



Pergamon

Tetrahedron Letters 41 (2000) 1971–1974

TETRAHEDRON  
LETTERS

## Palladium catalyzed [2+2+1] cyclotrimerization of alkynes: selective synthesis of fulvenes

Ukkiramapandian Radhakrishnan, Vladimir Gevorgyan and Yoshinori Yamamoto\*

*Department of Chemistry, Graduate School of Science, Tohoku University, Sendai 980-8758, Japan*

Received 1 November 1999; accepted 11 January 2000

---

### Abstract

This is the first report on the selective synthesis of fulvenes via a [2+2+1] cyclotrimerization of alkynes under catalytic conditions. The reactions of aliphatic terminal alkynes **1a–e** in the presence of a palladium catalyst in toluene gave the cyclotrimerization products **2a–e**, not easily available through the previously known methods, in good to fair yields. © 2000 Elsevier Science Ltd. All rights reserved.

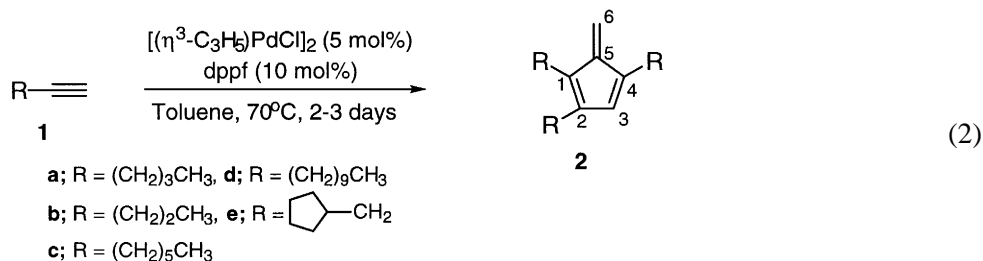
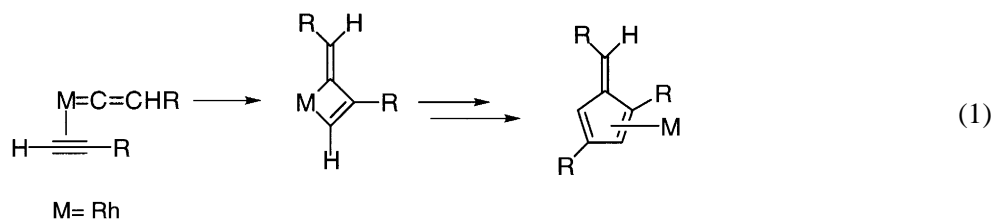
*Keywords:* cyclotrimerization; alkynes; palladium; fulvenes.

---

Transition metal mediated [2+2+2] cyclotrimerization has been an area of extensive investigation and has been utilized efficiently in the synthesis of aromatic compounds and many useful natural products.<sup>1</sup> On the other hand, there are only very few reports on transition metal mediated [2+2+1] cyclotrimerization of alkynes which leads to the formation of thermodynamically unstable fulvenes.<sup>2</sup> The formation of metal complexes coordinated by fulvenes has been observed in the reactions of stoichiometric amounts of iridium and rhodium complexes with alkynes (Eq. (1)).<sup>2</sup> It has been proposed that these reactions proceed via the metallacyclobutene intermediate to give the metal complexes of fulvenes in which one of the three substituents (*R*) is present at the *exo*-cyclic double bond of the fulvene (Eq. (1)).<sup>2b</sup> Rothwell et al. reported that the trimerization of *t*-butylacetylene catalyzed by titanium aryloxides leads to the formation of 1,3,6-tri(*t*-butyl) fulvene along with some other products.<sup>3</sup> To the best of our knowledge there is no report of a catalytic method for the [2+2+1] cyclotrimerization of alkynes for the selective synthesis of fulvenes. Herein we report an unprecedented palladium catalyzed [2+2+1] cyclotrimerization of alkynes **1** to give relatively inaccessible fulvenes **2**, in which all three substituents are present on the five-membered ring, in good yields (Eq. (2)).

---

\* Corresponding author. Fax: +81-22-217-6784; e-mail: yoshi@yamamoto1.chem.tohoku.ac.jp (Y. Yamamoto)



Our studies were initiated by the treatment of 1-hexyne **1a** with 5 mol% Pd(OAc)<sub>2</sub> in toluene at 70°C, since it was reported that the reaction of phenylacetylene with Pd(OAc)<sub>2</sub> as catalyst gave a mixture of 1,3,6-, 1,4,6- and 2,3,6-trisubstituted fulvenes in 60–80% combined as yields.<sup>4</sup> The reaction progress was monitored by GC–MS, but the formation of several unidentified products including **2a** was observed even at the beginning of the reaction. The use of Pd(OAc)<sub>2</sub> (5 mol%) and dppf (10 mol%) as the catalyst system gave small amounts of 2-*n*-butyl-1-octen-3-yne. No reaction took place in the case of the Pd(PPh<sub>3</sub>)<sub>4</sub>-dppf catalyst system even after two days and the starting material was recovered. Other catalyst systems, such as [Pd<sub>2</sub>(dba)<sub>3</sub>]CHCl<sub>3</sub>-dppf, PdCl<sub>2</sub>(PhCN)<sub>2</sub>-dppf, [(η<sup>3</sup>-C<sub>3</sub>H<sub>5</sub>)PdCl]<sub>2</sub>-dppb and [(η<sup>3</sup>-C<sub>3</sub>H<sub>5</sub>)PdCl]<sub>2</sub>-tdmpp, gave unsatisfactory results: a mixture of several products including **2a** was produced. Finally, we discovered that the [(η<sup>3</sup>-C<sub>3</sub>H<sub>5</sub>)PdCl]<sub>2</sub> (5 mol%)-dppf (10 mol%) catalyst system gave **2a** in 58% isolated yield (entry 1, Table 1): only two peaks of **1a** and **2a** appeared in the GC and GC–MS of the crude reaction mixture even after two days, and no other peaks due to isomers and unidentified products were obtained.

Table 1  
Palladium catalyzed [2+2+1] cyclotrimerization of terminal alkynes

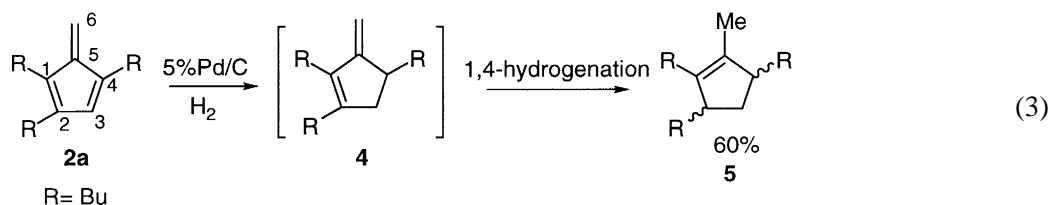
entry	R	Yield <sup>[a]</sup>
1	-(CH <sub>2</sub> ) <sub>3</sub> CH <sub>3</sub> ( <b>1a</b> )	58% ( <b>2a</b> )
2	-(CH <sub>2</sub> ) <sub>2</sub> CH <sub>3</sub> ( <b>1b</b> )	62% ( <b>2b</b> )
3	-(CH <sub>2</sub> ) <sub>5</sub> CH <sub>3</sub> ( <b>1c</b> )	58% ( <b>2c</b> )
4	-(CH <sub>2</sub> ) <sub>9</sub> CH <sub>3</sub> ( <b>1d</b> ) <sup>[b]</sup>	50% ( <b>2d</b> )
5	( <b>1e</b> )	52% ( <b>2e</b> )

[a] All yields are of pure products isolated by column chromatography. The presence of remaining unreacted alkynes was observed in GC and GC-MS of the reaction mixture. [b] The reaction was carried out for 3 days although the standard method required 2 days.

The [2+2+1] cyclotrimerization of other aliphatic terminal alkynes **1b–e** proceeded smoothly to give fulvenes **2b–e** in good yields and the results are presented in Table 1. In all cases the regioselective

formation of fulvenes, unsubstituted at the *exo*-cyclic double bond, was observed. The reaction of 1-pentyne **1b** and 1-octyne **1c** proceeded smoothly to give the corresponding fulvenes **2b** and **2c**, respectively, in good yields (entries 2 and 3). The yields of fulvenes **2** decreased slightly as the length of the aliphatic chain in the alkynes increased; the reaction of 1-dodecyne **1d** gave **2d** in 50% yield (entry 4). The reaction of 3-cyclopentyl-1-propyne **1e** gave the corresponding fulvene **2e** in 52% yield (entry 5). Again, even after two days only two peaks due to **1** and **2** were observed in the GC-MS of the crude reaction mixture. Decomposition of **2** started slowly on prolonged heating of the reaction mixture. Unfortunately, even under the optimized conditions, the reactions of aromatic alkynes did not produce the corresponding fulvenes regioselectively, but gave mixtures of products.

The structures of fulvenes **2a–e** were unambiguously established by extensive NMR studies and by hydrogenation. The DEPT spectrum of **2a** showed the presence of one =CH<sub>2</sub> (C<sub>6</sub>, exomethylene), one =CH- (C<sub>3</sub>) and four RR'-C= (C<sub>1</sub>, C<sub>2</sub>, C<sub>4</sub>, C<sub>5</sub>, quaternary) olefinic carbons, and furthermore the NOE and COLOC study also confirmed the structure of **2a**. The hydrogenation of **2a** using 5% palladium on carbon gave a (~1:2) diastereomeric mixture of cyclopentene derivative **5** in 60% yield (Eq. (3)). In this reaction the double bond between C<sub>3</sub> and C<sub>4</sub> would have been reduced first to give diene **4**, and then subsequent 1,4-reduction would give **5**.<sup>5</sup> The confirmation of structure **5** was carried out by the combination of DEPT, C-H COSY and COLOC experiments.



A representative procedure is as follows: a mixture of  $[(\eta^3\text{-C}_3\text{H}_5)\text{PdCl}]_2$  (0.05 mmol, 18.3 mg), dppf (0.1 mmol, 55.4 mg) and 1-hexyne (1 mmol, 82 mg) in toluene (1 mL) was heated at 70°C for two days under an argon atmosphere. Upon cooling, the reaction mixture was filtered and concentrated. The residue was purified by flash column chromatography on silica gel using hexane as an eluent to give 47.6 mg (58% yield) of fulvene **2a** as a yellow oil. Although the mechanism of this reaction is not yet clear, we are now in a position to synthesize certain fulvenes not easily available through the previously known methods.<sup>6,7</sup>

## References

- Diercks, R.; Eaton, B. E.; Gurtzgen, S.; Jalisatgi, S.; Matzger, A. J.; Radde, R. H.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1998**, *120*, 8247. (b) Fruhauf, H.-W. *Chem. Rev.* **1997**, *97*, 523. (c) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49. (d) Grotjahn, D. B. In *Comprehensive Organometallic Chemistry II*; Abel, E. W.; Stone, F. G. A.; Wilkinson, G., Eds.; Hegedus, L. S., Volume Ed.; Pergamon: Oxford, 1995; Vol. 12, pp. 741. (e) Bose, R.; Matzger, A. J.; Mohler, D. L.; Vollhardt, K. P. C. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1478. (f) Vollhardt, K. P. C. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 539.
- O'Connor, J. M.; Hiibner, K.; Merwin, R.; Gantzel, P. K.; Fong, B. S.; Adams, M.; Rheingold, A. L. *J. Am. Chem. Soc.* **1997**, *119*, 3631. (b) Moran, G.; Green, M.; Orpen, A. G. *J. Organomet. Chem.* **1983**, *250*, C15. (c) Moreto, J.; Maruya, K.; Bailey, P. M.; Maitlis, P. M. *J. Chem. Soc., Dalton Trans.* **1982**, 1341.
- Johnson, E. S.; Balaich, G. J.; Fanwick, P. E.; Rothwell, I. P. *J. Am. Chem. Soc.* **1997**, *119*, 11086.
- Chukhadzhyan, G. A.; Abramyan, Zh. I.; Tonyan, G. M.; Matosyan, V. A. *Zh. Org. Khim.* **1974**, *10*, 1994.
- In our hydrogenation reaction, the partial reduction may be due to the presence of tetrasubstituted alkenes. In general, the tetrasubstituted alkenes need elevated temperature and high pressure of hydrogen: March, J. *Advanced Organic Chemistry*, 4th ed.; Wiley Interscience: New York, 1992; pp. 771–780. (b) The 1,3,6-trisubstituted fulvene, prepared using modified Heck

reaction, was hydrogenated using Pd/C catalysts. Lee, G. C. M.; Tobias, B.; Holmes, J. M.; Harcourt, D. A.; Garst, M. *J. Am. Chem. Soc.* **1990**, *112*, 9330.

6. For reviews, see: (a) Neuenschwander, M. *The Chemistry of Double bonded Functional Groups*; Patai, S., Ed. Fulvenes. John Wiley: New York, 1989; p. 1131. (b) Yates, P. *Advanced Alicyclic Chemistry*; Academic Press: New York, 1968; Vol. 2, p. 59. (c) Bergman, E. D. *Chem. Rev.* **1968**, *68*, 41.
7. Erden, I.; Xu, F.; Sadoun, A.; Smith, W.; Sheff, G.; Ossun, M. *J. Org. Chem.* **1995**, *60*, 813 and references cited therein. (b) Stone, K. J.; Little, R. D. *J. Org. Chem.* **1984**, *49*, 1849.