

Novel Role of Carbon Dioxide as a Selective Agent in Palladium-Catalyzed Cyclotrimerization of Alkynes

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Carbon dioxide was found as a selective agent to promote the palladium-catalyzed cyclotrimerization of alkynes in water. Both aryl and alkylacetylenes afforded the corresponding cyclotrimerization products regioselectively in high yields using PdCl₂, CuCl₂, and CO₂ as the catalytic system. However, *tert*-butylacetylene bearing a bulky group gave a dimerization product. Mechanism of this reaction was also discussed.

Keywords carbon dioxide, a selective agent, palladium, cyclotrimerization, alkyne

In the earlier reports on carbon dioxide (CO₂), most of the studies concerned the use of CO₂ as raw materials¹ or reaction media² in organic synthesis. So the development of new routes to apply CO₂ to the modern organic synthesis is considered to be one of the most challenges for the synthetic chemists. Although CO₂ has been displayed to be a selective agent in the earlier reports as either a raw material or reaction media,¹⁻³ few examples succeeded in applying CO₂ only as a selective agent to shift the reaction selectivity in organic synthesis.⁴ Very recently, we found that CO₂ could be used as a selective agent to improve the diiodination of alkynes^{4b} and homocoupling of aryl halides,^{4c} respectively. The results encouraged us to investigate and broaden this role of CO₂ in organic synthesis.

Transition metal mediated [2+2+2] cyclotrimerization of alkynes has been an area of extensive investigation, and utilized efficiently in the synthesis of aromatic compounds and many natural products.⁵⁻¹² Recently, a novel palladium-catalyzed cyclotrimerization of alkynes has been reported,¹² which is useful for the regioselective synthesis of symmetric benzene derivatives in C₆H₆/*n*-BuOH. Unfortunately, phenylacetylene could not undergo the cyclotrimerization reaction, and only red oil was obtained. On the other hand, harmful solvents such as benzene or dichloromethane were used in all cases.⁵⁻¹² Thus, development of new and environmentally benign procedures for the palladium-catalyzed cyclotrimerization of alkynes is still an attractive area. Herein we reported our new results of using CO₂ as a selective agent in the palladium-catalyzed cyclotrimerization of alkynes (Scheme 1 and Table 1).

Our recent studies showed that the solvent effects played an important role in influencing the selectivity (chemo-, stereo-, and regio-selectivity) of the Pd(II)-

Scheme 1

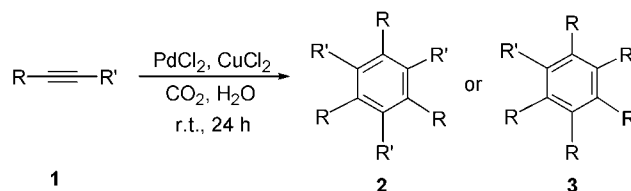


Table 1 Palladium-catalyzed cyclotrimerization of alkynes^a

Entry	Alkyne	Isolated yield/%
1 ^b	PhC≡CH (1a)	7 (2a) ^c
2 ^d	PhC≡CH (1a)	31 (2a) ^c
3	PhC≡CH (1a)	90 (2a)
4	<i>p</i> -MeC ₆ H ₄ C≡CH (1b)	95 (2b)
5	PhC≡CMe (1c)	91 (3)
6	<i>n</i> -C ₅ H ₁₁ C≡CH (1d)	87 (2d)
7 ^e	<i>n</i> -C ₅ H ₁₁ C≡CH (1d)	^c
8	<i>n</i> -C ₃ H ₇ C≡C(<i>n</i> -C ₃ H ₇) (1e)	99 (2e)

^a Reaction conditions: alkyne **1** (1 mmol), PdCl₂ (5 mol%), CuCl₂ (2 equiv.), CO₂ (1.0 MPa), and H₂O (5 mL) at room temperature for 24 h. ^b Without both CuCl₂ and CO₂. ^c The product was red oil and unidentified. ^d Without CO₂. ^e Without CuCl₂.

catalyzed processes.¹²⁻¹⁵ Indeed, we found that cyclotrimerization of phenylacetylene (**1a**) occurred regioselectively by altering the reaction solvent from benzene to water in the presence of PdCl₂ and CuCl₂, although the yield of the corresponding cyclotrimerization product **2a** was low (1,3,5-triphenylbenzene, 31% yield), and some red oil was still obtained (Entry 2 in Table 1). Cyclotrimerization of **1a** could occur in the absence of CuCl₂, but the yield of **2a** was decreased to 7% and a large amount of red oils were obtained (Entry 1). It is

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water, PdCl₂ was partly changed to CIPd(OH) species [Eq. (1)],⁸ which led to decreasing complex of catalysts with alkynes to give the desired products **2**. Trace of **2** was obtained in the absence of CuCl₂ and CO₂ due to poor solubility of the catalysts in H₂O. The presence of CuCl₂ could not only regenerate the palladium species *in situ* but also increase the solubility of catalysts due to the generation of CuPdCl₄ [Eq. (2)]. The formation of CIPdHCO₃R from the reaction of CO₂ with PdCl₂ and H₂O decreased the complex of the catalysts with alkynes,¹⁶ which resulted in the shift from the chemoselectivity to the cyclotrimerization reaction besides the acidity of H₂CO₃ by the reaction of CO₂ with water [Eq. (3)].⁴ A dimerization product **4** was obtained from *tert*-butylacetylene **1f** due to the steric hindrances.

In conclusion, we have developed a new general and environmentally benign protocol to synthesize some benzene derivatives. Currently, further efforts associated with this new role of carbon dioxide in organic synthesis are in progress in our laboratory.

Experimental

All ¹H NMR spectra were recorded on an INOVA-400 (Varian) spectrometer with CDCl₃ as solvent. All reagents were used directly as obtained commercially.

Typical procedure for the palladium-catalyzed cyclotrimerization of alkynes

Alkyne **1** (1 mmol) was added to a mixture of PdCl₂ (5 mol%), CuCl₂ (2 equiv.), and H₂O (5 mL) in HF-25 autoclave. Liquid CO₂ was then transferred into the autoclave to 1.0 MPa. The reaction mixture was stirred at room temperature for 24 h. After the gas was vented, the residue was extracted (ether), dried (anhydrous Na₂SO₄) and then purified by flash column chromatography (hexane/ethyl acetate). Under the above reaction conditions, alkyne **1** was consumed completely detected by GC analysis.

1,3,5-Triphenylbenzene (2a): A white solid, m.p. (uncorrected) 174—177 °C (lit.¹⁷ 176 °C); ¹H NMR (CDCl₃, 400 MHz) δ: 7.30—7.36 (m, 11H), 7.51—7.53 (m, 7H); MS *m/z* (%): 306 (M⁺, 100).

1,3,5-Tri(p-methylphenyl)benzene (2b): A white solid, m.p. (uncorrected) 175—178 °C (lit.¹⁷ 178 °C); ¹H NMR (CDCl₃, 400 MHz) δ: 2.37 (s, 9H), 7.16 (d, *J*=8.4 Hz, 6H), 7.27 (s, 3H), 7.60 (d, *J*=8.4 Hz, 6H); MS *m/z* (%): 348 (M⁺, 100).

1,3,5-Tripentylbenzene (2d): A colorless oil; ¹H NMR (CDCl₃, 400 MHz) δ: 0.88 (t, *J*=7.6 Hz, 9H), 1.24—1.32 (m, 12H), 1.55—1.61 (m, 6H), 2.38 (t, *J*=4.8 Hz, 6H), 6.39 (s, 3H); MS *m/z* (%): 288 (M⁺, 8) 262 (7), 241 (16), 227 (12), 205 (23), 192 (19), 171 (11), 149 (33), 135 (37), 113 (18), 99 (67), 91 (100).

Hexapropylbenzene (2e): A white solid, m.p. (uncorrected) 101—104 °C (lit.¹⁸ 102—102.5 °C); ¹H NMR (CDCl₃, 400 MHz) δ: 1.02 (t, *J*=7.6 Hz, 18H), 1.48—1.54 (m, 12H), 2.45 (t, *J*=4.8 Hz, 12H); MS *m/z* (%): 330 (M⁺, 5), 301 (9), 287 (18), 273 (8), 259 (11),

217 (15), 175 (8), 133 (25), 119 (56), 105 (100).

1,2,4-Trimethyl-3,5,6-triphenylbenzene (3): A white solid, m.p. (uncorrected) 223—225 °C (lit.¹⁹ 224 °C); ¹H NMR (CDCl₃, 400 MHz) δ: 1.71 (s, 6H), 2.03 (s, 3H), 6.95—7.44 (m, 15H); MS *m/z* (%): 348 (M⁺, 100).

1,4-Di(tert-butyl)buta-1,3-diyne (4): A white solid, m.p. (uncorrected) 129—132 °C (lit.²⁰ 131 °C); ¹H NMR (CDCl₃, 400 MHz) δ: 1.23 (s, 18H); MS *m/z* (%): 162 (M⁺, 8), 161 (25), 133 (37), 119 (55), 91 (100).

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