Catalytic Carbonylation Reactions of Benzyne Derivatives

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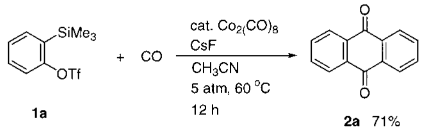
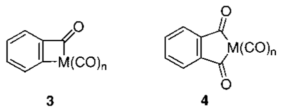
Received August 9, 2001

Alkynes can be used as two-carbon assembling units in cycloaddition reactions, and a variety of transition metal-catalyzed cycloaddition reactions using alkynes have been reported.[1] In contrast, benzyne derivatives (arynes) have not been used extensively in the area of transition metal-catalyzed cycloaddition chemistry despite their ability to undergo cycloaddition reactions.[2] The high reactivity and short lifetime of benzyne suggest that its use as a component of a catalytic reaction might be difficult. During our ongoing studies of catalytic carbonylative cycloaddition reactions,[3] we have investigated the use of benzyne as a reactive partner in carbonylative cycloadditions. In 1999, Pérez and Guitián reported that the treatment of 2-trimethylsilylphenyl trifluoromethansulfonate (**1a**) with CsF and a catalytic amount of Pd(0) in CH_3CN gives triphenylene, possibly via the [2 + 2 + 2] homo-cyclotrimerization of benzyne.[4] They also reported on the preparation of phenanthrene or naphthalene derivatives via the Pd-catalyzed [2 + 2 + 2] co-cyclotrimerization of benzyne−benzyne−alkyne or benzyne−alkyne−alkyne.[5,6] Yamamoto independently reported on a similar co-cyclotrimerization of benzyne−benzyne−alkyne, catalyzed by a Pd(0) complex.[7] Yamamoto later confirmed that these co-cyclotrimerization reactions do not proceed via an all-free benzyne mechanism; rather, the initial step of the catalytic cycle involves the oxidative addition of an Ar−OTf bond in benzyne precursor **1a** to Pd(0).[8] Yamamoto also reported that the Pd-catalyzed reaction of **1a** with allyl chlorides in the presence of CsF gives phenanthrene derivatives and that this reaction proceeded via a free benzyne mechanism.[8,9] On the other hand, no report on the catalytic carbonylation of benzyne has appeared in the literature to date. Stoichiometric reactions of benzyne−transition metal complexes with CO are, however, known.[10] If benzyne could be utilized as a two-carbon assembly unit in the same manner as alkynes, a new type of carbonylative cycloaddition reaction is possible. We wish to report, to the best of our knowledge, the first example of transition metal-catalyzed carbonylation reactions of benzyne.

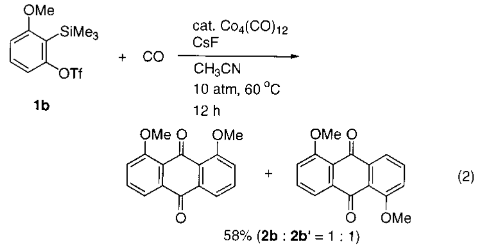
Although a wide variety of reaction systems were examined in the hope of achieving the three-component cycloaddition of benzyne, various alkenes (or alkynes), and CO, we were not able to achieve the carbonylative cycloaddition reaction. However, it was found that a few complexes show catalytic activity for carbonylation reactions of benzyne itself. A cobalt complex was found to be extremely active for the carbonylation of benzyne. Thus, the reaction of **1a** (0.5 mmol) with CO (5 atm) in CH_3CN (3 mL) in the presence of $Co_2(CO)_8$ (0.01 mmol) and CsF (1 mmol) at 60 °C for 12 h gave anthraquinone (**2a**)[11] in 71% isolated yield, along with a trace amount of triphenylene (eq 1). It was found that $Co_4(CO)_{12}$ is more active. The use of $Co_4(CO)_{12}$ as the catalyst gave **2a** in 80% yield. Increasing the CO pressure (10 and 15 atm) had no significant effect on the product yield (82 and 80%, respectively); however, the reaction under 1 atm dramatically decreased the yield. A reaction at 80 °C gave a slightly lower yield (70%).

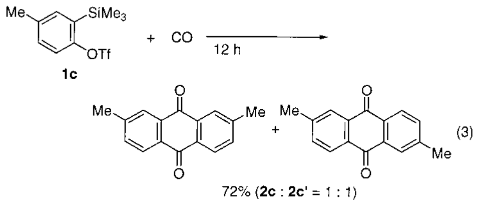




While details of the reaction mechanism are not clear at this time, the formation of these products is consistent with the intermediacy of **3** and **4**, in a manner similar to the transition metal-mediated synthesis of quinones from alkynes and CO.[12] Thus, the incorporation of the second benzyne into **4** followed by reductive elimination affords **2**.

The reaction of a methoxy derivative **1b** gave a mixture of regioisomers **2b** and **2b′** in a ratio of 1:1 (eq 2). The reaction of **1c** also gave a 1:1 mixture of **2c** and **2c′** (eq 3). These results are consistent with benzyne as an intermediate. However, the possibility that the reaction is initiated by the oxidative addition of a C−OTf bond to the cobalt complex and subsequent steps, which involve the insertion of CO, benzyne, and CO, followed by coupling, cannot be excluded, as Yamamoto has demonstrated.[8]





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[1] Recent reviews on cycloaddition of alkynes, see: Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49. Ojima, I.; Tzamarioudaki, M.; Li, Z.; Donovan, R. J. *Chem. Rev.* **1996**, *96*, 635. Saito, S.; Yamamoto, Y. *Chem. Rev.* **2000**, *100*, 2901.

[2] A recent review on benzyne nickel and platinum complexes, see: Bennett, M. A.; Wenger, E. *Chem. Ber./Rec.* **1997**, *130*, 1029.

[3] For our recent papers on carbonylative cycloaddition, see: Chatani, N.; Morimoto, T.; Fukumoto, Y.; Murai, S. *J. Am. Chem. Soc.* **1998**, *120*, 5335. Morimoto, T.; Chatani, N.; Murai, S. *J. Am. Chem. Soc.* **1999**, *121*, 1758. Chatani, N.; Tobisu, M.; Asaumi, T.; Fukumoto, Y.; Murai, S. *J. Am. Chem. Soc.* **1999**, *121*, 7160. Tobisu, M.; Chatani, N.; Asaumi, T.; Amako, K.; Ie, Y.; Fukumoto, Y.; Murai, S. *J. Am. Chem. Soc.* **2000**, *122*, 12663. Kamitani, A.; Chatani, N.; Morimoto, T.; Murai, S. *J. Org. Chem.* **2000**, *65*, 9230.

[4] Peña, D.; Escudero, S.; Pérez, D.; Guitián, E.; Castedo, L. *Angew. Chem., Int. Ed.* **1998**, *37*, 2659. Peña, D.; Pérez, D.; Guitián, E.; Castedo, L. *Org. Lett.* **1999**, *1*, 1555.

[5] Peña, D.; Pérez, D.; Guitián, E.; Castedo, L. *J. Am. Chem. Soc.* **1999**, *121*, 5827.

[6] Peña, D.; Pérez, D.; Guitián, E.; Castedo, L. *Synlett* **2000**, 1061.

[7] Radhakrishnan, K. V.; Yoshikawa, E.; Yamamoto, Y. *Tetrahedron Lett.* **1999**, *40*, 7533.

[8] Yoshikawa, E.; Radhakrishnan, K. V.; Yamamoto, Y. *J. Am. Chem. Soc.* **2000**, *122*, 7280.

[9] Yoshikawa, E.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2000**, *39*, 173.

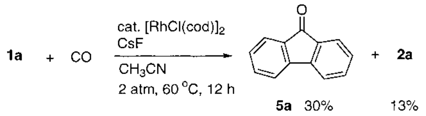
[10] Bennett, M. A.; Hockless, D. C. R.: Humphrey, M. G.; Schultz, M.; Wenger, E. *Organometallics* **1996**, *15*, 928.

[11] All compounds were characterized by NMR, IR, and mass spectral data. For new compounds, elemental analyses or high-resolution mass were also measured. See Supporting Information.

[12] For a review, Liebeskind, L. S.; Baysdon, S.; South, M. S.; Iyer, S. *Tetrahedron* **1985**, *41*, 5839.

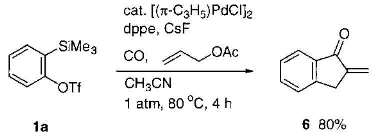
10.1021/ja011923c CCC: $20.00

Although various transition metal complexes were examined for their ability to catalyze the carbonylation of the benzyne precursor, the carbonylations proved to be less clean than those with the cobalt carbonyl complex, as shown in eq 1. For example, when a rhodium complex, such as $[RhCl(cod)]_2$, was used as the catalyst, a mixture of fluorenone (**5a**) in 30% yield and **2a** in 13% was obtained (eq 4). A palladium complex, $Pd(PPh_3)_4$, was also found to catalyze the formation of **2a** (3%) and **5a** (16%), while the main product was triphenylene (33%). The use of $Pt(dba)_2/4PPh_3$ as the catalyst gave triphenylene in 73% yield along with **2a** in 3% yield and **5a** in 13% yield.



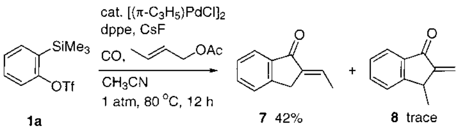
(4)

On the other hand, and quite interestingly, the use of the palladium complex in conjunction with allyl acetate resulted in a new type of carbonylation reaction. Thus, the reaction of **1a** (0.5 mmol) with allyl acetate (0.75 mmol) under CO (1 atm) in CH_3CN (3 mL) in the presence of $[(\pi\text{-}C_3H_5)PdCl]_2$ (0.0125 mmol), dppe (0.025 mmol), and CsF (1 mmol) at 80 °C for 4 h gave 2-methyleneindanone (**6**) in 80% yield (eq 5). It should be noted that the insertion of CO is very effective, even when 1 atm of CO is used. Furthermore, no phenanthrene derivatives were formed, in contrast to the results of Yamamoto.[8] The use of other phosphines, such as dppm, dppp, and dppb, in place of dppe failed to improve the product yield. Other allyl compounds, such as allyl chloride, bromide, and carbonate, were also not effective.

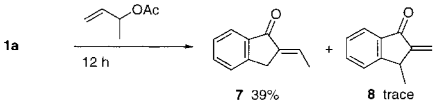


(5)

The reaction can be applicable to some substituted allyl acetates. The reaction of crotyl acetate gave **7** as a major product, along with a trace amount of **8** (eq 6). It was found that **7** is also obtained as a major product when 1-methyl-3-propenyl acetate is used, although the yield was somewhat low (eq 7). The use of cinnamyl acetate gave **9** in high yield (eq 8). In contrast, 2-methyl-2-butenyl acetate and 3-methyl-2-butenyl acetate did not serve as a coupling partner, and no carbonylation products were obtained.



(6)



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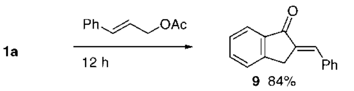
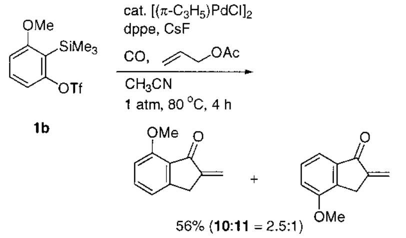


(8)

To examine the possibility that the reaction takes place through a benzyne mechanism, the reaction of **1b** was examined. The reaction of **1b** gave a mixture of regiosiomers **10** and **11** (eq 9). While the ratio of **10** and **11** was not the expected 1:1, the slightly predominant formation of **10** was rationalized as being due to the directing effect of the methoxy group (described later). The reaction of **1c** gave a nearly 1:1 mixture of **12** and **13** (eq 10). These results clearly support the intervention of a free benzyne or similar species.



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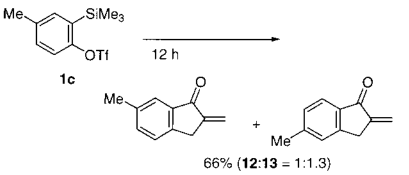
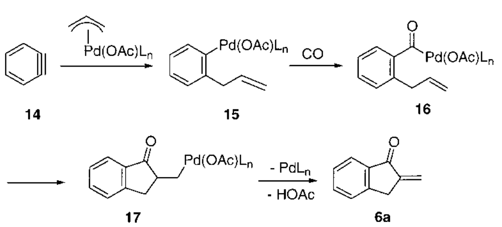
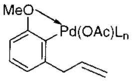


(10)

The proposed reaction mechanism is shown in Scheme 1. Carbopalladation of benzyne **14** with the π-allyl palladium complex gives the 2-allylphenylpalladium complex **15**, to which CO is inserted to give the acyl palladium **16**. Intramolecular cyclization followed by β-hydride elimination affords the final product **6a**. In the case of substituted allyl acetates, benzyne reacts predominantly at the less substituted terminus of the π-allylpalladium complex. The insertion of CO in **15**, which leads to the acyl complex **16** takes place much faster than the insertion of another molecule of benzyne into the C−Pd bond in **15**, which results in the formation of phenanthrene via several steps.[13] The predominant formation of **10** over **11** can be rationalized by the formation of the ortho-metalated complex **18** on the basis of coordination of the methoxy group to palladium.[14]

Scheme 1





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In summary, the present reaction demonstrates the first example, to our knowledge, of the catalytic carbonylation of benzyne. Further investigations are currently in progress concerning the use of benzyne for carbonylative cycloaddition as the two-atom assembling unit, as well as the development of a much more efficient entry to benzyne for catalytic use.

Acknowledgment. This research was supported by a Grant-in-Aid for Scientific Research on Priority Areas (A) “Exploitation of Multi-Element Cyclic Molecules” from the Monbusho.

Supporting Information Available: Experimental details (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(13) It was found that the presence of the Pd(II) catalyst, dppe, and CO results in the slow generation of benzyne, probably because of the trapping of F^- by Pd(II) to the palladate complex. In the reaction of **1a** with benzofuran in the presence of CsF in CH_3CN at 80 °C under N_2, **1a** was completely consumed within 30 min and the Diels−Alder adduct was obtained. On the other hand, 40% of **1a** still remained after 30 min when the reaction of **1a** with benzofuran was carried out in CH_3CN in the presence of $[(\eta^3\text{-}C_3H_5)PdCl]_2$, CsF, and dppe under CO.

(14) A similar methoxy-directing effect has been observed in catalytic reactions. Takeuchi, R.; Yasue, H. *J. Org. Chem.* **1993**, *58*, 5386. Sonoda, M.; Kakiuchi, F.; Chatani, N.; Murai, S. *Bull. Chem. Soc. Jpn.*, **1997**, *70*, 3117.