

Communications to the Editor

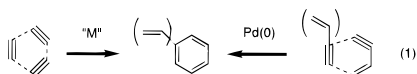
A New Palladium-Catalyzed Benzannulation of Conjugated Enynes

Shinichi Saito, Matthew M. Salter, Vladimir Gevorgyan,
Norie Tsuboya, Kazushi Tando, and Yoshinori Yamamoto*

Department of Chemistry, Graduate School of Science
Tohoku University, Sendai 980-77, Japan

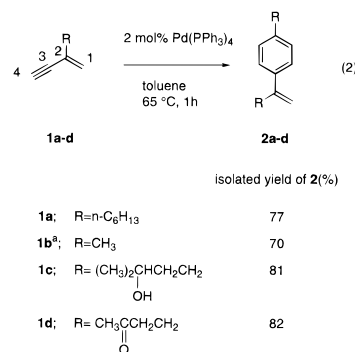
Received January 5, 1996

The transition metal catalyzed synthesis of aromatic rings is mainly accomplished by cyclotrimerization of alkynes (eq 1).^{1–3} We wish to report an entirely new route; the Pd(0)-catalyzed reaction of conjugated enynes gives the corresponding disubstituted aromatic compounds in good to high yields.



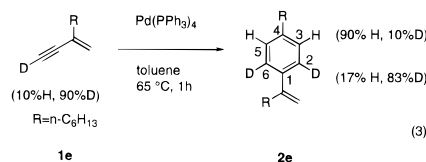
We have recently reported that the palladium (Pd₂dba₃·CHCl₃–dppf) catalyzed reaction of conjugated enynes with pronucleophiles affords the corresponding 1,4-addition products (allenes) in high yields.⁴ We also examined the reaction between conjugated enynes and pronucleophiles by using the Trost catalyst system (bis- π -allylpalladium chloride dimer–KO^tBu–dppf).⁵ Very interestingly, an aromatic compound derived from dimerization of enyne was obtained as a minor product along with the major product (allenes)! Accordingly, we investigated the reaction of 2-hexyl-1-buten-3-yne (**1a**) under various catalyst systems to find the optimum condition for obtaining this unprecedented reaction product in higher yields. Among the catalyst systems we examined, Pd(PPh₃)₄/toluene or Pd₂dba₃·CHCl₃–tris(2,6-dimethoxyphenyl)phosphine/toluene gave better results. The best solvent for the reaction was toluene, benzene, or acetonitrile; the rate of the reaction was slower in THF, DMSO, and DMF.

The results of the reactions of several enynes **1** under Pd(PPh₃)₄ catalyst are shown in eq 2. The reaction proceeded very smoothly and rapidly to give 1,4-disubstituted benzene **2** in good to high yield. Isomeric products such as 1,3-disubstituted benzene or trisubstituted benzenes, which may be formed via cyclotrimerization, were not detected. Even in the presence of functional groups such as the hydroxyl (**1c**) and carbonyl group (**1d**) in the alkyl chain at the 2-position, the reaction proceeded smoothly to give **2c** and **2d**, respectively, in high yields.⁶ However, 1- and/or 4-substituted enynes did not dimerize under the present catalyst systems. The preparation of **2a** is representative. To a solution of **1a** (1 mmol) in dry toluene (2 mL) was added Pd(PPh₃)₄ (20 μ mol, 2 mol %) under Ar at rt. The yellow solution was heated to 65 °C for 1 h, and the product was isolated by column chromatography to give 1,4-disubstituted benzene **2a** in 77% yield.



^a Using 2 mmol of **1b** in the presence of 1 mol % Pd(PPh₃)₄.

To help clarify the mechanism of this unprecedented cyclodimerization, the reaction of enyne **1e** in which the deuterium content was 90% at the 4-position was carried out. Disubstituted benzene **2e**, which contained deuterium mainly at the 2- and 6-positions (83% deuterium content at each position), was obtained in high yield. Deuterium was not distributed to other positions except for the protons attached to the benzene ring. The formation of **2e** indicates that the acetylenic C–H(D) bond is not cleaved in the present benzannulation (eq 3). Transition metal catalysts effective for the cyclotrimerization of alkynes (CpCo(CO)₂¹ or RhCl(PPh₃)₂⁷) were not effective for the cyclodimerization of enynes. Taken together, it seems difficult to explain the unprecedented cyclodimerization by the ordinary accepted mechanisms.



Two plausible mechanisms are shown in eqs 4 and 5, although they are highly speculative. The reaction of **1** with the Pd(0) species would produce a π -complex intermediate **3**, which might act as a nucleophilic diene and undergo (formal) Diels–Alder reaction (eq 4).^{8,9} Alternatively, this reaction may involve a metallacycle such as **4** as an intermediate (eq 5).¹⁰

The wide applicability of this new benzannulation procedure is demonstrated in the synthesis of cyclophanes (eq 6). The bis-enyne **5**, synthesized in one step from 1,8-dibromooctane

(7) Neeson, S. J.; Steverson, P. J. *Tetrahedron* **1989**, 45, 6239–6248 and references cited therein.

(8) The structure and reactivity of the corresponding alkyne–Pt(0) complex are well established. See: Glanville, J. O.; Stewart, J. M.; Grim, S. O. *J. Organomet. Chem.* **1967**, 7, P9–P10. Mann, B. E.; Shaw, B. L.; Tucker, N. I. *J. Chem. Soc. A* **1971**, 2667–2673. Greaves, E. O.; Lock, C. J. L.; Maitlis, P. M. *Can. J. Chem.* **1968**, 46, 3879–3891. Tripathy, P. B.; Renoe, B. W.; Adzaml, K.; Roundhill, d. M. *J. Am. Chem. Soc.* **1971**, 93, 4406–4410. Chatt, J.; Rowe, G. A.; Williams, A. A. *Proc. Chem. Soc.* **1957**, 208–209. Cook, C. D.; Allen, A. D. *Can. J. Chem.* **1964**, 42, 1603–1608.

(9) For examples of transition metal catalyzed [4 + 2] cycloadditions and Diels–Alder reactions, see: Wender, P. A.; Jenkins, T. E.; Suzuki, S. *J. Am. Chem. Soc.* **1995**, 117, 1843–1844. McKinstry, L.; Livinghouse, T. *Tetrahedron* **1994**, 50, 6145–6154. Jolly, R. S.; Luedtke, G.; Sheehan, D.; Livinghouse, T. *J. Am. Chem. Soc.* **1990**, 112, 4965–4966. Wender, P. A.; Jenkins, T. E. *J. Am. Chem. Soc.* **1989**, 111, 6432–6434. Matsuda, I.; Shibata, M.; Sato, S.; Izumi, Y. *Tetrahedron Lett.* **1987**, 28, 3361–3362. Mach, K.; Antropiusová, Petrusová, L.; Turecek, F.; Hanus, V.; Sedmera, P.; Schraml, J. *J. Organomet. Chem.* **1985**, 289, 331–339. tom Dieck, H.; Diercks, R. *Angew. Chem., Int. Ed. Engl.* **1983**, 22, 778–779. van Leeuwen, P. W. N. M.; Roobeek, C. F. *Tetrahedron* **1981**, 50, 1973–1983.

(1) Vollhardt, K. P. C. *Angew. Chem., Int. Ed. Engl.* **1984**, 23, 539–644.

(2) Schore, N. E. *Chem. Rev.* **1988**, 88, 1081–1119.

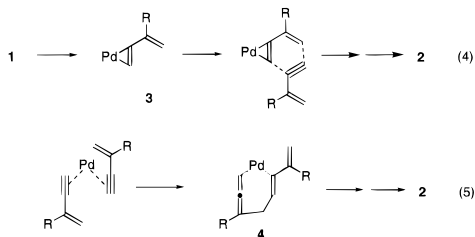
(3) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987; Section 18.3c, pp 870–879.

(4) Salter, M. M.; Gevorgyan, V.; Saito, S.; Yamamoto, Y. *J. Chem. Soc., Chem. Commun.* **1996**, 17–18.

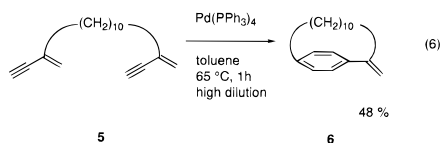
(5) (a) Trost, B. M.; Zhi, L. *Tetrahedron Lett.* **1992**, 33, 1831–1834.

(b) Trost, B. M.; Gerusz, V. J. *J. Am. Chem. Soc.* **1995**, 117, 5156–5157.

(6) The reaction of 2-*tert*-butyl-1-buten-3-yne and 2-(trimethylsilyl)-1-buten-3-yne afforded corresponding cyclodimerized products in lower yields, together with inseparable linear oligomers.



and 2-methyl-1-buten-3-yne,¹¹ gave a paracyclophane **6** in 48% yield. To the best of our knowledge, this is the shortest synthesis of a paracyclophane.¹²



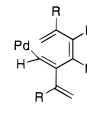
Although further investigation is needed to settle the mechanism, the present procedure provides a new convenient route to 1,4-disubstituted benzenes and paracyclophanes.

Acknowledgment. M.M.S. and S.S. gratefully acknowledge fellowships from the Japan Society for the Promotion of Science for Young Scientists.

Supporting Information Available: Spectroscopic and analytical data on compounds **1c–d**, **2a–d**, **5**, and **6** (8 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

JA9600486

(10) A referee has suggested another mechanism; hydridopalladation of enyne **1** would give a 4-pallado-2-R-diene, which then could carbopalladate the starting enyne to give a palladiohexatriene **7** as an intermediate, and then electrolytic closure of **7** and β -elimination would regenerate the PdH catalyst and provide the observed aromatic compound.



(11) Klusener, P. A. A.; Kulik, W.; Brandsma, L. *J. Org. Chem.* **1987**, 52, 5261–5266.

(12) For a review of cyclophane chemistry, see: Fögtle, J. P. *Cyclophane Chemistry*; Wiley: Chichester, England, 1993.