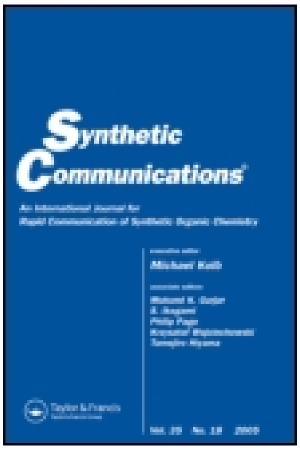

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Carbon Dioxide Promoted Palladium-Catalyzed Cyclotrimerization of Alkynes in Water

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ABSTRACT

In water, CO_2 was found to promote the palladium-catalyzed cyclotrimerization of alkynes. In the presence of $PdCl_2$, $CuCl_2$, and CO_2, both aryl and alkylalkynes afforded the corresponding cyclotrimerization products regioselectively in high yields. However, *tert*-butylacetylene bearing a bulk group gave a dimerization product.

Key Words: Cyclotrimerization; Palladium-catalyzed; Alkynes; Regioselectivity; Carbon dioxide.

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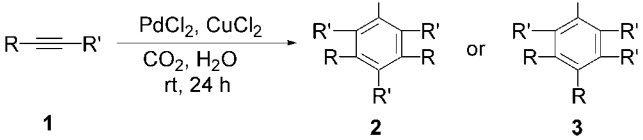
INTRODUCTION

Transition metal mediated [2 + 2 + 2] cyclotrimerization of alkynes has been an area of extensive investigation, and has been utilized efficiently in the synthesis of aromatic compounds and many natural products.[1–8] Recently, we reported a novel palladium-catalyzed cyclotrimerization of alkynes, which is useful for the regioselective synthesis of symmetric benzene derivatives in C_6H_6/n-BuOH.[8] Unfortunately, phenylacetylene did not undergo cyclotrimerization reaction and only red oils were obtained. On the other hand, harmful solvents such as benzene or dichloromethane were used in all case. Thus, development of new and environmentally benign methods for palladium-catalyzed cyclotrimerization of alkynes is still interesting. In this paper, we reported our new results of palladium-catalyzed cyclotrimerization of alkynes, which were promoted by CO_2 in water (Sch. 1 and Table 1).

Our recent studies[8–11] shown that the solvent effects played an important role in influencing selectivity (chemo-, stereo-, and regio-selectivity) of the Pd(II)-catalyzed process. Indeed, we found that cyclotrimerization of phenylacetylene occurred regioselectively by altering the reaction solvent form C_6H_6/n-BuOH to water in the presence of $PdCl_2$ and $CuCl_2$, although yield of the corresponding cyclotrimerization product **2a** is low (1,3,5-triphenylbenzene, 31%) and some red oils were still obtained (entry 2 in Table 1). The cyclotrimerization could occur in the absence of $CuCl_2$, but the yield of **2a** was decreased to 7% and a large amount of red oils were obtained (entry 1). Very interestingly, we found that the presence of CO_2 could enhance yields of the palladium-catalyzed cyclotrimerization of alkynes (the effect of CO_2 has already displayed in the application of CO_2 as either a reaction material[12–14] or reaction media.[15–17] In the 1.0 MPa of CO_2, the yield of **2a** was increased sharply to 90% in the presence of $PdCl_2$ and $CuCl_2$ in water (Entry 3).

Under the above optimum reaction conditions, cyclotrimerization of other alkynes was carried out smoothly and excellent yields were obtained. The cyclotrimerization of p-$MeC_6H_4C{\equiv}CH$, $C_5H_{11}C{\equiv}CH$, $C_3H_7C{\equiv}CC_3H_7$ afforded symmetric benzenes **2b**, **2c**, and **2d**, respectively (Entries 4, 6, and 8),



Scheme 1.

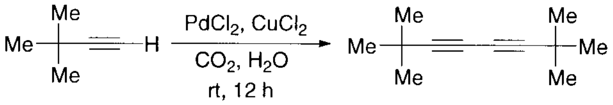
Table 1. Palladium-catalyzed cyclotrimerization of alkynes under CO_2 in water.[a]

Entry	R	R′	Isolated yield (%)
1[b]	Ph	H	7 (**2a**) + *c*
2[c,d]	Ph	H	31 (**2a**) + *c*
3	Ph	H	90 (**2a**)
4	*p*-MeC_6H_4	H	95 (**2b**)
5	Ph	Me	91 (**3**)
6	C_5H_{11}	H	87 (**2c**)
7[e]	C_5H_{11}	H	*c*
8	C_3H_7	C_3H_7	99 (**2d**)

[a] Reaction conditions: alkyne **1** (1 mmol), $PdCl_2$ (5 mol%), $CuCl_2$ (2 mmol), CO_2 (1.0 MPa), and H_2O (5 mL) at room temperature for 24 hr.
[b] In the absence of $CuCl_2$ and CO_2.
[c] The products were red oils and unidentified.
[d] In the absence of CO_2.
[e] In the absence of $CuCl_2$.

but $PhC{\equiv}CCH_3$ gave a unsymmetrical benzene **3** (1,3,5-triphenyl-2,4,6-trimethylbenzene, Entry 5). $CuCl_2$ is still crucial in cyclotrimerization of alkylacetylene ($C_5H_{11}C{\equiv}CH$).[8] In its absence, only red oils were obtained (entry 7). However, *tert*-butylacetylene, a bulky alkyne, was dimerized to afford **4** (1,4-di(*tert*-butyl)but-1,3-diyne) in 98% yield (Sch. 2).

Based upon the above results, several points should be noteworthy: (1) compared with our previous results,[8] the effect of solvents on the selectivity of the reaction is obvious. In C_6H_6/alcohol, phenylacetylene did not cyclotrimerize and *tert*-butylacetylene gave 1,3,5-tri(*tert*-butyl)benzene, whereas in water, phenylacetylene was cyclotrimerized to 1,3,5-triphenylbenzene and *tert*-butylacetylene was dimerized to 1,4-di(*tert*-butyl)but-1,3-diyne. (2) The presence of CO_2 can increase yields of the reaction. In its presence, the yield of 1,3,5-triphenyl-2,4,6-trimethylbenzene was increased from 31% to



4 (98%)

Scheme 2.

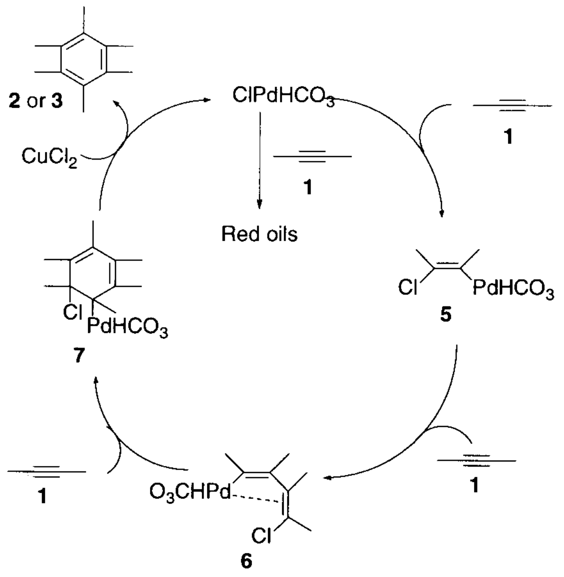
90%. However, the effect of CO_2 on the reaction is very difficult to understand. (3) The structure of alkynes influences both the chemo- and regioselectivity of the reaction to some extent. (4) $CuCl_2$ can also affect the yields of the reaction.[8]

A possible mechanism was proposed as shown in Sch. 3.[1–8] In water, some of $PdCl_2$ generally change to ClPd(OH) species (Eq. 1),[4] which leads to decreasing complex of catalysts with alkynes to give the desired products **2**. Trace of **2** was obtained in the absence of $CuCl_2$ and CO_2 due to poor solubility of the catalysts in H_2O. Addition of $CuCl_2$ could not only regenerate the palladium species in situ but also increase the solubility of catalysts (Eq. 2). Both the reaction of CO_2 with $PdCl_2$ and H_2O might be occurred to form $ClPdHCO_3$ (Eq. 3)[12] to decrease the complex of the catalysts with alkynes resulting in shifting the chemoselectivity to the cyclotrimerization reaction. Another increased yields of the reaction might be explained in terms of acidity of H_2CO_3 from the reaction of CO_2 with water. A dimeriza-

$$PdCl_2 + H_2O \rightleftharpoons ClPd(OH) + HCl \qquad (1)$$

$$PdCl_2 + CuCl_2 \rightleftharpoons CuPdCl_4 \qquad (2)$$

$$PdCl_2 + CO_2 + H_2O \rightleftharpoons ClPdHCO_3 + HCl \qquad (3)$$



Scheme 3.

tion product was obtained in the cyclotrimerization of *tert*-butylacetylene due to the steric hindrance.

Although further investigation is needed to settle the mechanism, the present procedure provides a new general and environmentally benign route to synthesize some benzene derivatives.

EXPERIMENTAL

All ^{1}H spectra were recorded at 400 MHz with $CDCl_3$ as solvent. TLC was performed using commercially prepared 100–400 mesh silica gel plates (HF_{254}) and visualization was effected at 254 nm. All reagents were used directly as obtained commercially.

A Typical Procedure for the Cyclotrimerization of Alkynes

Alkyne **1** (1 mmol) was added to a mixture of $PdCl_2$ (5 mol%), $CuCl_2$ (2 mmol), and H_2O (5 mL) in HF-25 autoclave. Liquid CO_2 was then transferred into the autoclave to 1.0 MPa. The reaction mixture was stirred at room temperature for 24 hr. After the gas was vented, the residue was extracted (ether), dried (anhydrous Na_2SO_4), and purified by preparative TLC on silica gel (light petroleum–ethyl ether). Under the above reaction conditions, alkyne **1** was consumed completely after 24 hr, which was detected by GC analyses.

Caution: Be careful in working at high pressure.

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REFERENCES

1. Tsuji, J. *Organic Synthesis with Palladium Compounds*; Springer-Verlag: New York, 1980, 162.
2. Schore, N.E. Transition metal-mediated cycloaddition reactions of alkynes in organic synthesis. Chem. Rev. **1988**, *88*, 1081.

3. Schore, N.E In *Comprehensive Organic Synthesis*; Trost, B.M., Fleming, I., Paquatte, L.A., Eds.; Pergamon: Elmsford, NY, 1991; Vol. 5, Chapter 7.3, 1129.
4. Grotijahn, D.B. *Comprehensive Organometallic Chemistry II*; Abel, E.W., Stone, F.G.A., Wilkinson, G., Hegedus, L.S., Eds.; Pergamon: Tarrytown, NY, 1995; Vol. 12, 741.
5. Gevorgyan, V.; Yamamoto, Y. Palladium-catalyzed enyne-yne $[4+2]$ benzannulation as a new and general approach to polysubstituted benzenes. J. Organometallic. Chem. **1999**, *576*, 232.
6. Sigmen, M.S.; Fatlant, A.W.; Eaton, B.E. Cobalt-catalyzed cyclotrimerization of alkynes in aqueous solution. J. Am. Chem. Soc. **1998**, *120*, 5130, and references cited therein.
7. Yokota, T.; Sakurai, Y.; Sakaguchi, S.; Ishii, Y. Cyclotrimerization of alkynes using a multicatalytic system, Pd(II)/chlorohydroquinone/NPMOV, under dioxygen. Tetrahedron Lett. **1997**, *38*, 3923.
8. Li, J.; Jiang, H.; Chen, M. $CuCl_2$-induced regiospecifical synthesis of benzene derivatives in the palladium-catalyzed cyclotrimerization of alkynes. J. Org. Chem. **2001**, *66*, 3627, and references cited therein.
9. Li, J.; Jiang, H.; Feng, A.; Jia, L. Novel stereospecific syntheses of 3-chloroacrylate esters via palladium-catalyzed dicarbonylation of terminal acetylenes. J. Org. Chem. **1999**, *64*, 5984.
10. Li, J.; Li, G.; Jiang, H.; Chen, M. A novel and efficient synthesis of maleic anhydrides by palladium-catalyzed dicarbonylation of terminal acetylenes in H_2O/dioxane. Tetrahedron Lett. **2001**, *42*, 6923.
11. Li, J.; Jiang, H.; Chen, M. Effect of solvent and acid-base on palladium (II)-catalyzed dicarbonylation of terminal acetylenes: a general and efficient synthesis of maleic diesters and maleic anhydrides. Chin. J. Chem. **2001**, *19*, 689.
12. Gabriele, B.; Salerno, G.; Costa, M.; Chiusoli, G.P. Palladium-catalysed formation of maleic anhydrides from CO, CO_2 and alk-l-ynes. Chem. Commun. **1999**, 1381.
13. Matsuda, T.; Ohashi, Y.; Harada, T.; Yanagihara, R.; Nagasawa, T.; Nakamura, K. Conversion of pyrrole to pyrrole-2-carboxylate by cells of *Bacillus megaterium* in supercritical CO_2. Chem. Commun. **2001**, 2194, and references cited therein.
14. Abia, M.; Choi, J.C.; Sakakura, T. Halogen-free process for the conversion of carbon dioxide to urethanes by homogeneous catalysis. Chem. Commun. **2001**, 2238, and references cited therein.
15. Jessop, P.G.; Leitner, W. *Chemical Synthesis Using Supercritical Fluids*; Wiley-VCH: Weinheim, 1999.
16. Li, J.; Jia, L.; Jiang, H. Transition metal-catalyzed organic reactions in supercritical carbon dioxide. Chinese J. Org. Chem. **2000**, *20*, 293.

17. Oakes, R.S.; Clifford, A.A.; Rayner, C.M. The use of supercritical fluids in synthetic organic chemistry. J. Chem. Soc. Perkin Trans. 1 **2001**, 917.

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