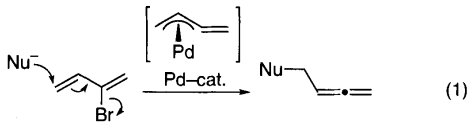
Palladium-Catalyzed Synthesis of Butatrienes

Masamichi Ogasawara, Hisashi Ikeda, Kazunori Ohtsuki, and Tamio Hayashi*
Department of Chemistry, Graduate School of Science, Kyoto University, Sakyo-ku, Kyoto 606-8502

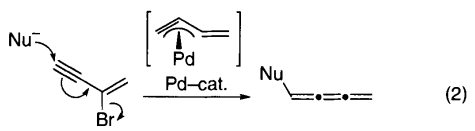
(Received April 12, 2000; CL-000345)

Palladium-catalyzed synthesis of functionalized butatrienes was achieved starting from 2-bromo-1-buten-3-yne derivatives and nucleophiles. The reaction proceeded under very mild conditions giving the products in moderate to good yields. The reactivity of the bromobutenyne substrates was highly dependent on substituents at 1-position. A subtle balance of nucleophilicity and basicity in the nucleophiles was also important for the success of the reactions.

Compounds with cumulated double bonds, such as allene or ketene, are fairly reactive because of their strained structures, thus, effective synthesis of these compounds is still challenging in organic chemistry.[1] Construction of three cumulated carbon–carbon double bonds is a more difficult problem, and the effective synthetic methods of butatrienes are still very few.[1,2] In addition, reported examples of transition metal-catalyzed synthesis of butatrienes are limited to dimerization of terminal acetylenes.[3] We have recently established a new synthetic method of functionalized allenes starting from 2-bromo-1,3-butadienes (eq 1).[4] The reaction is catalyzed by a π-allylpalladium species, and the allenic product obtained by this method always comes with a methylene unit between the allenyl moiety and the Nu substituent due to the structural requirement of the substrate. We started the project reported here with intention to utilize this extra carbon for preparation of higher cumulenes: i.e., butatrienes may be prepared by the analogous method starting from 2-bromo-1-buten-3-yne (eq 2). Indeed, the reaction proceeded effectively in certain cases to give the functionalized butatrienes in moderate to good yield. In this report, we describe the new synthetic method of butatrienes with its scope and limitation.



(1)

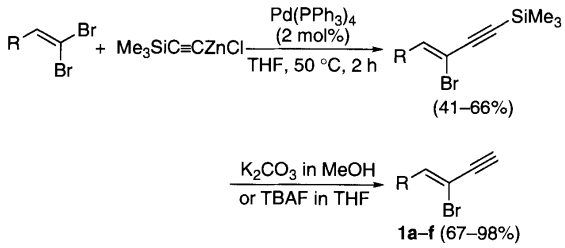


(2)

The substrates, (*Z*)-2-bromo-1-buten-3-ynes (**1a**–**f**), were easily prepared in moderate yield by two-step reactions starting from readily available 1,1-dibromoalkenes[5] as shown in Scheme 1. The first step, palladium-catalyzed cross-coupling of the dibromoalkene with trimethylsilylethynylzinc chloride, proceeded with high stereoselectivity giving the (*Z*)-product exclusively.[4,6] The trimethylsilyl protecting group was easily removed with either catalytic amount of K_2CO_3 in methanol or stoichiometric tetrabutylammonium fluoride in THF.

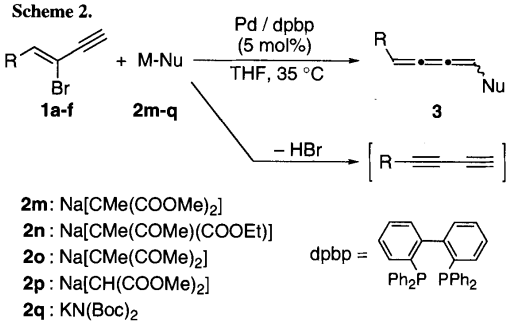
The obtained substrate **1a** (R = Ph) was allowed to react

Scheme 1.



with nucleophile **2m** under analogous reaction conditions employed for the allene synthesis.[4] It was found that the reaction was efficiently catalyzed by a palladium–dpbp[7] complex generated *in situ* from $[PdCl(\eta^3\text{-}C_3H_5)]_2$ and 1.05 equiv (to Pd) of dpbp. Thus, a mixture of **1a** (104.1 mg, 503 μmol), **2m** (97.9 mg, 582 μmol), $[PdCl(\eta^3\text{-}C_3H_5)]_2$ (4.6 mg, 25.1 μmol/Pd, 5 mol% Pd), and dpbp (13.2 mg, 25.3 μmol) in THF (5 mL) was stirred at 35 °C for 18 h. After removing the precipitated sodium salt by filtration, the residue was purified by silica gel chromatography to give 223 mg (45% yield) of **3am** (entry 1 in Table 1). The obtained butatriene **3am** was a mixture of two geometrical isomers and the *E*/*Z* isomeric ratio in **3am** was determined to be 52/48 by ^{1}H NMR.[8,9]

Scheme 2.



The R substituents in **1** played a very important role in controlling the reactivity of the substrates. The substrates with aryl groups gave **3** in moderate to good yield (entries 1–4), while no butatrienyl products were isolated with benzyl or alkyl R groups (entries 5 and 6). Comparison of the reactivity between **1a**, **1c**, and **1d** is interesting: introduction of an electron-withdrawing CF_3 on the phenyl group increased the yield of the cumulene (entries 1 vs 3), while **3** was obtained in much lower yield with the more electron-donating *p*-anisyl group (entry 4). This remote electronic effect is quite unique to this reaction, i.e., formally, the electronic characteristics of the R groups at 1-position control nucleophilic attacks to the carbons at 4-position. Meanwhile steric characteristics of the R substituents is less important. The bromoenyne **1b**, which is with a bulkier 1-naphthyl substituent, gave **3bm** in 46% yield (entry 2), which is almost identical to that for **3am**. However, introduction of a substituent to the terminal sp carbon diminished the reactivity of the enyne. (*Z*)-PhCH=CBr-C≡C-

$^{n}C_4H_9$, which was prepared from the corresponding dibromoalkene and 1-hexynylzinc chloride by the Pd-catalyzed cross-coupling in 67% yield, was completely inert to the Pd-catalyzed butatriene formation reaction with **2m**.

Table 1. Palladium-catalyzed synthesis of butatrienes **3** from bromoenynes **1** and nucleophiles **2**[a]

Entry	Substrate (R-)	Nucleophile	Yield/%[b]	*E*/*Z*[c]
1	**1a** (Ph-)	**2m**	45 (**3am**)	52/48
2	**1b** (1-naphthyl-)	**2m**	46 (**3bm**)	51/49
3	**1c** (*p*-CF_3-C_6H_4-)	**2m**	73 (**3cm**)	60/40
4	**1d** (*p*-MeO-C_6H_4-)	**2m**	29 (**3dm**)	54/46
5	**1e** ($PhCH_2$-)	**2m**	0[d]	---
6	**1f** ($PhCH_2CH_2$-)	**2m**	trace[e]	---
7	**1c** (*p*-CF_3-C_6H_4-)	**2n**	64 (**3cn**)[f]	50/50
8	**1c** (*p*-CF_3-C_6H_4-)	**2o**	~10[g]	---
9	**1c** (*p*-CF_3-C_6H_4-)	**2p**	no reaction	---
10	**1c** (*p*-CF_3-C_6H_4-)	**2q**	0[d,h]	---

[a]Reaction was carried out in THF in the presence of 5 mol% of the catalyst generated from $[PdCl(\eta^3\text{-}C_3H_5)]_2$ and dpbp. [b]Isolated yield by column chromatography on silica gel. [c]Determined by ^{1}H NMR. [d]No substrate was detected after the reaction. [e]Although a very small amount of the butatriene was detected by ^{1}H NMR and GS-MS analyses, the product was not isolated. [f]16% of substrate was recovered. [g]Many uncharacterized products, which were not completely separable, were formed with the butatriene product. The yield of the butatriene was estimated from ^{1}H NMR and GC-MS analyses. [h]Main product was dehydrobrominated diyne (ArC≡C–C≡CH).

The reaction is very sensitive to nucleophiles **2**: while **1c** reacted with **2m** to give **3cm** in 73% yield, the closely related nucleophile **2p** was completely inert under the same reaction condition and unreacted **1c** was recovered from the reaction mixture (entries 3 and 9). Because the nucleophilic center in **2m** is more hindered than that in **2p**, the higher reactivity of **2m** in the reaction cannot be accounted for by the steric factors. The unusual reactivity was double-checked by an independent experiment. An equimolar mixture of **1c**, **2m**, and **2p** was reacted for 22 h in THF at 35 °C in the presence of 5 mol% of the Pd–dpbp catalyst, and **3cm** was obtained with *E*/*Z* = 60/40 selectivity as a sole butatriene product.[10] The corresponding butatriene from **1c** and **2p** was not detected at all by NMR and GC–MS analyses. In the reactions with more basic nucleophiles, such as **2q** or Grignard reagents, dehydrobromination from **1** was a dominant reaction giving conjugated diyne as main products (entry 10).

The reaction reported here can be regarded as a skeletal rearrangement of the conjugated enynes to the butatriene frameworks. Considering ca. 20 kcal/mol energy difference between 1,4-dimethylbutatriene and the corresponding enynes,[3a] the represented reaction is very unique and the difference of bond energy between C–Br and C–Nu must be mainly contributory to the formation of the butatrienes. Since the butatrienes obtained here keep some energy in their skeletons, they must be reactive molecules, and thus their application to further organic transformations will be an interesting subject.

Judging from similarity between this reaction and the allene synthesis,[4] a probable intermediate of the Pd-catalyzed reaction is a π-allenylpalladium species. Establishment of the intermediate will be our next goal.

This work was supported by "Research for the Future" Program (the Japan Society for the Promotion of Science), a Grant-in-Aid for Scientific Research (the Ministry of Education, Science, Sports and Cullture, Japan), and Mitsubishi Chemical Corporation Fund (to M. O.).

References and Notes

1 "The Chemistry of Ketenes, Allenes, and Related Compounds," ed. by S. Patai, Wiley, New York (1980).

2 a) H.-F. Chow, X.-P. Cao, and M.-K. Leung, *J. Chem. Soc., Chem. Commun.*, 2121 (1994), and references cited therein. b) H.-F. Chow, X.-P. Cao, and M.-K. Leung, *J. Chem. Soc., Perkin Trans. 1*, 193 (1995). c) R. W. Saalfrank, A. Welch, and M. Haubner, *Angew. Chem., Int. Ed. Engl.*, **34**, 2709 (1995).

3 a) Y. Wakatsuki, H. Yamazaki, N. Kumegawa, T. Satoh, and J. Y. Satoh, *J. Am. Chem. Soc.*, **113**, 9604 (1991). b) Y. Wakatsuki, H. Yamazaki, N. Kumegawa, and P. S. Johar, *Bull. Chem. Soc. Jpn.*, **66**, 987 (1993). c) Y. Wakatsuki, N. Koga, H. Yamazaki, and K. Morokuma, *J. Am. Chem. Soc.*, **116**, 8105 (1994). d) C. S. Yi and N. Liu, *Organometallics*, **15**, 3968 (1996). e) Y. Suzuki, R. Hirotani, H. Komatsu, and H. Yamazaki, *Chem. Lett.*, 1299 (1999). f) T. Ohmura, S. Yorozuya, Y. Yamamoto, and N. Miyaura, *Organometallics*, **19**, 365 (2000).

4 M. Ogasawara, H. Ikeda, and T. Hayashi, *Angew. Chem., Int. Ed. Engl.*, **39**, 1042 (2000).

5 a) F. Ramirez, N. B. Desai, and N. McKelvie, *J. Am. Chem. Soc.*, **84**, 1745 (1962). b) E. J. Corey and P. L. Fuchs, *Tetrahedron Lett.*, **13**, 3769 (1972).

6 Palladium-catalyzed selective substitutions of one of the two halides from 1,1-dihalo-1-alkene have been reported. See, a) A. Minato, K. Suzuki, and K. Tamao, *J. Am. Chem. Soc.*, **109**, 1257 (1987). b) J. Uenishi, R. Kawahama, O. Yonemitsu, and J. Tsuji, *J. Org. Chem.*, **61**, 5716 (1996). c) J. Uenishi, R. Kawahama, Y. Shiga, O. Yonemitsu, and J. Tsuji, *Tetrahedron Lett.*, **37**, 6759 (1996).

7 a) dpbp = 2,2'-bis(diphenylphosphino)-1,1'-biphenyl. b) M. Ogasawara, K. Yoshida, and T. Hayashi, *Organometallics*, **19**, 1567 (2000), and references cited therein.

8 The assignment of the *E*- and *Z*-isomers was made by comparison of $^5J_{HH}$ values of the olefinic protons.[9] **3am**: ^{1}H NMR ($CDCl_3$, 23 °C): δ 1.67 (s, 3H of *Z*-isomer), 1.78 (s, 3H of *E*-isomer), 3.78 (s, 6H of *Z*-isomer), 3.79 (s, 6H of *E*-isomer), 6.12 (d, ^5J = 7.7 Hz, 1H of *E*-isomer), 6.19 (d, ^5J = 7.3 Hz, 1H of *Z*-isomer), 6.55 (d, ^5J = 7.7 Hz, 1H of *E*-isomer), 6.58 (d, ^5J = 7.3 Hz, 1H of *Z*-isomer), 7.24–7.28 (m, 1H of both isomers), 7.31–7.36 (m, 2H of both isomers), 7.41–7.44 (m, 2H of both isomers). **3bm**: ^{1}H NMR ($CDCl_3$, 23 °C): δ 1.72 (s, 3H of *Z*-isomer), 1.80 (s, 3H of *E*-isomer), 3.79 (s, 6H of *Z*-isomer), 3.80 (s, 6H of *E*-isomer), 6.19 (d, ^5J = 7.8 Hz, 1H of *E*-isomer), 6.25 (d, ^5J = 7.5 Hz, 1H of *Z*-isomer), 7.29 (d, ^5J = 7.8 Hz, 1H of *E*-isomer), 7.32 (d, ^5J = 7.5 Hz, 1H of *Z*-isomer), 7.45–7.58 (m, 3H of both isomers), 7.73–7.75 (m, 1H of both isomers), 7.78–7.81 (m, 1H of both isomers), 7.85–7.87 (m, 1H of both isomers), 8.35–8.37 (m, 1H of both isomers). **3cm**: ^{1}H NMR ($CDCl_3$, 23 °C): δ 1.68 (s, 3H of *Z*-isomer), 1.77 (s, 3H of *E*-isomer), 3.79 (s, 6H of both isomers), 6.25 (d, ^5J = 7.6 Hz, 1H of *E*-isomer), 6.33 (d, ^5J = 7.3 Hz, 1H of *Z*-isomer), 6.57 (d, ^5J = 7.6 Hz, 1H of *E*-isomer), 6.60 (d, ^5J = 7.3 Hz, 1H of *Z*-isomer), 7.50–7.54 (m, 2H of both isomers), 7.57–7.61 (m, 2H of both isomers). **3dm**: ^{1}H NMR ($CDCl_3$, 23 °C): δ 1.66 (s, 3H of *Z*-isomer), 1.76 (s, 3H of *E*-isomer), 3.78 (s, 6H of both isomers), 3.82 (s, 3H of *Z*-isomer), 3.83 (s, 3H of *E*-isomer), 6.01 (d, ^5J = 7.7 Hz, 1H of *E*-isomer), 6.08 (d, ^5J = 7.2 Hz, 1H of *Z*-isomer), 6.50 (d, ^5J = 7.7 Hz, 1H of *E*-isomer), 6.53 (d, ^5J = 7.2 Hz, 1H of *Z*-isomer), 6.86–6.89 (m, 2H of both isomers), 7.35–7.38 (m, 2H of both isomers). **3cn**: ^{1}H NMR ($CDCl_3$, 23 °C): δ 1.30 (t, *J* = 7.1 Hz, 3H of *Z*-isomer), 1.31 (t, *J* = 7.1 Hz, 3H of *E*-isomer), 1.60 (s, 3H of *Z*-isomer), 1.68 (s, 3H of *E*-isomer), 2.25 (s, 3H of *Z*-isomer), 2.26 (s, 3H of *E*-isomer), 4.25–4.30 (m, 2H of both isomers), 6.30 (d, ^5J = 7.7 Hz, 1H of *E*-isomer), 6.37 (d, ^5J = 7.3 Hz, 1H of *Z*-isomer), 6.57 (d, ^5J = 7.7 Hz, 1H of *E*-isomer), 6.59 (d, ^5J = 7.3 Hz, 1H of *Z*-isomer), 7.51–7.53 (m, 2H of both isomers), 7.57–7.62 (m, 2H of both isomers).

9 a) Although it was claimed previously that the *E*-isomer should have a larger $^5J_{HH}$ value than that of the corresponding *Z*-isomer,[9b] others reported that $^5J_{HH}$ values of *Z*- and *E*-isomers of corresponding butatrienes were almost identical.[9c] We could detect the slight, but meaningful differences between the $^5J_{HH}$ values of the two isomers of the obtained butatrienes using high-resolution NMR technique (at 500 MHz with 0.076 Hz of digital resolution). b) R. Mantione, A. Alves, P. P. Montijn, G. A. Wildschut, H. J. T. Bos, and L. Brandsma, *Rec. Trav. Chim. Pays-Bas*, **89**, 97 (1970). c) P. J. Bauer, O. Exner, R. Ruzziconi, T. D. An, C. Tarchini, and M. Schlosser, *Tetrahedron*, **50**, 1707 (1994).

10 The yield of **3cm** of this experiment is 34%, which is much lower than that of Entry 1 in Table 1. This negative effect of **2p** is unexpected and cannot be explained at this moment.