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# Selective Linear Triene Formation from Different Alkynes using Zr/Cu system

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Synthesis of stereocontrolled $\pi$-conjugated oligoenes from alkynes have been of growing interest in recent years.[1–3] We have recently reported selective linear triene formation[4] or linear tetraene formation from alkynes using zirconocene.[5]However, there is no report on metal mediated selective linear triene formation from different alkynes as shown in Scheme 1, to the best of our knowledge.

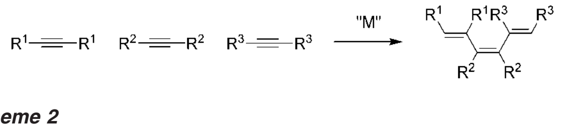
Oligomerization of alkynes using transition-metal complexes very often provides cyclotrimerization products, benzene or fulvene derivatives. In the case of benzene formation, we have developed selective cyclotrimerization of three different alkynes using zirconocene complexes.[4,6] These reactions are applicable for regioselective synthesis of highly substituted benzene and pyridine derivatives from three different alkynes or nitriles. During the course of our investigation for the formation of linear oligoenes, we found the control of the coupling of alkynes in the zirconocene/copper system.

We report herein linear triene formation from different alkynes using Zr/Cu system and tetraene formation is also demonstrated as depicted in Scheme 2.

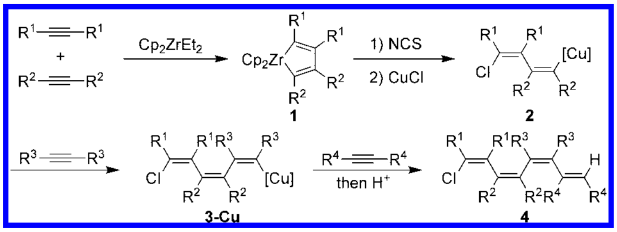
As shown in Scheme 2, two different alkynes can be selectively coupled on Zr using $Cp_2ZrEt_2$ to give an unsymmetrical zirconacyclopentadiene **1**, as we reported previously.[7] Differentiation of the two Zr−C bonds of the unsymmetrical zirconacyclopentadiene was important. Acid treatment, reaction with BuLi, or transmetalation to other transition metals of unsymmetrical zirconacyclopentadienes did not give the selective cleavage of the Zr−C bond of the two different Zr−C bonds in **1**. When $R^1$ is an alkyl group and $R^2$ is an aryl one, the Zr−C bond attached to $R^1$ was cleaved with NCS with excellent selectivity.[8] The following transmetalation of the remained Zr−C bond with CuCl gave **2**.[9] Insertion reaction of the third alkyne to **2** produced linear triene **3** after hydrolysis.[10] Before hydrolysis subsequent insertion of the fourth alkyne afforded the corresponding tetraene **4** after hydrolysis. In these insertion steps, prevention of multiple insertions of alkynes and control of the geometry of the formed double bonds are the key points to obtain the desired oligoenes with high selectivity.

To verify the strategy mentioned above, the reactions with tetraethylzirconacyclopentadiene **1a** were examined as shown in Scheme 3. Zirconacyclopentadiene **1a** was mixed with NCS, and the mixture was added with dimethyl acetylenedicarboxylate (DMAD) and CuCl. The mixture was stirred at –20 °C for 3 h. After hydrolysis, the desired linear triene **3a** was obtained as a single product in a good yield. On the other hand, when the reaction was carried out at 0 °C or room temperature, a mixture of the desired triene **3a** and higher oligoenes formed by further insertion to the other DMAD was obtained. At 50 °C, isomerization at the copper-attached C=C bond was also observed, and the triene **3a** was obtained as a mixture of *E/Z*-isomers in 34% yield (*Z*/*E* = 1:7.5). These results showed that the control of the reaction temperature is very important to restrict the number of the inserting DMAD molecules and prevention of *E,Z*-isomerization.

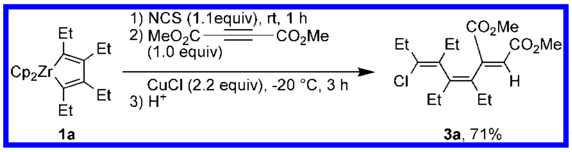
***Scheme 1***



***Scheme 2***



***Scheme 3***



Among the examined reagents for the ring opening of zirconacyclopentadiene **1a**, NCS gave the best results. When EtOH or HOAc was used instead of NCS, the yield of triene **3a** was significantly decreased. When NBS or NIS was used, formation of the corresponding benzene derivative occurred after addition of DMAD and CuCl.

When the reaction shown in Scheme 3 was quenched with the other electrophiles instead of hydrolysis, the corresponding triene derivatives were obtained as shown in Scheme 4. Iodine quenching of the alkenylcopper **3a-Cu** afforded iodotriene **3b**. Carbon−carbon bond formation is also possible. The reactions with benzoyl chloride and allyl bromide afforded the corresponding coupling products **3c** and **3d**, respectively.

This method was applied to the triene formation from three different alkynes. The results were summarized in Table 1. The triene formation was extended for that from three different alkynes. With two different alkynes the corresponding unsymmetrical zirconacyclopentadienes **1** were obtained in high yields and with excellent selectivity as we reported previously.[7] After

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***Scheme 4***

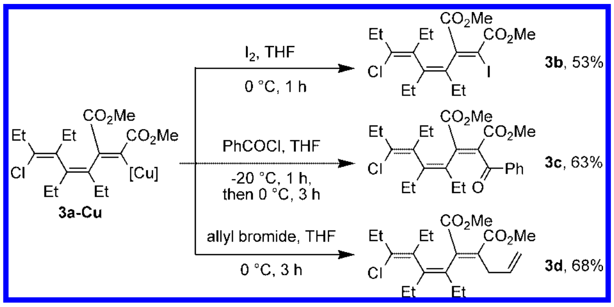
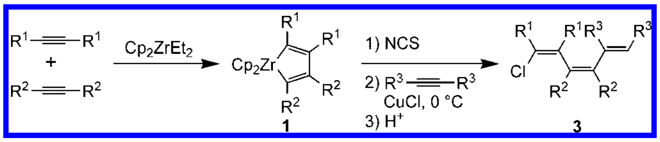
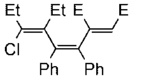
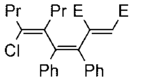
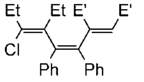
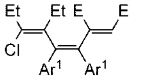
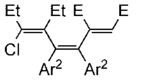
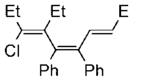
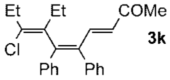
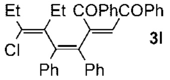
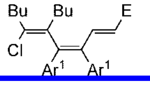


***Table 1.*** Synthesis of Linear Trienes with Three Different Alkynes

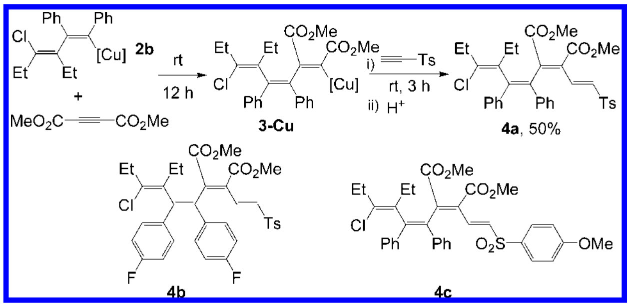


| enrty | alkyne[a] 1st | 2nd | 3rd | product[b] | | yield (%)[c] |
|---|---|---|---|---|---|---|
| 1 | Et≡Et | Ph≡Ph | E≡E |  | **3e** | 68 (57) |
| 2 | Pr≡Pr | Ph≡Ph | E≡E |  | **3f** | 72 (64) |
| 3 | Et≡Et | Ph≡Ph | E′≡E′ |  | **3g** | 70 (63) |
| 4 | Et≡Et | Ar$^1$≡Ar$^1$ (Ar$^1$ = *p*-F-$C_6H_4$-) | E≡E |  | **3h** | 71 (54) |
| 5 | Et≡Et | Ar$^2$≡Ar$^2$ (Ar$^2$ = *p*-MeO-$C_6H_4$-) | E≡E |  | **3i**[d] | 48 |
| 6 | Et≡Et | Ph≡Ph | ≡E |  | **3j** | 60 (53) |
| 7 | Et≡Et | Ph≡Ph | ≡COMe |  | **3k** | 42 (32) |
| 8 | Et≡Et | Ph≡Ph | COPh≡COPh |  | **3l** | 50 (42) |
| 9 | Bu≡Bu | Ar$^1$≡Ar$^1$ | ≡E |  | **3m** | 53 (47) |

[a] E = $CO_2Me$, E′ = $CO_2Et$, Ar$^1$ = *p*-F-$C_6H_4$-, Ar$^2$ = *p*-MeO-$C_6H_4$-. The insertion into the 3rd alkyne was carried out at 0 °C for 12 h. [b] Stereochemistry of the products were made by analogy from the structures of **3e** and **4a**. Ratio of three alkynes used: 1:1:1, except **3j** and **3m** (1:1:4). [c] NMR yields. Isolated yields were given in parentheses. Yields were based on first alkynes. [d] Triene **3i** was obtained as a mixture with the minor isomer in a ratio of 93:7.

quenching with NCS, the third alkyne was inserted in the presence of CuCl to afford the corresponding linear triene **3** after hydrolysis. When diphenylacetylene, 3-hexyne, and DMAD were employed for the reaction, the selective and successive coupling of these alkynes occurred to afford the desired triene **3e** in high yield (entry 1). The structure of triene **3e** was unambiguously confirmed by X-ray crystallography. The triene skeleton has *Z,Z,Z* geometry, and the three alkynes were connected in the expected order. As the same way, bis(*p*-fluoro-, and *p*-methoxyphenyl)acetylenes, methyl propiolate, 3-butyn-2-one, and dibenzoylacetylene were also applicable for the reactions without significant loss of selectivity (entries 4–9).

***Scheme 5.*** Synthesis of Linear Tetraenes with Four Different Alkynes



Furthermore, the zirconium-mediated successive coupling reaction was extended for linear tetraene formation as shown in Scheme 5. The alkenylcopper intermediate **3-Cu** prepared as above was reacted with tosylacetylene at room temperature to afford the corresponding tetraene **4a** in moderate to good yields with high regio- and stereoselectivity. The other tetraenes **4b** and **4c** were also obtained in 68 and 30% yields, respectively. X-ray crystallographical analysis was carried out for tetraene **4a** and confirmed the structure and stereochemistry.

**Supporting Information Available:** Detailed experimental procedures, spectral data for new compounds, and results of X-ray crystallographical analyses for **3e**, and **4a**. This material is available free of charge via the Internet at http://pubs.acs.org.

## References

(1) (a) Reviews for oligomerization of alkynes: Grotjahn, D. B. In *Comprehensive Organometallic Chemistry II*; Hegedus, L. S., Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: Oxford, U.K., 1995; Vol. 12, pp 753–770. (b) Shore, N. E. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming I., Eds.; Pergamon: Oxford, U.K., 1991; Vol. 5, pp 1152–1162.

(2) (a) Reviews for monodisperse $\pi$-conjugated oligomers, see : Tour, J. M. *Chem. Rev.* **1996**, *96*, 537–553. (b) Pu, L. *Chem. Rev.* **1998**, *98*, 2405–2494. (c) Martin, R. E.; Diederich, F. *Angew. Chem., Int. Ed.* **1999**, *38*, 1350–1377. (d) Berresheim, A. J.; Muller, M.; Mullen, K. *Chem. Rev.* **1999**, *99*, 1747–1786. (e) Roncali, J. *Acc. Chem. Res.* **2000**, *33*, 147–156.

(3) (a) Examples of metal-mediated linear oligomerization of alkynes: Eisch, J. J.; Ma, X.; Han, K. I.; Gitua, J. N.; Krüger, C. *Eur. J. Inorg. Chem.* **2001**, 77–88. (b) Bruce, M. I.; Hall, B. C.; Skelton, B. W.; White, A. H.; Zaitseva, N. N. *J. Chem. Soc., Dalton Trans.* **2000**, 2279. (c) Haskel, A.; Straub, T.; Dash, A. K.; Eisen, M. *S. J. Am. Chem. Soc.* **1999**, *121*, 3014. (d) Haskel, A.; Wang, J.; Straub, T.; Neyround, T. G.; Eisen, M. S. *J. Am. Chem. Soc.* **1999**, *121*, 3025. (e) Burrows, A. D.; Green, M.; Jeffery, J. C.; Lynam, J. M.; Mahon, M. F. *Angew. Chem., Int. Ed.* **1999**, *38*, 3043. (f) Biagini, P.; Caporusso, A. M.; Funaioli, T.; Fachinetti, G. *Angew. Chem.* **1989**, *101*, 1079. (g) Shirakawa, E.; Yoshida, H.; Nakao, Y.; Hiyama, T. *J. Am. Chem. Soc.* **1999**, *121*, 4290–4291.

(4) Takahashi, T.; Xi, Z.; Yamazaki, A.; Liu, Y.; Nakajima, K.; Kotora, M. *J. Am. Chem. Soc.* **1998**, *120*, 1672.

(5) Takahashi, T.; Liu, Y.; Iesato, A.; Chaki, S.; Nakajima, K.; Kanno, K. *J. Am. Chem. Soc.* **2005**, *127*, 11928.

(6) (a) Takahashi, T.; Kotora, M.; Xi, Z. *J. Chem. Soc.,Chem. Commun.* **1995**, 361–362. (b) Takahashi, T.; Tsai, F.-Y.; Li, Y.; Nakajima, K.; Kotora, M. *J. Am. Chem. Soc.* **1999**, *121*, 11093–11100. (c) Takahashi, T.; Tsai, F.-Y.; Kotora, M. *J. Am. Chem. Soc.* **2000**, *122*, 4994–4995. (d) Takahashi, T.; Tsai, F.-Y.; Li, Y.; Wang, H.; Kondo, Y.; Yamanaka, M.; Nakajima, K.; Kotora, M. *J. Am. Chem. Soc.* **2002**, *124*, 5059.

(7) (a) Xi, Z.; Hara, R.; Takahashi, T. *J. Org. Chem.* **1995**, *60*, 4444–4448. (b) Takahashi, T.; Kageyama, M.; Denisov, V.; Hara, R.; Negishi, E. *Tetrahedron Lett.* **1993**, *34*, 687–690.

(8) Ubayama, H.; Xi, Z.; Takahashi, T. *Chem. Lett.* **1998**, 517–518.

(9) Lipshutz, B. H.; Pfeiffer, S. S.; Noson, K.; Tomioka, T. *In Titanium and Zirconium in Organic Synthesis*; Marek, I. Ed.; Wiley-VCH; Weinheim, Germany, 2002; pp 110–148.

(10) (a) Gardette, M.; Alexakis, A.; Normant, J. F. *Tetrahedron Lett.* **1982**, *23*, 5155. (b) Normant, J. F.; Alexakis, A. *Synthesis* **1981**, 841–870.

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