JOC Article

Alkynylzirconation of Alkynes and Application to One-Pot Bisalkynylation of Alkynes

Yuanhong Liu, Zhenqi Zhong, Kiyohiko Nakajima,† and Tamotsu Takahashi*

Catalysis Research Center and Graduate School of Pharmaceutical Sciences, Hokkaido University and CREST, Science and Technology Corporation (JST), Sapporo 060-0811, Japan, and Department of Chemistry, Aichi University of Education, Igaya, Kariya 448-8542, Japan

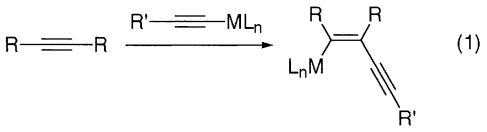
tamotsu@cat.hokudai.ac.jp

Received June 10, 2002

Stereocontrolled alkynylzirconation of unactivated alkynes was achieved by the reaction of an alkyne with Cp_2ZrEt_2 and alkynyl halide in this order. After hydrolysis of the alkynylzirconation product, trisubstituted enyne derivatives were obtained in good yields. Functionalized enynes were also prepared by the reaction of the alkynylzirconation products with a variety of electrophiles. Subsequent addition of the second alkynyl halide to the alkynylzirconation products provided an in situ protocol for bisalkynylation of alkynes into (*Z*)-enediynes in good yields.

Introduction

Stereoselective carbometalation of alkynes is an attractive method for the preparation of stereodefined alkenylmetal compounds.[1] This method has been successfully applied for the synthesis of stereodefined di-, tri-, or tetrasubstituted olefins. Especially, functionalized carbometalation, such as acyl-,[2] alkenyl-,[3] and allylmetalation,[4] and metalloesterification[5] of alkynes led to the convenient formation of functionalized alkenes. However, as for alkynylmetalation of alkynes (eq 1), only palladium or nickel-catalyzed alkynylstannylation of alkynes has been reported.[6] This alkynylstannylation of alkynes is useful for terminal or relatively electron-deficient alkynes.



(1)

There is no report, to our best knowledge, of alkynylmetalation of internal unactivated alkynes. In 1992, it was reported that the zirconocene−cation complex, $[Zr(C_5Me_5)_2Me\{B(4\text{-}C_6H_4F)_4\}]$, catalyzed the dimerization reaction of terminal alkynes.[7] The intermediate was isolated in the case of *t*-Bu-substituted terminal alkyne and it was shown that the intermediate was an alkynylzirconation product. From the viewpoint of organic synthesis, however, we had to wait for development of a more general method for the alkynylmetalation of unactivated internal alkynes.

On the other hand, we have investigated the zirconium approach for functionalization of unactivated alkynes via the formation of zirconacycles. Here we found the alkynylzirconation could be achieved using the combination of unactivated internal alkynes, alkynyl halides, and Cp_2ZrEt_2. In this paper we report the novel alkynylzirconation of internal alkynes (eq 2). We also demonstrate here

* Address correspondence to this author at Hokkaido University. Fax: +81-11-706-3274.

† Aichi University of Education.

(1) For reviews on carbometalation of alkynes, see (a) Knochel, P. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, UK, 1991; Vol. 4, pp 865−911. (b) Negishi, E. *Acc. Chem. Res.* **1987**, *20*, 65−72. (c) Normant, J. F.; Alexakis, A. *Synthesis* **1981**, 841−870. (d) Marek, I.; Normant, J. F. In *Metal-catalyzed Cross-coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wileyvch, Weinheim, Germany, 1998; pp 271−337. (e) Lipshutz, B. H.; Sengupta, S. *Org. React.* **1992**, *41*, 135−631.

(2) For acyl-metalation of alkynes, see: (a) Hoberg, H.; Schaefer, D.; Burkhart, G.; Krüger, C.; Romao, M. J. *J. Organomet. Chem.* **1984**, *266*, 203 and references therein. (b) Hoberg, H.; Apotecher, B. *J. Organomet. Chem.* **1984**, *270*, C15. (c) DeShong, P.; Sidler, D. R.; Rybczynski, P. J.; Slough, G. A.; Rheingold, A. L. *J. Am. Chem. Soc.* **1988**, *110*, 2575. (d) DeShong, P.; Sidler, D. R. *J. Org. Chem.* **1988**, *53*, 4892. (e) Takai, K.; Kataoka, Y.; Yoshizumi, K.; Oguchi, Y.; Utimoto, K. *Chem. Lett.* **1991**, 1479−1482.

(3) For alkenyl-metalation of alkynes, see the following. For Cu: (a) Negishi, E. *Acc. Chem. Res.* **1987**, *20*, 65−72. (b) Normant, J. F.; Cahiez, G.; Bourgain, M.; Chuit, C.; Villieras, J. *Bull. Soc. Chim. Fr.* **1974**, 1656−1666. (c) Alexakis, A.; Normant, J. F. *Tetrahedron Lett.* **1982**, *23*, 5151−5154. (d) Furber, M.; Taylor, R. J. K.; Burford, S. C. *Tetrahedron Lett.* **1985**, *26*, 3285−3288. (e) Furber, M.; Taylor, R. J. K.; Burford, S. C. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1809−1815. For Al: (f) Wilke, G.; Muller, H. *Chem. Ber.* **1956**, *89*, 444−447. (g) Eisch, J. J.; Kaska. W. C. *J. Am. Chem. Soc.* **1966**, *88*, 2213−2220. (h) Zweifel, G.; Snow, J. T.; Whitney, C. C. *J. Am. Chem. Soc.* **1968**, *90*, 7139−7141. For Mg: (i) Richey, H. G., Jr.; Von Rein, F. W. *J. Organomet. Chem.* **1969**, 20, P32−35. For Zr: (j) Takahashi, T.; Kondakov, D. Y.; Xi, Z.; Suzuki, N. *J. Am. Chem. Soc.* **1995**, *117*, 5871−5872.

(4) For allyl-metalation of alkynes, see the following. For Mg: (a) Richey, H. G.; Von Rein, F. W. *Tetrahedron Lett.* **1971**, 3777. (b) Eisch, J. J.; Merkley, J. H.; Galle, J. E. *J. Org. Chem.* **1979**, *44*, 587. For Zn: (c) Courtois, G.; Miginiac, L. *J. Organomet. Chem.* **1974**, *69*, 1. (d) Bernardou, F.; Miginiac, L. *J. Organomet. Chem.* **1977**, *125*, 23. (e) Negishi, E.; Miller, J. A. *J. Am. Chem. Soc.*, **1983**, *105*, 6761−6763. For Al: (f) Miller, J. A.; Negishi, E. *Tetrahedron Lett.* **1984**, *25*, 5863. For Zr: (g) Suzuki, N.; Kondakov, D. Y.; Kageyama, M.; Kotora, M.; Hara, R.; Takahashi, T. *Tetrahedron* **1995**, *51*, 4519−4540. (h) Takahashi, T.; Kotora, M.; Kasai, K.; Suzuki, N. *Tetrahedron Lett.* **1994**, *35*, 5685. (i) Yamanoi, S.; Imai, T.; Matsumoto, T.; Suzuki, K. *Tetrahedron Lett.* **1997**, 38, 3031−3034. For Sn: (j) Shirakawa, E.; Yamasaki, K.; Yoshida, H.; Hiyama, T. *J. Am. Chem. Soc.* **1999**, *121*, 10221−10222.

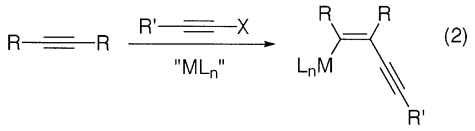
(5) Takahashi, T.; Xi, C.; Ura, Y.; Nakajima, K. *J. Am. Chem. Soc.* **2000**, *122*, 3228−3229.

(6) Shirakawa, E.; Yoshida, H.; Kurahashi, T.; Nakao, Y.; Hiyama, T. *J. Am. Chem. Soc.* **1998**, *120*, 2975−2976.

(7) Horton, A. D. *J. Chem. Soc., Chem. Commun.* **1992**, 185−187.

10.1021/jo026037e CCC: $22.00
Published on Web 09/25/2002

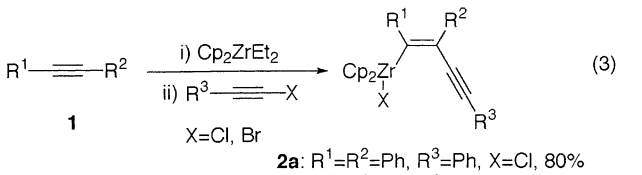
the further reactions of alkynylzirconation products for the stereoselective synthesis of conjugated enediynes.



(2)

Results and Discussion

Alkynylzirconation of Internal Alkynes via Zirconacycles. Treatment of internal alkynes **1** such as diphenylacetylene, di(*p*-tolyl)acetylene, and di(2-thienyl)acetylene with Cp_2ZrEt_2 and alkynyl chloride (or bromide) in this order afforded alkynylzirconation products **2a**−**d** in high yields as shown in eq 3. When diphenylacetylene was used as an internal alkyne and 1-phenylethynyl chloride was used as an alkynyl halide, alkynylzirconation product **2a** was formed in 80% NMR yield.



(3)

2a: $R^1=R^2$=Ph, R^3=Ph, X=Cl, 80%
2b: $R^1=R^2$=Ph, R^3=*p*-Tol, X=Cl, 83%
2c: $R^1=R^2$=*p*-Tol, R^3=Ph, X=Cl, 81%
2d: $R^1=R^2$=2-thienyl, R^3=Ph, X=Cl, 79%

The ^{1}H NMR spectrum of **2a** in C_6D_6/THF (2:1) solution showed a singlet peak at 6.3 ppm assigned to Cp protons. Its ^{13}C NMR spectrum revealed one singlet at 112.84 ppm assigned to Cp ligands. Other characteristic signals appeared at 89.75, 95.60, and 202.05 ppm which were assignable to the two carbons of the C≡C and one carbon of the Zr−C(sp^2) moiety, respectively. The chemical shift of the two alkynyl carbons in the sp carbon region indicated that the alkynyl substituent in **2a** has no interaction with the zirconium center. When di(*p*-tolyl)acetylene and di(2-thienyl)acetylene were used, the corresponding alkynylzirconation products **2c** and **2d** were formed in 81% and 79% yields, respectively, with 1-phenylethynyl chloride. In their ^{13}C NMR spectra, signals assigned to two carbons of the C≡C appeared in a similar region (89.37 and 95.84 ppm for **2c**; 87.77 and 91.24 ppm for **2d).** It is interesting to note that addition of 1 equiv of $MgBr_2$ to the solution of **2a** with 1 h of stirring at room temperature led to the halogen-exchange reaction of **2a**. As a result, the brominated analogue of **2a** was obtained as a mixture with **2a** in a ratio of 2.3:1. This result indicated that in order to obtain a clean chlorozirconium product of **2**, EtMgCl has to be used instead of EtMgBr to prepare Cp_2ZrEt_2 from Cp_2ZrCl_2, although it did not influence further reactions of **2** with electrophiles at all.

Hydrolysis of **2a** afforded 1,3,4-triphenylbut-3*E*-en-1-yne **3a** in 75% isolated yield with high stereoselectivity (isomerical purity >98%). Iodination of **2a** with 1 equiv of iodine gave iodinated product **4** in 74% yield. Bromination of **2a** was cleanly achieved by the reaction with NBS (88%). However, the use of NCS resulted in the formation of a mixture of the desired chlorinated compound **6** and hydrolysis product **3a** in the ratio of 1:1.7 after hydrolysis. Alkynes bearing phenyl, 2-thienyl, or alkyl substituents undergo alkynylzirconation with alkynyl halides to give enynes **3a**−**g** in 42−75% yields after hydrolysis. It was notable that aryl-substituted alkynyl halides usually afforded better results than alkyl-substituted halides. These results are summarized in Table 1.

Reactions of **2** with various electrophiles are shown in Scheme 1 and Table 1.[8] The alkynylzirconium product **2a** reacted with allyl chloride or benzyl chloride in the presence of a catalytic amount of CuCl to give the corresponding products **7** and **8** in 87% and 76% NMR yields, respectively. In the case of coupling with benzoyl chloride, a stoichiometric amount of CuCl (1 equiv) was used to obtain **9** in a good yield (72% isolated yield). The reaction of **2a** with *p*-trifluoromethyliodobenzene in the presence of 5 mol % of $Pd(PPh_3)_4$ and 1 equiv of CuCl gave the cross-coupling product **10** in 85% NMR yield. The structure of **10** was characterized by X-ray study to verify its stereochemistry.

Mechanism of Alkynylzirconation. We have recently reported allylzirconation,[4g,h] vinylzirconation,[3j] and esterzirconation reactions[5] via zirconacyclopentenes. On the basis of the results obtained here, it is reasonable to propose that the alkynylzirconation reactions also proceed in a similar way. The mechanism is shown in Scheme 2. It involves (i) the formation of zirconacyclopentene **12** by the reaction of an alkyne with Cp_2ZrEt_2,[9] (ii) replacement of ethylene by alkynyl halide through β,β'-C−C bond cleavage of **12** to form a zirconacyclopentadiene **13** with a halogen X at the β-position, which might be in equilibrium with the regioisomer **14**, and (iii) β-halogen elimination of **13** to afford **2**, which upon hydrolysis gives enyne **3**.

One-Pot Procedure for the Synthesis of Enediynes: *cis*-Enediynes. Alkynylzirconation described above could be used for an efficient synthesis of (*Z*)-enediynes in one pot from internal alkynes. Recently, enediyne derivatives have attracted much attention since they exist in bioactive compounds such as antitumor agents,[10] and as a substrate of the Masamune−Bergman reaction.[11] Although a variety of enediynes has been synthesized, for example, by Pd-catalyzed cross coupling of vinyl halides with terminal acetylenes,[12] by elimination of a silanol from α-silyl alcohols[13] or by conversion of 1,5-diynes into *cis*-enediynes after dehydration of prop-2-ynyl alcohols,[14] by reductive elimination,[15] by acid or base-induced elimination of alcohols, etc.,[16] one-pot synthesis of *Z*-enediynes from alkynes is very attractive. We

(8) (a) Takahashi, T.; Kotora, M.; Xi, Z. *J. Chem. Soc., Chem. Commun.* **1995**, 1503−1504. (b) Takahashi, T.; Xi, Z.; Kotora, M.; Xi, C.; Nakajima, K. *Tetrahedron Lett.* **1996**, *37*, 7521−7524. (c) Takahashi, T.; Hara, R.; Nishihara, Y.; Kotora, M. *J. Am. Chem. Soc.* **1996**, *118*, 5154−5155. (d) Hara, R.; NIshihara, Y.; Landre, P. D.; Takahashi, T. *Tetrahedron Lett.* **1997**, *38*, 447−450.

(9) Takahashi, T.; Suzuki, N.; Kageyama, M.; Nitto, Y.; Saburi, M.; Negishi, E. *Chem. Lett.* **1991**, 1579−1582.

(10) Wender, P. A.; Zercher, C. K.; Beckham, S.; Haubold, E.-M. *J. Org. Chem.* **1993**, *58*, 5867.

(11) Lockhart, T. P.; Bergman, R. G. *J. Am. Chem. Soc.* **1981**, *103*, 4091.

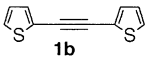
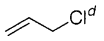
(12) (a) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, 4467−4470. (b) Sonogashira, K. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: New York, 1991; Vol 3, pp 521−549.

(13) Petasis, N. A.; Teets, K. A. *Tetrahedron Lett.* **1993**, *34*, 805.

(14) Yoshimatsu, M.; Yamada, H.; Shimizu, H.; Kataoka, T. *J. Chem. Soc., Chem. Commun.* **1994**, 2107−2108.

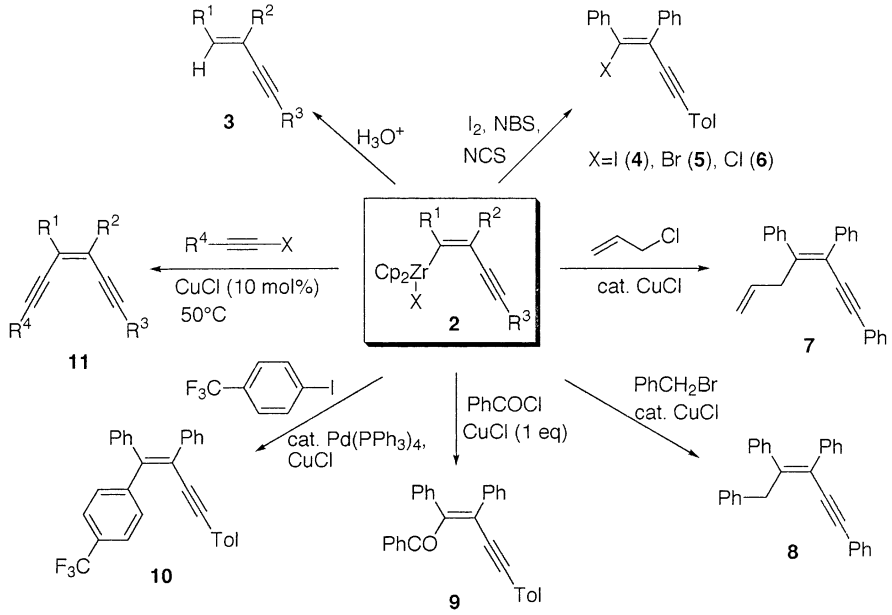
(15) Myers, A. G.; Dragovich, P. S. *J. Am. Chem. Soc.* **1992**, *114*, 5859−5860.

TABLE 1. Alkynylzirconation of Alkynes: Formation of Functionalized Enyne Derivatives

Alkyne R^1 R^2	Alkynyl Halide R^3	Electrophile	Temp./°C[a]	Time/h[a]	Product	Yield/%[b]
Ph—≡—Ph **1a**	Ph	HCl	r.t.	3	**3a**	(75)
1a	Tol	HCl	r.t.	3	**3b**	(66)
1a	Hex	HCl	50	3	**3c**	(42)
1a	Bu	HCl	50	6	**3d**	(47)
 **1b**	Tol	HCl	50	6	**3e**	(42)
Et—≡—Et **1c**	Ph	HCl	50	12	**3f**	(58)
Bu—≡—Bu **1d**	Ph	HCl	50	9	**3g**	(52)
1a	Tol	I_2	r.t.	12	**4**	74 (55)
1a	Tol	NBS	r.t.	6	**5**	88 (79)
1a	Tol	NCS	r.t.	6	**6**	78 (49)[c]
1a	Ph	 Cl[d]	50	3	**7**	87 (75)
1a	Ph	$PhCH_2Br$[d]	50	6	**8**	76 (62)
1a	Tol	PhCOCl[e]	50	1	**9**	84 (72)
1a	Tol	*p*-$CF_3C_6H_4I$[f]	50	1	**10**	85 (71)

[a] Except of hydrolysis, the reaction conditions shown here are the reactions of alkynylzirconation products with electrophiles. [b] NMR yields; isolated yields are given in parentheses. [c] EtMgCl was used to prepare Cp_2ZrEt_2. Combined yield. A mixture of chloro and hydrolysis products was obtained in the ratio of 1:1.7. [d] 10 mol % of CuCl was used. [e] 1 equiv of CuCl was used. [f] 5 mol % of $Pd(PPh_3)_4$ and 1 equiv of CuCl were added.

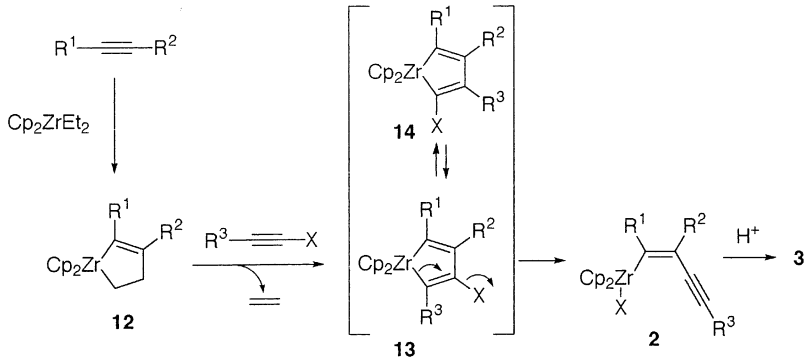
SCHEME 1



expected that zirconium product **2** could react with the second alkynyl halide to give *cis*-enediynes in one pot (Scheme 1, product **11**).

In the same way as described above for the formation of **2**, an alkyne was treated with Cp_2ZrEt_2 and the first alkynyl halide in this order. To achieve (*Z*)-enediyne formation cleanly, 1.0 equiv of the first alkynyl halide was used. After addition of the second alkynyl halide (1.25 equiv) and a catalytic amount of CuCl (0.1 equiv), the mixture was stirred at 50°C for an additional 6 h. The 1,3,4,6-tetrasubstituted en-1,5-diyne **11** was formed in moderate to good yields. In all cases, only (*Z*)-

SCHEME 2



enediynes were obtained. For example, the reaction of diphenylacetylene with phenylethynyl halide using Cp_2ZrEt_2 afforded 1,3,4,6-tetraphenyl-3-hexen-1,5-diyne **11a** in 63% isolated yield with exclusively cis configuration. (*Z*)-Di(2-thienyl) and dialkyl enediynes were also obtained (entries 2, 3, and 4). When two different alkynyl halides were used, the unsymmetrical (*Z*)-enediyne **11f** was formed in 72% yield.

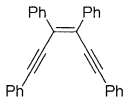
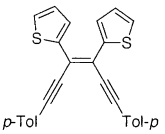
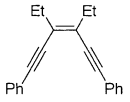
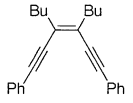
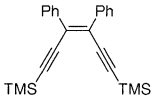
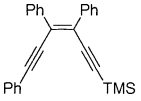
Cis−Trans Isomerization of Enediynes: Preparation of *trans*-Enediynes. It was known that *cis*-enediynes isomerize to trans under heating or irradiation.[17] (*Z*)-Enediynes obtained here also could be converted into trans isomers in organic solvents. For example, in a warm (50°C) THF solution of **11a**, a ca. 2.3:1 mixture of cis/trans isomers was obtained after 24 h. The trans isomer of **11a** crystallized from hexane/acetone (5/1) solution. Thus pure *trans*-**11a** could be obtained. Similarly, pure *trans*-**11c** was also prepared.

As described above, the alkynylzirconation reaction we report here can provide various kinds of enyne derivatives by the reaction of electrophiles. In particular, this method provides a convenient route to a one-pot procedure for bisalkynylation of internal alkynes.

Experimental Section

All reactions were carried out with standard Schlenk techniques under nitrogen. THF was distilled over sodium/benzophenone. All commercial reagents were used without further purification. Flash chromatography was performed with Merck silica gel 60 (40−60 μm). Alkynyl halide was prepared by the reaction of alkynyllithium with NCS or NBS. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ (containing 1% TMS) solutions at 400 and 100 MHz, respectively. All melting points were determined by a micro melting point apparatus and are uncorrected. IR spectra were measured with a FT-IR spectrometer. Single-crystal X-ray diffraction data were collected in Enraf-Nonius CAD4 diffractometers with molybdenum or copper cathodes.

TABLE 2. One-Pot Preparation of (*Z*)-Enediynes from Unactivated Internal Alkynes[a]

Entry	Alkyne	Alkynyl halide R^3	Alkynyl halide R^4	Product	Yield/%[b] of **11**	Stereochemistry
1	**1a**	Ph	Ph	 **11a**	63	only cis
2	**1b**	*p*-Tol	*p*-Tol	 **11b**	45	only cis
3	**1c**	Ph	Ph	 **11c**	61	only cis
4	**1d**	Ph	Ph	 **11d**	41	only cis
5	**1a**	TMS	TMS	 **11e**	56	only cis
6	**1a**	Ph	TMS	 **11f**	72	only cis

[a] Alkynylzirconation products were prepared in situ. [b] Isolated yields. Reactions were carried out at 50 °C for 3−9 h in the presence of 10 mol % CuCl.

A Typical Procedure for the Alkynylzirconation of Alkynes. 1,3,4-Triphenyl-4-[bis(η^5-cyclopentadienyl)chlorozirconium]but-3*Z*-en-1-yne (2a). To a solution of Cp_2ZrCl_2 (0.36 g, 1.25 mmol) in THF (5 mL) was added EtMgCl (1.0 M THF solution, 2.5 mmol) at −78°C and the mixture was stirred for 1 h at the same temperature. Diphenylacetylene (0.18 g, 1 mmol) was added and the mixture was warmed to 0 °C. After the mixture was stirred for 1 h, phenylethynyl chloride (0.17 g, 1.0 mmol) was added and stirring was continued at room temperature for 3 h or at 50°C for 1 h. Alkynylzirconation product **2a** was cleanly formed in 80% NMR yield. ^{1}H NMR

(16) (a) Yoshimatsu, M.; Yamada, H.; Shimizu, H.; Kataoka, T. *J. Chem. Soc., Chem. Commun.* **1994**, 2107−2108. (b) Audrain, H.; Skrydstrup, T.; Ulibarri, G.; Grierson, D. S. *Synlett* **1993**, 20−22. (c) Shibuya, M.; Sakai, Y.; Naoe, Y. *Tetrahedron Lett.* **1995**, *36*, 897−898. (d) Iida, K.; Hirama, M. *J. Am. Chem. Soc.* **1995**, *117*, 8875−8876.

(17) It has been reported that enediynes undergo cis−trans isomerization under heating or irradiation. (a) Vollhardt, K. P. C.; Winn. L. S. *Tetrahedron Lett.* **1985**, *26*, 709−712. (b) König, B.; Schofield, E.; Bubenitschek, P.; Jones, P. G. *J. Org. Chem.* **1994**, *59*, 7142−7143. (c) Martin, R. E.; Bartek, J.; Diederich, F.; Tykwinski, R. R.; Meister, E. C.; Hilger, A.; Lüthi, H. P. *J. Chem. Soc., Perkin Trans.* **1998**, 233. (d) Shimizu, T.; Miyasaka, D.; Kamigata, N. *Org. Lett.* **2000**, *2*, 1923−1925. (e) Diederich, F. *Chem. Commun.* **2001**, 219−227.

(C_6D_6/THF: 2/1, Me_4Si): δ 6.28 (s, 10H), 6.81−6.92 (m, 5H), 6.93−7.05 (m, 5H), 7.31−7.55 (m, 5H). ^{13}C NMR (C_6D_6/THF, Me_4Si): δ 89.75, 95.60, 112.84, 124.57, 126.32, 127.76, 127.94, 128.16, 128.30, 128.39, 128.60, 128.98, 129.06, 129.28, 131.60, 141.40, 202.11. HRMS calcd for $C_{32}H_{25}ClZr$ 534.0692, found 534.0698.

1-(*p*-Tolyl)-3,4-diphenyl-4-[bis(η^5-cyclopentadienyl)-chlorozirconium]but-3*Z*-en-1-yne (2b). NMR yield: 83%. ^1H NMR (C_6D_6/THF: 2/1, Me_4Si): δ 2.09 (s, 3H), 6.27 (s, 10H), 6.84−6.85 (m, 2H), 6.86−6.99 (m, 8H), 7.37−7.42 (m, 4H). ^{13}C NMR (C_6D_6/THF, Me_4Si) δ 21.27, 89.94, 94.96, 112.79, 121.59, 126.33, 127.80, 128.35, 128.63, 128.80, 129.01, 129.30, 129.80, 131.56, 131.92, 138.46, 141.45, 201.62. HRMS calcd for $C_{33}H_{27}ClZr$ 548.0848, found 548.0829.

1-Phenyl-3,4-di(*p*-tolyl)-4-[bis(η^5-cyclopentadienyl)chlorozirconium]but-3*Z*-en-1-yne (2c). NMR yield: 81%. ^1H NMR (C_6D_6/THF: 2/1, Me_4Si): δ 2.03 (s, 3H), 2.12 (s, 3H), 6.30 (s, 10H), 6.81−6.92 (m, 5H), 7.17−7.21 (m, 4H), 7.35 (d, J = 8.3 Hz, 2H), 7.53 (d, J = 8.3 Hz, 2H). ^{13}C NMR (C_6D_6/THF, Me_4Si): δ 20.93, 21.20, 89.37, 95.84, 112.49, 124.73, 128.35, 128.53, 128.84, 129.04, 129.53, 129.68, 131.59, 131.84, 132.24, 135.65, 136.42, 138.72, 201.85. HRMS calcd for $C_{34}H_{29}ClZr$ 562.1005, found 562.1013.

1-Phenyl-3,4-di(2-thienyl)-4-[bis(η^5-cyclopentadienyl)-chlorozirconium]but-3*Z*-en-1-yne (2d). NMR yield: 79%. ^1H NMR (C_6D_6/THF: 2/1, Me_4Si): δ 6.16 (s, 10H), 6.54 (d, J = 3.5 Hz, 1H), 6.76 (dd, J = 5.0, 3.8 Hz, 1H), 6.99 (dd, J = 5.0, 3.6 Hz, 1H), 7.16−7.23 (m, 5H), 7.45 (dd, J = 3.6, 1.0 Hz, 1H), 7.57−7.60 (m, 2H). ^{13}C NMR (C_6D_6/THF, Me_4Si): δ 87.77, 91.24, 109.88, 121.98, 123.74, 123.97, 124.13, 124.89, 126.34, 126.68, 126.78, 127.14, 127.89, 129.09, 129.69, 141.42, 189.99. HRMS calcd for $C_{28}H_{21}ClS_2Zr$ 545.9820, found 545.9818.

Formation of a Brominated Alkynylzirconation Product by Halogen-Exchange Reaction. To a solution of **2a** described above was added 1 mmol of $MgBr_2$. The mixture was stirred at room temperature for 1 h. The brominated product was formed in the ratio of 1:2.3 to **2a**. When Cp_2ZrEt_2 derived from EtMgBr and alkynyl chloride were used to prepare compound **2**, formation of a mixture of chloro- and bromozirconocene complexes with the same ratio was observed. **1,3,4-Triphenyl-4-[bis(η^5-cyclopentadienyl)bromozirconium]-but-3*Z*-en-1-yne**: ^1H NMR (C_6D_6/THF: 2/1, Me_4Si): δ 6.30 (s, 10H), 6.80−7.10 (m, 5H), 7.10−7.58 (m, 10H). ^{13}C NMR (C_6D_6/THF, Me_4Si) δ 89.45, 95.30, 112.36, 124.49, 126.48, 127.17, 127.65, 127.69, 128.44, 128.75, 128.96, 129.48, 129.74, 131.18, 131.82, 141.49, 202.30.

1,3,4-Triphenylbut-3*E*-en-1-yne (3a). Quenching the reaction mixture of **2a** with 3 N HCl afforded **3a**, which was purified by chromatography on silica (hexane) and afforded the product in 75% yield: white solid, mp 63−65 °C. ^1H NMR ($CDCl_3$, Me_4Si): δ 7.07−7.09 (m, 2H), 7.11 (s, 1H), 7.12−7.17 (m, 3H), 7.26−7.33 (m, 6H), 7.42−7.45 (m, 2H), 7.46−7.48 (m, 2H). ^{13}C NMR ($CDCl_3$, Me_4Si): δ 89.79, 92.22, 123.30, 124.20, 127.60, 127.84, 128.09, 128.16, 128.26, 128.51, 129.04, 129.34, 131.56, 136.05, 136.42, 137.71. IR (Nujol): 3020, 2305, 1595, 1490, 1442, 920, 756, 719 cm^{-1}. Anal. Calcd for $C_{22}H_{16}$: C, 94.25; H, 5.75. Found: C, 94.22; H, 5.73.

1-*p*-Tolyl-3,4-diphenylbut-3*E*-en-1-yne (**3b**): 66% (isolated); white needles, mp 91−92°C. ^1H NMR ($CDCl_3$, Me_4Si): δ 2.34 (s, 3H), 7.07−7.09 (m, 2H), 7.11 (s, 2H), 7.13−7.15 (m, 4H), 7.29−7.33 (m, 3H), 7.36 (m, 2H), 7.41−7.44 (m, 2H). ^{13}C NMR ($CDCl_3$, Me_4Si): δ 21.51, 90.04, 91.60, 120.22, 124.37, 127.52, 127.80, 128.08, 128.50, 129.05, 129.07, 129.33, 131.46, 136.08, 136.15, 137.83, 138.31. IR (Nujol): 3020, 2193, 1595, 1508, 1442, 814, 700 cm^{-1}. Anal. Calcd for $C_{23}H_{18}$: C, 93.84; H, 6.16. Found: C, 93.79; H, 6.15.

1,2-Diphenyldec-1*E*-en-3-yne (**3c**): 42% (isolated); yellow oil. ^1H NMR ($CDCl_3$, Me_4Si): δ 0.89 (t, J = 6.95 Hz, 3H), 1.27−1.35 (m, 4H), 1.39−1.44 (m, 2H), 1.46−1.61 (m, 2H), 2.37 (t, J = 7.10 Hz, 2H), 6.95 (s, 1H), 7.01−7.04 (m, 2H), 7.12−7.13 (m, 3H), 7.25−7.28 (m, 3H), 7.32−7.37 (m, 2H). ^{13}C NMR ($CDCl_3$, Me_4Si) δ 14.07, 19.57, 22.56, 28.63, 28.73, 31.34, 83.32, 91.16, 124.76, 127.20, 127.60, 128.00 (2C), 128.34, 128.99, 129.21, 135.05, 136.36, 138.30. IR (neat): 3024, 2922, 2181, 1599, 1495, 760, 696 cm^{-1}. Anal. Calcd for $C_{22}H_{24}$: C, 91.61; H, 8.39. Found: C, 91.28, H, 8.47.

1,2-Diphenyloct-1*E*-en-3-yne (**3d**): 47% (isolated); pale yellow oil. ^1H NMR ($CDCl_3$, Me_4Si): δ 0.93 (t, J = 7.26 Hz, 3H), 1.41−1.50 (m, 2H), 1.53−1.60 (m, 2H), 2.38 (t, J = 7.05 Hz, 2H), 6.95 (s, 1H), 7.02−7.05 (m, 2H), 7.11−7.16 (m, 3H), 7.23−7.29 (m, 3H), 7.32−7.36 (m, 2H). ^{13}C NMR ($CDCl_3$, Me_4Si) δ 13.65, 19.26, 22.04, 30.86, 83.29, 91.08, 124.76, 127.21, 127.62, 128.01, 128.36, 128.99, 129.21, 135.08, 136.36, 138.29. IR (neat): 3019, 2276, 1599, 1496, 1442, 918, 756, 698 cm^{-1}. HRMS calcd for $C_{20}H_{20}$ 260.1565, found 260.1566.

1-(*p*-Tolyl)-3,4-di(2-thienyl)but-3*E*-en-1-yne (**3e**): 42% (isolated); yellow oil. ^1H NMR ($CDCl_3$, Me_4Si): δ 2.35 (s, 3H), 6.92−6.94 (m, 1H), 7.06−7.08 (m, 2H), 7.12 (d, J = 8.06 Hz, 2H), 7.18 (d, J = 5.00 Hz, 1H), 7.21 (dd, J = 3.5, and 0.91 Hz, 1H), 7.26 (d, J = 8.06 Hz, 1H), 7.35 (d, J = 8.07 Hz, 2H), 7.43 (d, J = 5.08 Hz, 1H). ^{13}C NMR ($CDCl_3$, Me_4Si) δ 21.53, 90.70, 90.80, 114.46, 120.02, 126.53, 127.22, 127.30, 127.83, 128.01, 129.06, 130.20, 131.41, 131.58, 138.44, 139.15. IR (Nujol): 3096, 2191, 1601, 1508, 1228, 700 cm^{-1}. Anal. Calcd for $C_{19}H_{14}S_2$: C, 74.47; H, 4.60; S, 20.93. Found: C, 74.28; H, 4.81; S, 20.73.

1-Phenyl-3-ethylhex-3*E*-en-1-yne (**3f**): 58% (isolated); pale yellow oil. ^1H NMR ($CDCl_3$, Me_4Si): δ 1.02 (t, J = 7.52 Hz, 3H), 1.15 (t, J = 7.52 Hz, 3H), 2.15 (q, J = 7.52 Hz, 2H), 2.23 (q, J = 7.52 Hz, 2H), 5.93 (t, J = 7.48 Hz, 1H), 7.25−7.32 (m, 3H), 7.41−7.44 (m, 2H). ^{13}C NMR ($CDCl_3$, Me_4Si): δ 13.33, 13.93, 21.57, 23.93, 86.76, 91.47, 123.86, 124.09, 127.65, 128.21, 131.43, 139.36. IR (Nujol): 2995, 2168, 1599, 758, 712 cm^{-1}. HRMS calcd for $C_{14}H_{16}$ 184.1263, found 184.1252.

1-Phenyl-3-butyloct-3*E*-en-1-yne (**3g**): 52% (isolated); pale yellow oil. ^1H NMR ($CDCl_3$, Me_4Si): δ 0.91−0.96 (m, 6H), 1.33−1.42 (m, 6H), 1.52−1.60 (m, 2H), 2.14−2.24 (m, 4H), 5.96 (t, J = 7.56 Hz, 1H), 7.25−7.32 (m, 3H), 7.41−7.43 (m, 2H). ^{13}C NMR ($CDCl_3$, Me_4Si): δ 13.97, 14.05, 22.33, 22.40, 28.04, 30.39, 30.71, 31.50, 86.48, 91.90, 123.06, 123.91, 127.61, 128.20, 131.42, 138.56. IR (Nujol): 2950, 2202, 1599, 758, 690 cm^{-1}. HRMS calcd for $C_{18}H_{24}$ 240.1877, found 240.1892.

Reaction of Vinylzirconocene Product 2 with Electrophiles. To a solution of vinylzirconocene **2** in THF were added electrophiles such as allyl chloride, benzyl bromide, *p*-trifluoromethyliodobenzene, and acyl chloride in the presence of a catalytic amount of $Pd(PPh_3)_4$ and/or CuCl. In the cases of I_2, NBS, and NCS, direct halogenation occurred without CuCl. The reaction mixture was stirred for an additional 3−6 h at 50°C, quenched with 3 N HCl, and extracted with hexane. Combined organic extracts were washed with aqueous $NaHCO_3$ and water, dried over $MgSO_4$, and concentrated in a vacuum. Column chromatography on silica gel afforded the corresponding products.

4-Iodo-1-(*p*-tolyl)-3,4-diphenylbut-3*Z*-en-1-yne (**4**): 55% (isolated); brown oil. ^1H NMR ($CDCl_3$, Me_4Si): δ 2.36 (s, 3H), 7.10−7.16 (m, 8H), 7.18−7.25 (m, 4H), 7.46 (d, J = 7.9 Hz, 2H). ^{13}C NMR ($CDCl_3$, Me_4Si): δ 21.58, 94.79, 95.11, 108.16, 119.87, 127.46, 127.93, 128.03, 129.12, 129.50, 129.96, 131.55, 133.08, 137.64, 138.97, 143.00. IR (Nujol): 3050, 2199, 1597, 1494, 928, 702 cm^{-1}. Anal. Calcd for $C_{23}H_{17}I$: C, 65.73; H, 4.08; I, 30.19. Found: C, 65.54; H, 4.19; I, 30.44.

4-Bromo-1-(*p*-tolyl)-3,4-diphenylbut-3*Z*-en-1-yne (**5**): 79% (isolated). ^1H NMR ($CDCl_3$, Me_4Si): δ 2.38 (s, 3H), 7.16−7.20 (m, 8H), 7.24−7.27 (m, 4H), 7.46 (d, J = 7.9 Hz, 2H). ^{13}C NMR ($CDCl_3$, Me_4Si): δ 21.56, 90.78, 96.29, 119.92, 126.41, 127.57, 127.98, 128.05, 128.48, 129.11, 129.35, 129.49, 130.10, 131.58, 137.75, 138.91, 139.45. IR (Nujol): 3085, 2189, 1597, 1442, 898, 708 cm^{-1}. Anal. Calcd for $C_{23}H_{17}Br$: C, 74.00; H, 4.59; Br, 21.41. Found: C, 73.89; H, 4.65; Br, 21.30.

4-Chloro-1-(*p*-tolyl)-3,4-diphenylbut-3*Z*-en-1-yne (**6**): 49% (combined yield with hydrolysis product). ^1H NMR ($CDCl_3$, Me_4Si): δ 2.36 (s, 3H), 7.16−7.20 (m, 8H), 7.24−7.27 (m, 4H), 7.41−7.43 (m, 2H). ^{13}C NMR ($CDCl_3$, Me_4Si): δ 21.51, 88.72,

97.13, 119.93, 122.96, 127.63, 127.97, 128.12, 128.64, 129.09, 129.60, 129.81, 131.60, 137.37, 137.45, 137.66, 138.85. IR (Nujol): 3026, 2189, 1595, 1442, 1188, 814, 700 cm^{-1}. HRMS calcd for $C_{23}H_{17}Cl$ 328.1019, found 328.1017.

1,3,4-Triphenylhept-3*E*-3,6-dien-1-yne (**7**): 75% (isolated); white solid, mp 97−99°C. ^1H NMR ($CDCl_3$, Me_4Si): δ 3.73 (d, J = 6.60 Hz, 2H), 5.05 (dd, J = 10.08 and 1.40 Hz, 2H), 5.86−5.95 (m, 1H), 7.07−7.20 (m, 10H), 7.31−7.33 (m, 3H), 7.47−7.50 (m, 2H). ^{13}C NMR ($CDCl_3$, Me_4Si): δ 42.65, 90.27, 94.35, 116.34, 121.65, 123.64, 126.77, 127.02, 127.73, 127.92, 128.13, 128.32, 129.20, 129.85, 131.47, 134.97, 138.77, 140.66, 147.07. IR (Nujol): 3020, 2278, 1632, 1595, 916, 689 cm^{-1}. Anal. Calcd for $C_{25}H_{20}$: C, 93.71; H, 6.29. Found: C, 93.88; H, 6.19.

1,3,4,5-Tetraphenylpent-3*E*-1-yne (**8**): 62% (isolated); white needles, mp 106−107°C. ^1H NMR ($CDCl_3$, Me_4Si): δ 4.32 (s, 2H), 6.93−6.95 (m, 2H), 7.06−7.08 (m, 4H), 7.11−7.15 (m, 4H), 7.20−7.25 (m, 4H), 7.29−7.32 (m, 4H), 7.44−7.45 (m, 2H). ^{13}C NMR ($CDCl_3$, Me_4Si): δ 43.99, 90.83, 93.78, 122.08, 123.55, 126.08, 126.80, 126.95, 127.70, 127.83, 128.14, 128.30, 128.84, 129.33, 129.91, 131.51, 138.74, 139.19, 140.43, 148.16. IR (Nujol): 3080, 2310, 1597, 1487, 914, 754, 698 cm^{-1}. Anal. Calcd for $C_{29}H_{22}$: C, 94.01; H, 5.99. Found: C, 94.13; H, 5.93.

3,4-Diphenyl-4-phenylcarbonyl-1-(*p*-tolyl)but-3*Z*-en-1-yne (**9**): 72% (isolated); white solid, mp 134−136°C. ^1H NMR ($CDCl_3$, Me_4Si): δ 2.34 (s, 3H), 7.10 (d, J = 7.9 Hz, 2H), 7.14−7.20 (m, 3H), 7.22−7.24 (m, 2H), 7.26−7.34 (m, 3H), 7.35−7.41 (m, 3H), 7.45−7.47 (m, 2H), 7.76−7.78 (m, 2H), 7.86 (d, J = 7.8 Hz, 2H). ^{13}C NMR ($CDCl_3$, Me_4Si): δ 21.55, 89.07, 96.58, 119.82, 125.29, 128.18, 128.19, 128.28, 128.37, 128.46, 128.82, 129.08, 129.09, 129.59, 131.50, 133.10, 136.92, 137.43, 138.22, 138.94, 145.47, 197.95. IR (Nujol): 3082, 2200, 1661, 1597, 1269, 818, 696 cm^{-1}. Anal. Calcd for $C_{30}H_{22}O$: C, 90.42; H, 5.56. Found: C, 90.47; H, 5.65.

3,4-Diphenyl-4-(*p*-trifluoromethylphenyl)-1-(*p*-tolyl)-but-3*Z*-en-1-yne (**10**): 71% (isolated); white solid, mp 153−156°C. ^1H NMR ($CDCl_3$, Me_4Si): δ 2.32 (s, 3H), 6.97−7.00 (m, 2H), 7.05−7.10 (m, 4H), 7.11−7.24 (m, 6H), 7.33−7.35 (m, 2H), 7.61 (d, J = 8.3 Hz, 2H), 7.67 (d, J = 8.4 Hz, 2H). ^{13}C NMR ($CDCl_3$, Me_4Si): δ 21.50, 91.07, 94.22, 120.07, 123.12, 124.54, 124.58, 124.62, 124.65, 127.35, 127.51, 127.97, 129.07, 129.89, 130.84, 131.04, 131.25, 138.55, 139.10, 140.68, 146.49, 146.66. IR (Nujol): 3028, 2193, 1612, 1323, 698 cm^{-1}. Anal. Calcd for $C_{30}H_{21}F_3$: C, 82.17; H, 4.83; F, 13.00. Found: C, 82.19; H, 4.95; F, 12.86.

A Typical Procedure for the Preparation of Enediynes and Isomerization of *cis*-11a to *trans*-11a. To a solution of alkynylzirconation product **2a** described above were added phenylethynyl bromide (0.22 g, 1.25 mmol) and CuCl (0.01 g, 0.1 mmol) then the mixture was stirred at 50°C for 3 h. The reaction mixture was quenched with 3 N HCl and extracted with ethyl acetate. The extract was washed with brine and water and dried over $MgSO_4$. The solvent was evaporated in vacuo and the residue was purified by chromatography on silica (covered with aluminum foil to avoid the light) to afforded *cis*-**11a** in 63% yield. When the cis isomer was kept in hexane/acetone (5:1) solution for several days, the cis−trans isomerization occurred and *trans*-**11a** (**11a′**) was crystallized from the solution in 60% yield.

1,3,4,6-Tetraphenylhex-3*Z*-en-1,5-diyne (**11a**): 63% (isolated). Its NMR spectra were consistent with the published data.[17d]

1,3,4,6-Tetraphenylhexa-3*E*-en-1,5-diyne (**11a′**): 60% (isolated). Its NMR spectra were consistent with the published data.[17d]

3,4-Di(2-thienyl)-1,6-di(*p*-tolyl)hex-3*Z*-en-1,5-diyne (**11b**): 45% (isolated); yellow solid, mp 95−96°C. ^1H NMR ($CDCl_3$, Me_4Si): δ 2.35 (s, 6H), 6.96−6.98 (m, 2H), 7.11−7.13 (m, 4H), 7.19−7.22 (m, 2H), 7.31−7.32 (m, 2H), 7.43−7.45 (m, 4H). ^{13}C NMR ($CDCl_3$, Me_4Si): δ 21.55, 90.13, 97.37, 120.04, 121.83, 126.91, 127.87, 129.14, 129.24, 131.49, 138.87, 139.25. IR (Nujol): 2201, 1604, 1508, 814, 707 cm^{-1}. Anal. Calcd for $C_{28}H_{20}S_2$: C, 79.96; H, 4.79; S, 15.25. Found: C, 79.94; H, 4.84; S, 15.39.

3,4-Diethyl-1,6-diphenylhex-3*Z*-en-1,5-diyne (**11c**): 61% (isolated); white oil. ^1H NMR ($CDCl_3$, Me_4Si): δ 1.20 (t, J = 7.52 Hz, 6H), 2.60 (q, J = 7.52 Hz, 4H), 7.26−7.36 (m, 6H), 7.45−7.48 (m, 4H). ^{13}C NMR ($CDCl_3$, Me_4Si): δ 13.35, 25.32, 90.76, 94.30, 123.81, 128.02, 128.28, 130.22, 131.49. IR (Nujol): 2963, 2201, 1599, 758, 692 cm^{-1}. HRMS calcd for $C_{22}H_{20}$ 284.1574, found 284.1565.

3,4-Diethyl-1,6-diphenylhex-3*E*-en-1,5-diyne (11c′). This isomer was obtained by isomerization: 39% (isolated); white oil. ^1H NMR ($CDCl_3$, Me_4Si): δ 1.22 (t, J = 7.52 Hz, 6H), 2.60 (q, J = 7.52 Hz, 4H), 7.30−7.35 (m, 6H), 7.45−7.48 (m, 4H). ^{13}C NMR ($CDCl_3$, Me_4Si): δ 13.11, 28.43, 88.67, 98.77, 123.56, 128.15, 128.33, 130.25, 131.37. IR (Nujol): 2932, 2461, 1595, 1441, 756, 690 cm^{-1}. Anal. Calcd for $C_{22}H_{20}$: C, 92.91; H, 7.09. Found C, 92.87; H, 7.21.

3,4-Dibutyl-1,6-diphenylhex-3*Z*-en-1,5-diyne (**11d**): 41% (isolated); pale yellow oil. ^1H NMR ($CDCl_3$, Me_4Si): δ 0.96 (t, J = 7.30 Hz, 6H), 1.37−1.46 (m, 4H), 1.58−1.66 (m, 4H), 2.35 (t, J = 7.56 Hz, 4H), 7.24−7.32 (m, 6H), 7.47−7.50 (m, 4H). ^{13}C NMR ($CDCl_3$, Me_4Si): δ 14.02, 22.43, 30.89, 31.71, 91.04, 94.03, 123.79, 127.96, 128.24, 129.37, 131.46. IR (Nujol): 2932, 1599, 1450, 760, 696 cm^{-1}. Anal. Calcd for $C_{26}H_{28}$: C, 91.71; H, 8.29. Found: C, 91.76; H, 8.41.

3,4-Diphenyl-1,6-ditrimethylsilylhex-3*Z*-en-1,5-diyne (**11e**): 56% (isolated); white solid, mp 159−160°C. ^1H NMR ($CDCl_3$, Me_4Si): δ 0.15 (s, 18H), 7.02−7.14 (m, 10H). ^{13}C NMR ($CDCl_3$, Me_4Si): δ 0.03, 102.43, 106.04, 127.75, 127.92, 129.66, 129.84, 137.15. IR (Nujol): 2959, 2131, 1599, 1444, 842 cm^{-1}. Anal. Calcd for $C_{24}H_{28}Si_2$: C, 77.55; H, 7.57. Found: C, 77.85; H, 7.40.

1,3,4-Triphenyl-6-trimethylsilylhex-3*Z*-en-1,5-diyne (**11f**): 72% (isolated); white solid, mp 130−131°C. ^1H NMR ($CDCl_3$, Me_4Si): δ 0.26 (s, 9H), 7.17−7.20 (m, 6H), 7.22−7.27 (m, 4H), 7.33−7.34 (m, 3H), 7.52−7.54 (m, 2H). ^{13}C NMR ($CDCl_3$, Me_4Si): δ 0.02, 91.55, 96.71, 102.30, 106.24, 123.28, 127.75, 127.83, 127.95, 128.02, 128.26, 128.50, 128.96, 129.63, 129.72, 130.14, 131.73, 137.12, 137.35. IR (Nujol): 2959, 2187, 1595, 1442, 842, 696 cm^{-1}. Anal. Calcd for $C_{27}H_{24}Si$: C, 86.12; H, 6.42. Found: C, 86.11; H,6.31.

Supporting Information Available: Tables of crystallographic data, atomic coordinates, thermal parameters, and bond lengths and angles for **10** as well as spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

JO026037E