

Nickel-catalyzed cocyclootrimerization of arynes with diynes; a novel method for synthesis of naphthalene derivatives†

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The $\text{NiBr}_2(\text{dppe})\text{-Zn}$ system effectively catalyzes the [2 + 2 + 2] cocyclootrimerization of arynes with diynes, leading to substituted naphthalene derivatives in moderate to good yields. This cocyclootrimerization reaction shows excellent tolerance of functional groups and leads to products of 5- to 7-membered fused-ring sizes

The transition-metal mediated [2 + 2 + 2] cocyclootrimerization of alkynes is a powerful method for the construction of polycyclic compounds in one step.¹ Although this cycloaddition has been known for decades, the control of both regio- and chemoselectivity remains a great challenge to organic chemists. Recently, the cyclootrimerization of arynes and alkynes has attracted considerable attention. Perez *et al.* revealed the cyclootrimerization of arynes catalyzed by palladium to give triphenylenes.² Both the Perez and the Yamamoto groups reported the cyclootrimerization of benzynes and alkynes catalyzed by palladium complexes leading to the formation of phenanthrene derivatives.³ In the area of nickel-catalyzed trimerization, Ikeda and co-workers have developed an array of important methods.⁴ In addition, our interest in nickel and cycloaddition chemistry^{5,6} encouraged us to explore the possibility of using diynes in the cocyclootrimerization with benzynes. Herein, we wish to report the first example of a nickel-catalyzed [2 + 2 + 2] cocyclootrimerization of a benzyne with a diyne, providing an efficient method for the synthesis of naphthalene derivatives (Scheme 1). Notably, the naphthalene skeleton is found as a precursor in a number of active biological chemical products⁷ and polycyclic aromatic electronic materials.⁸

Treatment of benzyne precursor (**1a**, 0.50 mmol) with octa-1,7-diyne (**2a**, 1.0 mmol) in the presence of zinc powder (0.075 mmol),

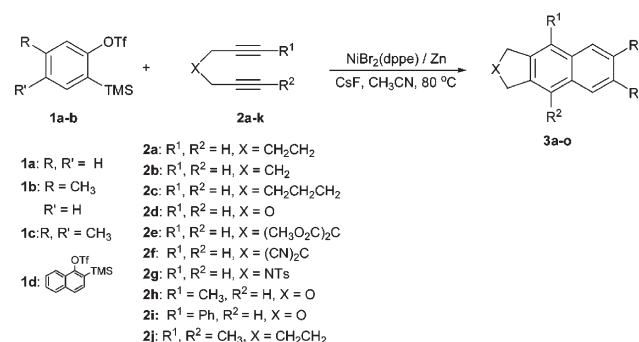
CsF (2.0 mmol) and $\text{NiBr}_2(\text{dppe})$ (0.025 mmol, dppe: bis(diphenylphosphino)ethane) in acetonitrile (2.0 mL) at 80 °C for 12 h afforded 1,2,3,4-tetrahydroanthracene (**3a**) in 86% yield in addition to a mixture of dimer (~ 0.2 mmol)⁹ and trimer (~ 0.02 mmol) of diyne **2a** (*vide infra*). The structure of **3a** was confirmed by its ¹H NMR, ¹³C NMR and mass data.

To understand the nature of this nickel-catalyzed carbocyclization, the effect of the solvent and metal complex used on the reaction of **1a** with **2a** was investigated. $\text{NiBr}_2(\text{PPh}_3)_2$ and $\text{NiBr}_2(\text{dppm})$ did not show any catalytic activity for the reaction, while $\text{NiBr}_2(\text{dppb})$ and $\text{Pd}(\text{PPh}_3)_4$ gave **3a** in 54 and 29% yields, respectively. The use of $\text{CoI}_2(\text{PPh}_3)_2$ as catalyst afforded only triphenylene without the desired cocyclootrimerization product. $\text{NiBr}_2(\text{dppe})$ was found to be the best catalyst producing product **3a** in 86% yield and with only a trace of triphenylene. The solvent used for the catalytic reaction was also critical. No reaction occurred in toluene, whereas THF afforded only a trace of **3a**. CH_3CN was the best solvent when $\text{NiBr}_2(\text{dppe})$ was used as the catalyst.

This nickel-catalyzed cocyclootrimerization reaction was successfully extended to various substituted diynes and the results are listed in Table 1. Thus, **1a** reacts with hepta-1,6-diyne (**2b**) and nona-1,8-diyne (**2c**) to provide the corresponding cocyclootrimerization products, **3b** and **3c**, in 89% and 84% yield. The results of entries 1 to 3 reveal a good fused-ring size tolerance within the present reaction. Similarly, functional diynes (**2d–g**) underwent [2 + 2 + 2] cycloaddition to produce naphthalene derivatives **3d–g** in good yields (Scheme 1, Table 1, entries 4–7).

Under similar reaction conditions, diynes **2h–j** possessing at least one internal alkyne moiety, also underwent [2 + 2 + 2] cocyclootrimerization with **1a** to give products **3h–3j** in 55, 47 and 41%, respectively. The observed lower product yield reflects that the present nickel-catalyzed cocyclootrimerization is sensitive to the substituent attached to the triple bond of the diynes. A small amount of homotrimerization product ([2 + 2 + 2]) of benzynes was observed in each of these reactions. No cocyclootrimerization of benzyne with more bulky disubstituted diynes, such as 1,8-diester and 1,8-diphenyl-1,7-octadiynes, was observed.

The present method can also be applied to the cocyclootrimerization of substituted benzynes. Treatment of 4-methylbenzyne, 4,5-dimethylbenzyne and naphthylne precursors (**1b–d**) with octa-1,7-diyne (**2a**) in the presence of $\text{NiBr}_2(\text{dppe})$, zinc powder and CsF in acetonitrile at 80 °C for 12 h furnished naphthalene derivatives **3k**, **3n**, and **3o** in 62, 59, and 37% yields. In the same fashion, **1b** reacted with hepta-1,6-diyne (**2b**) and dimethyl 2,2-(diprop-2-ynyl)malonate (**2e**) to give naphthalene derivatives **3l** and **3m** in 56 and 63% yields, respectively.

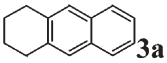
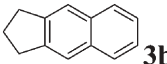
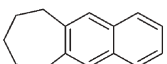
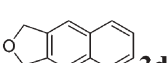
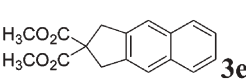
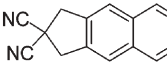
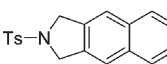
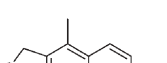
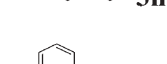
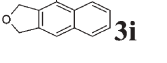
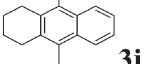
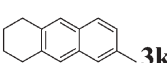
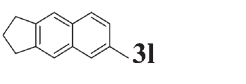
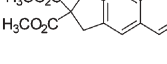
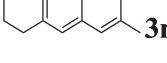


Scheme 1

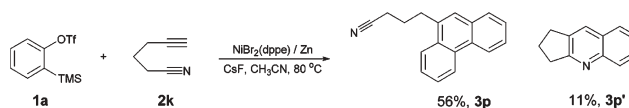
† Electronic supplementary information (ESI) available: experimental details. See <http://www.rsc.org/suppdata/cc/b4/b415691a/>

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Table 1 Results of [2 + 2 + 2] cocyclootrimerization of diynes with benzynes catalyzed by nickel complex NiBr₂(dppe)^a

Entry	1	2	Product	Yield (%) ^b
1	1a	2a		86
2	1a	2b		89
3	1a	2c		84
4	1a	2d		71
5	1a	2e		79
6	1a	2f		87
7	1a	2g		74
8	1a	2h		55
9	1a	2i		47
10	1a	2j		41
11	1b	2a		62
12	1b	2b		56
13	1b	2e		63
14	1c	2a		59
15	1d	2a		37

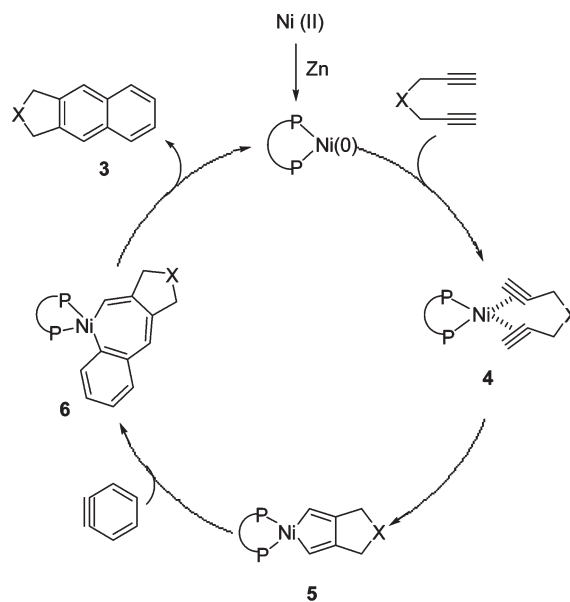
^a Unless stated otherwise, all reactions were carried out using benzyne precursor (1) (0.50 mmol), diyne (2) (1.0 mmol), NiBr₂(dppe) (5.0 mol%), CsF (2.0 mmol) and Zn (15.0 mol%) in CH₃CN (2.0 mL) at 80 °C under N₂ for 12 h. ^b Isolated yields based on benzyne precursor used.

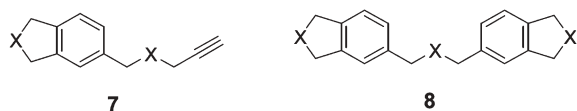
**Scheme 2**

The reaction of hex-5-ynitrile (**2k**) with **1a** is interesting. Two products **3p** and **3p'**, a phenanthrene and a naphthalene derivative, respectively, in 56 : 11 molar ratio were observed with a combined yield of 67% (Scheme 2). The major product **3p** was produced by the reaction of two benzynes with one hex-5-ynitrile during the cyclootrimerization. The minor product, a quinoline derivative, **3p'** was formed from a [2 + 2 + 2] cocyclootrimerization of the carbon-carbon triple and the nitrile group in a hex-5-ynitrile molecule and a benzyne moiety. The low reactivity of the nitrile moiety likely accounts for the low yield of **3p'**.

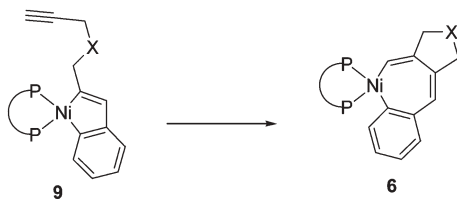
The foregoing results reveal that the present catalytic reaction is sensitive to the substituent on the diyne and benzyne moieties. Terminal diynes are most reactive and give high yields of the cocyclootrimerization products. Monosubstituted diynes undergo [2 + 2 + 2] cocyclootrimerization but with lower yields. For the disubstituted internal diynes, only deca-2,8-diyne (**2j**) reacts with benzyne to give the expected product; other bulkier disubstituted diynes gave no or trace amount of the desired products. *meta*-Substituted benzynes are also somewhat less reactive. It is also worth pointing out here that, whilst not specifically detailed, *ortho*-substituted benzyne derivatives gave no or very low yield of the expected products.

Based on the above results and known organometallic chemistry, a plausible mechanism is proposed to account for the formation of naphthalene products (Scheme 3). The catalytic reaction is likely to be initiated by the reduction of the Ni(II) species to a Ni(0) species by zinc metal. Coordination of both C–C triple bonds of diyne to the Ni(0) center **4** followed by cyclometalation produces a nickelacyclopentadiene intermediate **5**.¹⁰ Benzyne coordination and then insertion into a Ni(II)–carbon

**Scheme 3**



Scheme 4



Scheme 5

bond of **5** gives a nickelacycloheptatriene intermediate **6**. Subsequent reductive elimination of **6** affords product **3** and regenerates the Ni(0) catalyst. This mechanism appears likely in view of the formation of diyne dimer **7** and trimer **8**⁹ (Scheme 4) in the reaction that can only be formed from intermediate **5**.

An alternative mechanism (Scheme 5) involves the coordination of a triple bond of diyne **2** and a benzyne to the nickel center to produce a five-membered nickelacyclopentadiene intermediate **9**. An intramolecular insertion of the C–C triple bond into the adjacent Ni(II)–carbon bond yields intermediate **6**. Further reductive elimination affords the final product **3**. This pathway also explains very well the formation of product **3**, but fails to account for the formation of diyne dimer and trimer in the reaction.

In conclusion, we have developed a new methodology for the [2 + 2 + 2] cocyclootrimerization of arynes with diyne catalyzed by nickel complexes. This is the first report that a diyne can undergo cycloaddition with a benzyne with excellent tolerance of functional groups and fused-ring sizes to furnish naphthalene derivatives in moderate to good yields. Further studies to determine the exact mechanistic pathway for this useful reaction are currently under way.

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