Rhenium-catalyzed Regio- and Stereoselective Dimerization and Cyclotrimerization of Terminal Alkynes

Atsushi Kawata, Yoichiro Kuninobu,* and Kazuhiko Takai*
Division of Chemistry and Biochemistry, Graduate School of Natural Science and Technology,
Okayama University, Tsushima, Kita-ku, Okayama 700-8530

(Received May 29, 2009; CL-090527; E-mail: kuninobu@cc.okayama-u.ac.jp, ktakai@cc.okayama-u.ac.jp)

A combination of catalytic amounts of $[ReBr(CO)_3(thf)]_2$ and tetrabutylammonium fluoride (TBAF) promoted the dimerization of aryl- and alkenyl-substituted alkynes with high regio- and stereoselectivities, and gave only (*E*)-enynes. When terminal alkynes having a carbonyl group were employed as substrates, regioselective cyclotrimerization of the alkynes occurred to give 1,3,5-trisubstituted aromatic compounds.

Regio- and stereoselective dimerization and cyclotrimerization of terminal alkynes are efficient and useful methods to synthesize enynes and trisubstituted aromatic compounds. Therefore, there have been many reports on dimerization[1] and cyclotrimerization[2,3] of terminal alkynes. However, a mixture of (*E*)-1,4-disubstituted-, (*Z*)-1,4-disubstituted-, and 2,4-disubstituted-enynes from dimerization (Figure 1a) or a mixture of 1,3,5- and 1,2,4-trisubstituted aromatic compounds from trimerization (Figure 1b) is usually formed. Therefore, it is difficult to construct (*E*)-enyne and 1,3,5-tricarbonyl-substituted benzene skeletons regio- and stereoselectively. We report herein the regio- and stereoselective synthesis of (*E*)-enynes and 1,3,5-tricarbonyl-substituted benzenes from terminal alkynes using a mixture of a rhenium complex and tetrabutylammonium fluoride (TBAF) as a catalyst.

During our investigations of rhenium-catalyzed transformations using alkynes,[4] we found that the dimerization of terminal alkynes took place in the presence of a rhenium complex, $Re_2(CO)_{10}$, and TBAF as a catalyst. For example, treatment of phenylacetylene (**1a**) with catalytic amounts of the combination in toluene at 80 °C for 8 h gave (*E*)-enyne **2a** in 50% yield (eq 1).[5,6] In this reaction, (*Z*)-1,4-diphenyl-1-buten-3-yne and 2,4-diphenyl-1-buten-3-yne, which are stereo- and regioisomers of **2a**, were not generated at all. In addition, cyclotrimerization, oligomerization, and polymerization of phenylacetylene (**1a**) did not occur.

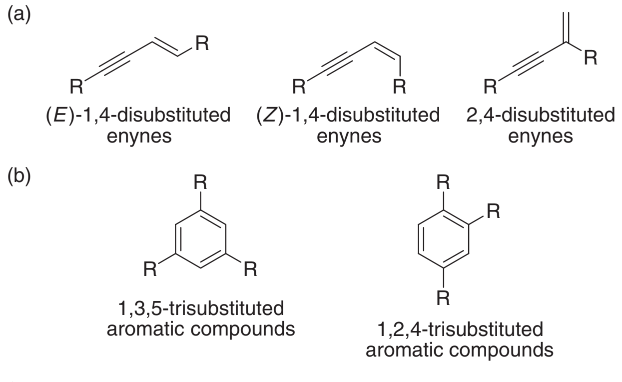
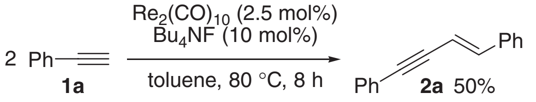
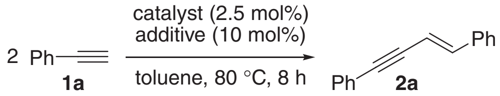


Figure 1. Isomers of dimerization and cyclotrimerization products of terminal alkynes.



(1)

Table 1. Investigation of several rhenium complexes and additives



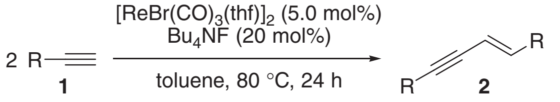
Entry	Catalyst	Additive	Yield/%[a]
1	$ReBr(CO)_5$[b]	Bu_4NF	6
2	$[ReBr(CO)_3(thf)]_2$	Bu_4NF	98
3	—	Bu_4NF	0
4	$[ReBr(CO)_3(thf)]_2$	—	0
5	$[ReBr(CO)_3(thf)]_2$	Bu_4NF[b]	4
6	$[ReBr(CO)_3(thf)]_2$	DMA	0
7	$[ReBr(CO)_3(thf)]_2$	DBU	10
8	$[ReBr(CO)_3(thf)]_2$	*i*-Pr_2NEt	0

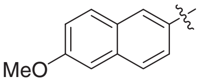
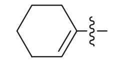
[a] ^1H NMR yield. [b] 5.0 mol %.

To improve the yield of (*E*)-enyne **2a**, several catalysts and additives were investigated (Table 1). When a rhenium complex, $ReBr(CO)_5$, was used, **2a** was formed only in 6% yield (Entry 1). By replacing some of the carbonyl groups with THF ligands, the yield of **2a** increased dramatically to 98% (Entry 2). (*E*)-Enyne **2a** was not formed using only the rhenium catalyst, $[ReBr(CO)_3(thf)]_2$, or TBAF (Entries 3 and 4). In these reactions, **1a** was recovered quantitatively. These results show that a combination of $[ReBr(CO)_3(thf)]_2$ and TBAF is necessary to promote the reaction. In addition, the ratio between $[ReBr(CO)_3(thf)]_2$ and TBAF is important. When using 2.5 mol % of $[ReBr(CO)_3(thf)]_2$ and 5.0 mol % of TBAF, (*E*)-enyne **2a** was formed in only 4% yield (Entry 5). This result is in sharp contrast to Entry 2, in which 10 mol % of TBAF was employed. Other additives were not effective for the reaction (Entries 6–8).

Next, we investigated several terminal alkynes (Table 2). Arylacetylenes bearing electron-donating groups, **1b** and **1c**, provided (*E*)-enynes **2b** and **2c** in excellent to quantitative yields (Entries 1 and 2). By using 1-bromo-4-ethynylbenzene (**1d**), the corresponding (*E*)-enyne **2d** was obtained in 92% yield without loss of bromine (Entry 3). Enyne **2e** was produced in 92% yield when an arylacetylene having an electron-withdrawing group, **1e**, was employed (Entry 4). Arylacetylenes with substituents at either the meta- or ortho-positions, **1f** and **1g**, also afforded (*E*)-enynes **2f** and **2g** in 92 and 94% yields, respectively (Entries 5 and 6). (*E*)-Enyne **2h** was also produced from 2-ethynyl-6-methoxynaphthalene (**1h**) (Entry 7). Enyne **1i** generated trieneyne **2i**, albeit in low yield (Entry 8). However, alkylacetylene, such

Table 2. Investigation of several terminal alkynes **1**



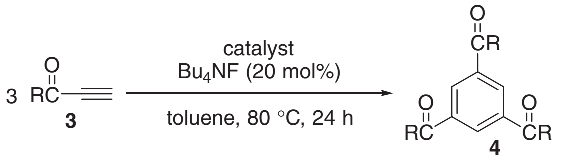
Entry	R		Yield/%^{a}
1	4-(MeO)C_6H_4	**1b**	**2b** 90 (94)
2	4-MeC_6H_4	**1c**	**2c** 98 (>99)
3	4-BrC_6H_4	**1d**	**2d** 92 (96)
4	4-(CF_3)C_6H_4	**1e**	**2e** 92 (94)
5	3-MeC_6H_4	**1f**	**2f** 92 (98)
6	2-(MeO)C_6H_4	**1g**	**2g** 94 (96)
7		**1h**	**2h** 90 (96)
8^b		**1i**	**2i** 35 (38)

^{a}Isolated yield. Yield determined by ^{1}H NMR is reported in parentheses. ^{b}$Re_2(CO)_{10}$ (5.0 mol %) was used as a catalyst. 115 °C.

as 4-phenyl-1-butyne, and triisopropylsilylacetylene did not produce the corresponding (*E*)-enyne, and those alkynes were recovered quantitatively.

When ethyl propiolate (**3a**) was used as the terminal alkyne, and treated with a catalytic amount of the rhenium complex, $[ReBr(CO)_3(thf)]_2$ (2.5 mol %), and TBAF (10 mol %) in toluene at 80 °C for 24 h, the corresponding (*E*)-enyne was not formed. Instead, the cyclotrimerization of alkyne **3a** proceeded, and the 1,3,5-trisubstituted aromatic compound **4a** was obtained in 60% yield (eq 2).[7,8] In this reaction, the regioisomeric 1,2,4-trisubstituted aromatic compound was not formed. Benzene-1,3,5-tricarboxylate **4a** was formed in a trace amount in the absence of TBAF, but produced in 12% yield in the presence of TBAF. By using $MnBr(CO)_5$ as a catalyst, the yield of **4a** improved slightly (eq 2). An alkyne with an electron-withdrawing group, 3-butyn-2-one (**3b**), also afforded the corresponding 1,3,5-trisubstituted aromatic compound **4b** in 95% yield when $Re_2(CO)_{10}$ was employed as a catalyst (eq 2).

In summary, we have succeeded in rhenium and TBAF-catalyzed regio- and stereoselective synthesis of (*E*)-enynes or 1,3,5-tricarbonyl-substituted benzenes from terminal alkynes.[9,10] In these reactions, other regio- and stereoisomers were not produced. We hope that the reactions will become useful methods to synthesize (*E*)-enynes and benzene-1,3,5-tricarboxylates.



(2)

Catalyst	R		Yield/%
$MnBr(CO)_5$ (10 mol%)	OEt	**3a**	**4a** 69
$Re_2(CO)_{10}$ (5.0 mol%)	Me	**3b**	**4b** 95

Financial support was provided by a Grant-in-Aid for Scientific Research on Priority Areas (No. 20036037, "Synergy of Elements") from the Ministry of Education, Culture, Sports, Science and Technology of Japan. A. K. also thanks the Japan Society for the Promotion of Science (JSPS) for a Research Fellowship for Young Scientists.

References and Notes

1 For recent examples, see: a) T. Ohmura, S. Yorozuya, Y. Yamamoto, N. Miyaura, *Organometallics* **2000**, *19*, 365. b) M. Rubina, V. Gevorgyan, *J. Am. Chem. Soc.* **2001**, *123*, 11107. c) S. Ogoshi, M. Ueta, M. Oka, H. Kurosawa, *Chem. Commun.* **2004**, 2732. d) C.-C. Lee, Y.-C. Lin, Y.-H. Liu, Y. Wang, *Organometallics* **2005**, *24*, 136. e) X. Chen, P. Xue, H. H. Y. Sung, I. D. Williams, M. Peruzzini, C. Bianchini, G. Jia, *Organometallics* **2005**, *24*, 4330. f) W. Weng, C. Guo, R. Çelenligil-Çetin, B. M. Foxman, O. V. Ozerov, *Chem. Commun.* **2006**, 197. g) E. Bustelo, P. H. Dixneuf, *Adv. Synth. Catal.* **2007**, *349*, 933. h) K. Ogata, O. Oka, A. Toyota, N. Suzuki, S. Fukuzawa, *Synlett* **2008**, 2663.

2 For recent reviews, see: a) S. Saito, Y. Yamamoto, *Chem. Rev.* **2000**, *100*, 2901. b) P. R. Chopade, J. Louie, *Adv. Synth. Catal.* **2006**, *348*, 2307. For recent examples, see: c) E. Rüba, R. Schmid, K. Kirchner, M. J. Calhorda, *J. Organomet. Chem.* **2003**, *682*, 204. d) K. Tanaka, K. Toyoda, A. Wada, K. Shirasaka, M. Hirano, *Chem.—Eur. J.* **2005**, *11*, 1145. e) A. Saito, H. Seino, H. Kajitani, F. Takagi, A. Yashiro, T. Ohnishi, Y. Mizobe, *J. Organomet. Chem.* **2006**, *691*, 5746. f) V. Cadierno, S. E. Garcia-Garrido, J. Gimeno, *J. Am. Chem. Soc.* **2006**, *128*, 15094.

3 There has been an example of the synthesis of 1,3,5-trisubstituted aromatic compounds by oxidative cyclotrimerization of acrylate. See: K. Tamaso, Y. Hatamoto, S. Sakaguchi, Y. Obora, Y. Ishii, *J. Org. Chem.* **2007**, *72*, 3603.

4 We have recently reported on several rhenium-catalyzed transformations using alkynes. See: a) Y. Kuninobu, A. Kawata, K. Takai, *J. Am. Chem. Soc.* **2005**, *127*, 13498. b) Y. Kuninobu, A. Kawata, K. Takai, *Org. Lett.* **2005**, *7*, 4823. c) Y. Kuninobu, A. Kawata, K. Takai, *J. Am. Chem. Soc.* **2006**, *128*, 11368. d) S. Yudha S., Y. Kuninobu, K. Takai, *Org. Lett.* **2007**, *9*, 5609. e) Y. Kuninobu, H. Takata, A. Kawata, K. Takai, *Org. Lett.* **2008**, *10*, 3133. f) Y. Kuninobu, A. Kawata, M. Nishi, H. Takata, K. Takai, *Chem. Commun.* **2008**, 6360. In Ref. 4f, notes and references section, rhenium-catalyzed dimerization of phenylacetylene has already been reported.

5 Results for temperature and reaction time are as follows: 80 °C, 3 h: 30%; 50 °C, 8 h: 16%; and 25 °C, 8 h: trace.

6 Results for other solvents are as follows: 1,2-dichloroethane, <1%; THF, 79%.

7 Results for temperature are as follows: 50 °C, 9% and 25 °C, trace.

8 Ethyl propiolate (**3a**) was not recovered because of the polymerization of **3a**.

9 The role of TBAF and the reason for the high selectivity is not clear.

10 Supporting Information is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.