.5 mmol) and ethyl (*Z*)-3-iodopropenoate (0.5 mmol) reacted with the organozinc reagent formed by the treatment of 1-phenylprop-1-yne (0.85 mmol) with *n*-BuLi (0.94 mmol) and $ZnBr_2$ under the catalysis of $Pd(PPh_3)_4$ (29 mg, 0.025 mmol), it afforded a mixture of 1,1-diphenylpropa-1,2-diene and (*Z*)-**4a** in a ratio of 4:1, indicating that the coupling reaction of phenyl iodide is much faster than that of ethyl (*Z*)-3-iodopropenoate (Scheme 5).

It has been reported that in most cases the oxidative addition reaction of Pd(0) with allenic bromides or propargylic halides afforded completely or predominantly η^1-allenyl palladium species.[7] However, the equilibrium between η^1-allenyl palladium, η^1-propargyl palladium, and η^3-propargyl palladium complexes depends on the ligands[8] used as well as the substituents at the propargyl moiety;[9,10] thus, a unified mechanism (Scheme 6) was proposed for this reaction. With 3-phenylprop-1-yne (R = H), the 6-phenylhex-5-yn-2-enoates **4** were formed via the reductive elimination of η^1-propargyl-type of palladium intermediate **10**,[11] while with 3-phenylhex-1-yne, probably due to the steric hindrance of R, 2,4,5-trienoates **7** were formed exclusively via the reductive elimination of η^1-allenyl-type of palladium intermediate **9**.[12] The different regioselectivity observed here may be derived from the competing reactivity of either two isomeric organozincs or two isomeric palladium species.

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[6] (a) Kawakami, Y.; Tsuruta T. *Tetrahedron Lett.* **1971**, 1173. (b) Kawakami, Y.; Tsuruta T. *Tetrahedron Lett.* **1971**, 1959. (c) Tsuruta T.; Kawakami, Y. *Tetrahedron* **1973**, *29*, 1173. (d) Malzieu, R. *Bull. Soc. Chim. Fr.* **1966**, 2682. (e) Daviaud, G.; Miginiac P. *Bull. Soc. Soc. Fr.* **1970**, 1617. Moreau, J.-L.; Frangin, Y.; Gaudemar, M. *Bull. Soc. Chim. Fr.* **1970**, 4511. (f) Daviaud, G.; Massy M.; Miginiac, P. *Tetrahedron Lett.* **1970**, 5169. (g) Daviaud, G.; Massy-Bardot, M.; Miginiac, P. *C. R. Hebd. Seances Acad. Sci., Ser. C* **1971**, *272*, 969. (h) Gaudemar-Bardone, F.; Mladenova, M.; Gaudemar, M. *Synthesis* **1988**, 611. (i) Frangin, Y.; Guimbal, G.; Wissocq, F.; Zamarlik, H. *Synthesis* **1986**, 1046. (j) Barbot, F.; Paraiso, E.; Miginiac, P. *Tetrahedron Lett.* **1984**, *25*, 4369.

[7] (a) Jeffery-Luong, T.; Linstrumelle, G.*Tetrahedron Lett.* **1980**, *21*, 5019. (b) Tsuji J.; Watanabe H.; Minami I.; Shimizu I. *J. Am. Chem. Soc.* **1985**, *107*, 2196. (c) For the synthesis of pure η^1-allenyl palladium complexes from the oxidative addition reaction of Pd(0) with allenylic bromides, see: Wouters, J. M. A.; Klein, R. A.; Elsevier: C. J.; Häming, L.; Stam, C. H. *Organometallics* **1994**, *13*, 4586. (d) For the synthesis of η^1-allenyl palladium complexes from the oxidative additon reaction of Pd(0) with propargyl halides, see: Elsevier: C. J.; Kleijn, H.; Ruitenberg, K.; Vermeer, P. *J. Chem. Soc., Chem. Commun.* **1983**, 1529.

[8] Tsutsumi, K.; Ogoshi, S.; Nishiguchi, S.; Kurosawa, H. *J. Am. Chem. Soc.* **1998**, *120*, 1938.

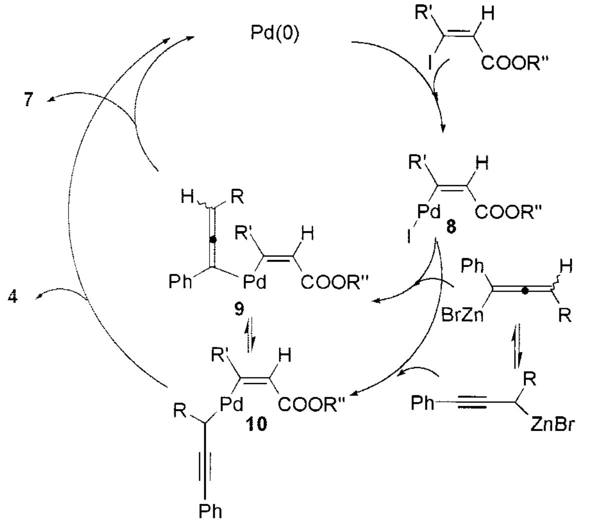
[9] Ogoshi, S.; Tsutsumi, K.; Kurosawa, H. *J. Organomet. Chem.* **1995**, *493*, C19.

[10] Elsevier, C. J.; Kleijn, H.; Boersma, J.; Vermeer, P. *Organometallics* **1986**, *5*, 716.

[11] It should be noted that under procedure A 1-phenylprop-1-yne afforded a mixture of allenic and propargylic zinc reagents; see ref 5.

[12] Russel, C. E.; Hegedus, L. S. *J. Am. Chem. Soc.* **1983**, *105*, 943.

Scheme 6



In conclusion, we have observed two different types of coupling patterns for the Pd(0)-catalyzed reaction of allenic/propargylic zinc reagents with organic halides; the regioselectivity of the coupling reaction depends not only on the structure of organic halides, but also on that of 1-arylalk-1-ynes. The tendency for the migration of C═C double bond in products **4a** depends largely on the excess amount of zinc reagent and the reaction temperature. Although the rational has been discussed, the real effect on the regioselectivity still needs further attention. In most cases, the configurations of the C═C bonds in the alkenyl halides remained intact. By the methodology described in this paper, 6-phenylhex-5-yn-2-enoates/enitriles and 4-phenyl-6-substitutedhexa-2,4,5-trienoates can be prepared highly regio- and stereoselectively.

Experimental Section

Materials. *n*-BuLi (solution in hexane), (*E*)-1-iodostyrene,[13] (*E*)-1-iodohexene,[13] methyl (*Z*)-3-iodopropenoate,[14] ethyl (*Z*)-3-iodopropenoate,[14] ethyl (*Z*)-3-bromopropenoate,[14] ethyl (*Z*)-3-chloropropenoate,[14] methyl (*Z*)-3-iodobutenoate,[14] methyl (*Z*)-3-phenyl-3-iodopropenoate,[14] and (*Z*)-3-iodopropenitrile[14] were prepared according to the literature methods. α-Bromostyrene and α-iodostyrene were commercially available and used after they were dried via the azeotropic evaporation with benzene. ^{1}H NMR spectra (δ) were measured using $CDCl_3$ as the solvent and Me_4Si as the internal standard, unless otherwise stated.

Ethyl (*E*)-3-iodopropenoate (**2c**), ethyl (*E*)-3-bromopropenoate, and 4-nitrobenzyl (*E*)-3-iodopropenoate were prepared via the reaction of (*E*)-3-halopropenoic acid,[15] K_2CO_3, and the corresponding organic halides in DMF.

Pd(PPh$_3$)$_4$-Catalyzed Coupling Reaction of α-Iodostyrene with Organozinc Formed by the Reaction of 1-Phenylprop-1-yne with *n*-BuLi and ZnBr$_2$ in the Presence of HgCl$_2$. To a solution of $HgCl_2$ (2 mg, 0.007 mmol, 1.5 mol %) and 1-phenylprop-1-yne (58 mg, 0.5 mmol) in THF (2 mL) in a dry Schlenk tube was added *n*-BuLi (0.35 mL, 1.6 M in hexane, 0.55 mmol) at −78 °C under N_2. After 100 min at −78 °C, dry $ZnBr_2$ (169 mg, 0.75 mmol) in THF (3 mL) was added. After 10 min at this temperature, the reaction mixture was warmed to room temperature and stayed at rt for 20 min, and a solution of Pd(PPh$_3$)$_4$ (29 mg, 0.025 mmol) and α-iodostyrene (112 mg, 0.5 mmol) in THF (1 mL) was added subsequently at rt. After the reaction was complete, as monitored by TLC (eluent: petroleum ether), it was quenched with water and extracted with petroleum ether. Drying over $MgSO_4$, rotary evaporation, and chromatography on silica gel (eluent: petroluem ether) afforded 36 mg (33%) of 2,3-diphenylpenta-1,3,4-triene (**3a**): ^{1}H NMR 7.55−7.05 (m, 10H), 5.70 (s, 1H), 5.40 (s, 1H), 5.15 (s, 2H); MS *m/e* 218 (M$^+$, 100); IR (neat) 1938, 1600 cm^{-1}; HRMS calcd for $C_{17}H_{14}$ 218.1092, found 218.1100.

Ethyl 6-phenylhex-5-yn-2(*Z*)-enoate ((*Z*)-4a) was prepared similarly, starting from **1** (99 mg, 0.85 mmol) and **2a** (113 mg, 0.5 mmol) to afford 71 mg (66%) of (*Z*)-**4a**: ^{1}H NMR 7.40−7.20 (m, 5H), 6.28 (dt, *J* = 11.3, 6.7 Hz, 1H), 5.80 (dt, *J* = 11.3, 1.9 Hz, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 3.80 (dd, *J* = 6.7, 1.9 Hz, 2H), 1.30 (t, *J* = 7.1 Hz, 3H); MS *m/e* 214 (M$^+$, 46.13), 141 (100); IR (neat) 2200, 1720, 1645, 1600, 1200 cm^{-1}. Anal. Calcd for $C_{14}H_{14}O_2$: C, 78.48; H, 6.59. Found: C, 78.50; H, 6.71.

Methyl 6-phenylhex-5-yn-2(*Z*)-enoate ((*Z*)-4b) was prepared similarly, starting from **1** (99 mg, 0.85 mmol) and **2b** (106 mg, 0.5 mmol) to afford 62 mg **(**62%) of (*Z*)-**4b**: ^{1}H NMR 7.45−7.20 (m, 5H), 6.38 (dt, *J* = 11.3, 6.8 Hz, 1H), 5.90 (dt, *J* = 11.3, 2.1 Hz, 1H), 3.85 (dd, *J* = 6.8, 2.1 Hz, 2H), 3.75 (s, 3H); MS *m/e* 200 (M$^+$, 68.21), 115 (100); IR (neat) 2240, 1730, 1655, 1600, 1220, 1180 cm^{-1}; HRMS calcd for $C_{13}H_{12}O_2$ 200.0834, found 200.0847.

Methyl 3,6-diphenylhex-5-yn-2(*Z*)-enoate ((*Z*)-4e) was prepared similarly, starting from **1** (99 mg, 0.85 mmol) and **2e** (144 mg, 0.5 mmol) to afford 67 mg **(**49%) of (*Z*)-**4e**: ^{1}H NMR 7.65−7.55 (m, 2H), 7.45−7.35 (m, 3H), 7.25−7.15 (m, 5H), 6.20 (s, 1H), 4.32 (s,2H), 3.80 (s, 3H); MS *m/e* 276 (M$^+$, 57.01), 215 (100); IR (neat) 2200, 1720, 1630, 1600, 1190, 1170 cm^{-1}; HRMS calcd for $C_{19}H_{16}O_2$: 276.1146, found 276.1139.

Pd(PPh$_3$)$_4$-Catalyzed Coupling Reaction of Ethyl (*E*)-3-Iodopropenoate with Organozinc Formed by the Subsequent Reaction of 1-Phenylprop-1-yne with *n*-BuLi and ZnBr$_2$ in the Presence of HgCl$_2$. Starting from **1** (99 mg, 0.85 mmol) and **2c** (113 mg, 0.5 mmol) to afford 27 mg (25%) of (*E*)-**4a**, 22 mg (21%) of (*Z*)-**5a**, and 13 mg (12%) of (*E*)-**5a**. **Ethyl 6-phenylhex-5-yn-3(*Z*)-enoate ((*Z*)-5a):** ^{1}H NMR 7.45−7.15 (m, 5H), 6.15 (dt, *J* = 10.9, 7.1 Hz, 1H), 5.85 (dt, *J* = 10.9, 1.1 Hz, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 3.45 (dd, *J* = 7.1, 1.1 Hz, 2H), 1.25 (t, *J* = 7.1 Hz, 3H); MS *m/e* 214 (M$^+$, 43.45), 141 (100); IR (neat) 2190, 1731, 1661, 1595, 1180 cm^{-1}; HRMS calcd for $C_{14}H_{14}O_2$ 214.0990, found 214.0995. **Ethyl 6-phenylhex-5-yn-3(*E*)-enoate ((*E*)-5a):** ^{1}H NMR 7.45−7.20(m, 5H), 6.30 (dt, *J* = 15.8, 7.3 Hz, 1H0, 5.84 (dt, *J* = 15.8, 1.6 Hz, 1H), 4.17 (q, *J* = 7.2, 2H), 3.20 (dd, *J* = 7.3, 1.6 Hz, 2H), 1.25 (t, *J* = 7.2 Hz, 3H); MS *m/e* 214 (M$^+$, 43.45), 141 (100); IR (neat) 1731, 1595, 1257, 1164 cm^{-1}; HRMS calcd for $C_{14}H_{14}O_2$ 214.0990, found 214.0988.

Pd(PPh$_3$)$_4$-Catalyzed Coupling Reaction of *p*-Nitrobenzyl (*E*)-3-Iodopropenoate with Organozinc Formed by the Reaction of 1-Phenylprop-1-yne with *n*-BuLi and ZnBr$_2$ in the Presence of HgCl$_2$. Starting from **1** (99 mg, 0.85 mmol) and *p*-nitrobenzyl (*E*)-3-iodopropenoate (167 mg, 0.5 mmol) to afford **4c**, (*Z*)-**5b**, and (*E*)-**5b** in an NMR ratio of 0.54:2:1 in 80% combined yield. Recrystallization with the mixture of petroleum ether and ethyl acetate afforded the single crystals of (*E*)-**5b**. ***p*-Nitrobenzyl 6-phenylhex-5-yn-3(*E*)-enoate ((*E*)-5b):** ^{1}H NMR 8.23 (d, *J* = 8.8 Hz, 2H), 7.52 (d, *J* = 8.8 Hz, 2H), 7.48−7.35 (m, 2H), 7.35−7.25 (m, 3H), 6.28 (dt, *J* = 15.8, 7.2 Hz, 1H), 5.82 (dt, *J* = 15.8, 1.3 Hz, 1H), 5.20 (s, 2H), 3.30 (dd, *J* = 7.2, 1.3 Hz, 2H); MS *m/e* 321 (M$^+$, 48.17), 141 (100); IR (neat) 1735, 1605, 1190, 1160 cm^{-1}. Anal. Calcd for $C_{19}H_{15}NO_4$: C, 71.02; H, 4.71; N, 4.36. Found: C, 70.90; H, 4.70; N, 4.52.

The detailed information for the X-ray structure determination of (*E*)-**5b** was included in the Supporting Information.

Pd(PPh$_3$)$_4$-Catalyzed Coupling Reaction of Ethyl (*E*)-3-Iodopropenoate with Organozinc Formed by the Subsequent Reaction of 1-Phenylprop-1-yne with *n*-BuLi and ZnBr$_2$ in Absence of HgCl$_2$. To a solution of 1-phenylprop-1-yne (99 mg, 0.85 mmol) in THF (2 mL) in a dry Schlenk tube was added *n*-BuLi (0.7 mL, 1.6 M in hexane, 0.94 mmol) at −78 °C under N_2. After 100 min at −78 °C, dry $ZnBr_2$ (278

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mg, 1.275 mmol) in THF (3 mL) was added. After 10 min at this temperature, the reaction mixture was warmed to room temperature and stayed at room temperature for 20 min, and a solution of $Pd(PPh_3)_4$ (29 mg, 0.025 mmol) and ethyl (*E*)-3-iodopropenoate (113 mg, 0.5 mmol) in THF(1 mL) was added at 0 °C. After the reaction was complete, as monitored by TLC (eluent: petroleum ether/ethyl acetate = 100:1), it was quenched with water and extracted with ether. Drying over $MgSO_4$, rotary evaporation, and chromatography on silica gel (eluent: petroluem ether/ethyl acetate = 100:1) afforded 82 mg (76%) of ethyl 6-phenylhex-5-yn-2(*E*)-enoate **((*E*)-4a)**: ^{1}H NMR 7.45−7.20 (m, 5H), 6.90(dt, J = 15.5, 5.0 Hz, 1H), 6.15(dt, J = 15.5, 1.9 Hz, 1H), 4.15(q, J = 7.2 Hz, 2H), 3.28(dd, J = 5.0, 1.9 Hz, 2H), 1.20(t, J = 7.2 Hz, 3H); MS *m*/*e* 214 (M^+, 36.06), 141 (100); IR (neat) 2200, 1720, 1660, 1600, 1270, 1170 cm^{-1}. Anal. Calcd for $C_{14}H_{14}O_2$: C, 78.48; H, 6.59. Found: C, 78.40; H, 6.55.

$Pd(PPh_3)_4$-Catalyzed Coupling Reaction of (*Z*)-3-Iodopropenitrile with Organozinc Formed by the Reaction of 1-Phenylprop-1-yne with *n*-BuLi and $ZnBr_2$ in the Presence of $HgCl_2$. To a solution of $HgCl_2$ (3 mg, 0.011 mmol, 1.5 mol %) and 1-phenylprop-1-yne (99 mg, 0.85 mmol) in THF (2 mL) in a dry Schlenk tube was added *n*-BuLi (0.7 mL, 1.6 M in hexane, 0.94 mmol) at −78 °C under N_2. After 100 min at −78 °C, dry $ZnBr_2$ (278 mg, 1.275 mmol) in THF (3 mL) was added. After 10 min at this temperature, the reaction mixture was warmed to room temperature and stayed at rt for 20 min, and then $Pd(PPh_3)_4$ (29 mg, 0.025 mmol) and (*Z*)-3-iodopropenitrile (90 mg, 0.5 mmol) in THF (1 mL) were added at −15 °C. After the reaction was complete, as monitored by TLC (eluent: petroleum ether/ethyl acetate = 100:1), it was quenched with water and extracted with ether. Drying over $MgSO_4$, evaporation, and chromatography on silica gel (eluent: petroluem ether/ethyl acetate = 100:1) afforded 76 mg (90%) of 6-phenylhex-5-yn-2(*Z*)-enitrile **((*Z*)-4f)**: ^{1}H NMR 7.45−7.25 (m, 5H), 6.55 (dt, J = 10.8, 7.1 Hz, 1H), 5.55 (dt, J = 10.8, 1.6 Hz, 1H), 3.55 (dd, J = 7.1, 1.6 Hz, 2H); MS *m*/*e* 167 (M^+, 100); IR (neat) 2221, 1621, 1597, 1569, 1489, 1300 cm^{-1}; HRMS calcd for $C_{12}H_9N$ 167.0733, found 167.0720.

$Pd(PPh_3)_4$-Catalyzed Coupling Reaction of Methyl (*Z*)-3-Iodopropenoate with Organozinc Formed by the Reaction of 1-Phenylhex-1-yne with *n*-BuLi and $ZnBr_2$ in the Presence of $HgCl_2$. To a solution of $HgCl_2$ (3 mg, 0.011 mmol, 1.5 mol %) and 1-phenylhex-1-yne (134 mg, 0.85 mmol) in THF (2 mL) in a dry Schlenk tube was added *n*-BuLi (0.7 mL, 1.6 M in hexane, 0.94 mmol) at rt under N_2. After 100 min at rt, dry $ZnBr_2$ (278 mg, 1.275 mmol) in THF (3 mL) was added at −78 °C. After 10 min at this temperature, the reaction mixture was warmed to room temperature and stayed at rt for 20 min, and then $Pd(PPh_3)_4$ (29 mg, 0.025 mmol) and methyl (*Z*)-3-iodopropenoate (106 mg, 0.5 mmol) in THF (1 mL) were added at rt. After the reaction was complete, as monitored by TLC (eluent: petroleum ether/ethyl acetate = 100:1), it was quenched with water and extracted with ether. Drying over $MgSO_4$, rotary evaporation, and chromatography on silica gel (eluent: petroluem/ethyl acetate = 100:1) afforded 103 mg (85%) of methyl 4-phenylnona-2(*E*),4,5-trienoate **((*E*)-7b)**: ^{1}H NMR 7.35−7.15 (m, 6H), 6.43 (s, 1H), 5.95 (d, J = 15.84 Hz, 1H), 3.75 (s, 3H), 2.35−2.20 (m, 2H), 1.70−1.50 (m, 2H), 1.00 (t, J = 7.24 Hz, 3H); MS *m*/*e* 242 (M^+, 8.94), 153 (100); IR (neat) 1922, 1714, 1618, 1192, 1172 cm^{-1}; HRMS calcd for $C_{16}H_{18}O_2$ 242.1302, found 242.1290.

Ethyl 4-phenylnona-2(*E*),4,5-trienoate ((*E*)-7a) was prepared similarly, starting from **6** (134 mg, 0.85 mmol) and **2c** (113 mg, 0.5 mmol) to afford 110 mg (86%) of (*E*)-**7a**: ^{1}H NMR 7.40−7.20 (m, 6H), 6.43 (s, 1H), 5.95 (dd, J = 15.8, 1.5 Hz, 1H), 4.20 (q, J = 7.1 Hz, 2H), 2.35−2.20 (m, 2H), 1.70−1.50 (m, 2H), 1.30 (t, J = 7.1 Hz, 3H), 1.00(t, J = 7.4 Hz, 3H); ^{13}C NMR 212.23, 166.75, 143.29, 133.27, 128.76, 128.40, 128.07, 118.13, 108.26, 96.19, 60.35, 30.75, 20.92, 14.30, 13.97; MS *m*/*e* 256 (M^+, 14.75), 183 (100); IR (neat) 1930, 1715, 1620 cm^{-1}; HRMS calcd for $C_{17}H_{20}O_2$ 256.1458, found 256.1463.

Methyl 3-methyl-4-phenylnona-2(*Z*),4,5-trienoate ((*Z*)-7d) was prepared similarly, starting from **6** (134 mg, 0.85 mmol) and **2d** (113 mg, 0.5 mmol) to afford 99 mg (77%) of (*Z*)-**7d**: ^{1}H NMR 7.45−7.10 (m, 5H), 6.50 (s, 1H), 5.90 (s, 1H), 3.75 (s, 3H), 2.45−2.20 (m, 5H), 1.70−1.45 (m, 2H), 0.95 (t, J = 7.30 Hz, 3H); MS *m*/*e* 256 (M^+, 27.87), 43 (100); IR (neat) 1930, 1720, 1620, 1170 cm^{-1}; HRMS calcd for $C_{17}H_{20}O_2$ 256.1458, found 256.1490.

Methyl 3,4-diphenylnona-2(*Z*),4,5-trienoate ((*Z*)-7e) was prepared similarly, starting from **6** (134 mg, 0.85 mmol) and **2e** (143 mg, 0.5 mmol) to afford 71 mg of **2e** and 37 mg (47%, based on 50% conversion) of (*Z*)-**7e**: ^{1}H NMR 7.35−7.05 (m, 10H), 6.12 (s, 1H), 6.07 (s, 1H), 3.55 (s, 3H), 2.45−2.30 (m, 2H), 1.70−1.50 (m, 2H), 1.00 (t, J = 7.3 Hz, 3H); MS *m*/*e* 318 (M^+, 27.87), 289 (100); IR (neat) 1945, 1730, 1615, 1180, 1160 cm^{-1}; HRMS calcd for $C_{22}H_{22}O_2$ 318.1614, found 318.1651.

Isomerization Reaction of Ethyl 6-Phenylhex-5-yn-2(*Z*)-enoate ((*Z*)-4a). (*Z*)-**4a** (30 mg, 0.14 mmol) was added to DMF (1 mL) in a dry Schlenk tube and heated to 50 °C. After 2 h at this temperature, the reaction mixture was extracted with ether and washed with water. After the mixture was dried over $MgSO_4$, rotary evaporation afforded 26 mg of a mixture of ethyl 6-phenylhex-5-yn-3(*Z*)-enoate ((*Z*)-**5a**) and ethyl 6-phenylhex-5-yn-3(*E*)-enoate ((*E*)-**5a**) in a ratio of 1:4.

$Pd(PPh_3)_4$-Catalyzed Coupling Reaction of Ethyl (*Z*)-3-Iodopropenoate and Phenyl Iodide with Organozinc Formed by the Subsequent Reaction of 1-Phenylprop-1-yne with *n*-BuLi and $ZnBr_2$ in the Presence of $HgCl_2$. To a solution of $HgCl_2$ (3 mg, 0.011 mmol, 1.5 mol %) and 1-phenylprop-1-yne (99 mg, 0.85 mmol) in THF (2 mL) in a dry Schlenk tube was added *n*-BuLi (0.7 mL, 1.6 M in hexane, 0.94 mmol) at −78 °C under N_2. After 100 min at −78 °C, dry $ZnBr_2$ (278 mg, 1.275 mmol) in THF (3 mL) was added. After 10 min at this temperature, the reaction mixture was warmed to room temperature and stayed at rt for 20 min, and then $Pd(PPh_3)_4$ (29 mg, 0.025 mmol), ethyl (*Z*)-3-iodopropenoate (113 mg, 0.5 mmol), and phenyl iodide (102 mg, 0.5 mmol) in THF (1 mL) were added at rt. After the reaction was complete, as monitored by TLC (eluent: petroleum ether/ethyl acetate = 100:1), it was quenched with water and extracted with ether. the mixture was dried over $MgSO_4$, rotary evaporation afforded 1,1-diphenylpropa-1,2-diene[5] and ethyl 6-phenylhex-5-yn-2(*Z*)-enoate ((*Z*)-**4a**) in an NMR ratio of 4:1.

Isomerization of Ethyl 6-Phenylhex-5-yn-2(*E*)-enoate. To a solution of 1-phenylprop-1-yne in THF (1 mL) in a dry Schlenk tube was added *n*-BuLi at −78 °C under N_2. After 100 min at −78 °C, dry $ZnBr_2$ (for the specific amounts of all the reagents in this procedure see Scheme 4) in THF (2 mL) was added. After 10 min at this temperature, the reaction mixture was warmed to room temperature and stayed at rt for 20 min, a solution of ethyl 6-phenylhex-5-yn-2(*E*)-enoate (53 mg, 0.25 mmol) in THF (1 mL) was added at the temperature specified in Scheme 4. After the reaction was complete as monitored by TLC, it was quenched with water and extracted with ether. Drying over $MgSO_4$ and rotary evaporation afforded the crude product, which was analyzed by 300 MHz ^{1}H NMR spectra using CH_2Br_2 as the internal standard.

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Supporting Information Available: The ^{1}H NMR spectra of the compounds **3a**, (*Z*)-**4a**, (*E*)-**4a**, (*Z*)-**5a**, (*E*)-**5a**, (*Z*)-**4b**, (*E*)-**5b**, (*Z*)-**4e**, (*Z*)-**4f**, (*E*)-**7a**, (*E*)-**7b**, (*Z*)-**7d**, and (*Z*)-**7e**, 2D ^{1}H−^{1}H NOSEY spectra of (*Z*)-**7d**, HMBC spectra of (*Z*)-**4a** and (*Z*)-**5a**, and detailed information for the X-ray structure determination of (*E*)-**5b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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