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Synthesis of Biaryls Using Nickel-Catalyzed [2+2+2] Cocyclization

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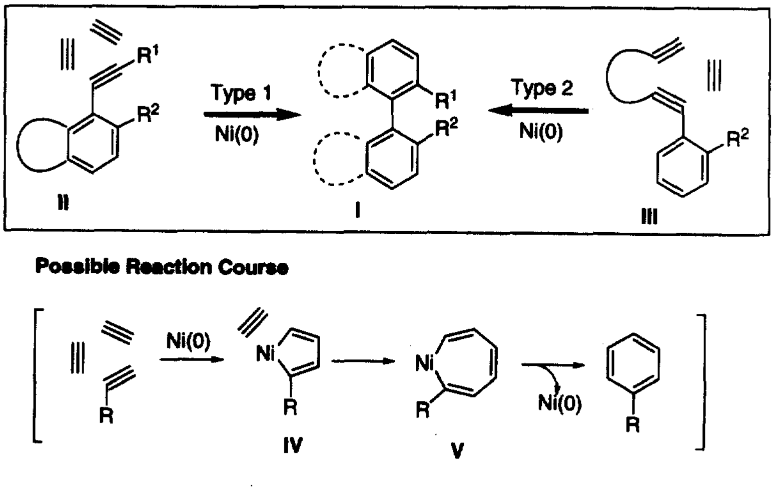
Abstract: Methods of synthesizing biaryls using nickel-catalyzed [2+2+2] cocyclization were developed. Two ways for the synthesis of biaryl using [2+2+2] cocyclization were investigated: one method is that biaryls synthesized from alkyne having a phenyl group and 2 equivalents of acetylene, and the other method is that those were synthesized from α,ω-diyne having a phenyl group at an α-position and acetylene. The yield is good in each case. © 1999 Elsevier Science Ltd. All rights reserved.

Key Words: Biaryl, [2+2+2] Cocyclization, Cotrimerization, Cycloaddition, Nickel catalyst.

A [2+2+2] cocyclization of alkynes using a transition-metal complex is useful for the construction of the aromatic ring.[1] Recently, the syntheses of the aromatic ring using nickel-promoted[2] and nickel-catalyzed[3,4] [2+2+2] cocyclization were reported. Although the reaction mechanism was not clear, the intermediate is thought to be nickelacyclopentadiene **IV** generated from two alkynes by oxidative cyclization, and nickelacyclohepatatriene **V**, which was formed by insertion of alkyne into **IV**. These results prompted us to develop a conceptually new methodology for the synthesis of biaryls using a nickel-catalyzed [2+2+2] cocyclization. In general, biaryls are constructed by the attachment of two aryl groups.[5] However, we planed to construct biaryls by two methods shown in Scheme 1. One method is the synthesis of biaryls from alkynes **II** having an aryl group and 2 equivalents of acetylene (Type 1). The other method is the formation of biaryls from α,ω-diynes **III** having an aryl group at the terminal position and acetylene (Type 2).

Scheme 1. Plan for the Synthesis of Biaryls by Nickel-Catsalyzed [2+2+2]Cocyclization



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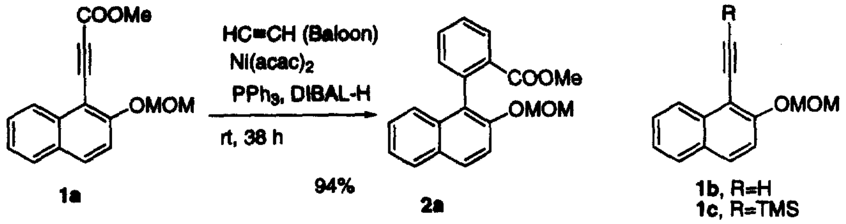
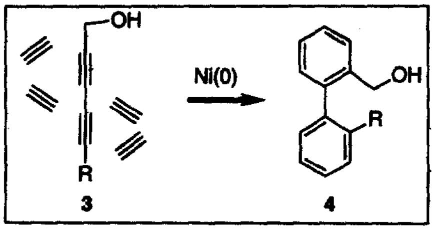
First, we examined the synthesis of biaryls from alkynes having an aryl group and 2 equivalents of acetylene (i.e., Type 1). When a THF solution of naphthalene derivative **1a** having alkyne at an α–position was stirred at room temperature in the presence of nickel catalyst prepared from $Ni(acac)_2$ (20 mol %), PPh_3 (80 mol %) and DIBAL-H (40 mol %) under acetylene gas (balloon) for 38 h, biaryl **2a** was obtained in 94% yield. The result was quite interesting because the biaryl skeleton was constructed with a excellent yield from alkyne and gaseous acetylene. On the other hand, the reaction of alkyne **1b** with acetylene under the similar conditions did not afford the desired biaryl but gave complex mixtures along with recovered starting material **1b** in 58%. In the reaction of **1c** under the similar conditions, the starting material **1c** was recovered in 99%. These results suggested that coordination of alkyne to the metal center is important in this cyclization, and that the alkyne moiety in **1a**, having an electron withdrawing substituent, would strongly coordinate to the metal center due to back donation.

Scheme 2. Synthesis of Biaryl from Alkyne +2 Acetylene (Type 1)



It was known that the reaction of α,ω-diyne and propargylic alcohol gave the aromatic compound in good yield because the hydroxy moiety would assist the alkyne to coordinate to the metal center.[2] Thus, we tried to construct biaryl **4** from 1,3-diyne **3**, having the hydroxymethyl group, and 4 equivalents of acetylene (Scheme 3).

Scheme 3 Plan for the Synthesis of Biaryls from 1,3-Diyne and Acetylene



Scheme 4. Nickel-Catalyzed [2+2+2]Cocyclization Using Diyne and Acetylene

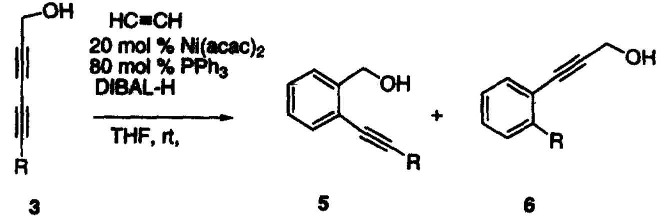
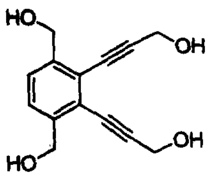


Table 1. Nickel-Catalyzed [2+2+2]Cocyclization of 1,3-Diyne and Acetylene

Run	R		Yield (%) 5	Yield (%) 6
1	CH_2OH	**3a**	84	-
2	TMS	**3b**	81	-
3	Bu	**3c**	80	-
4	Ph	**3d**	63	-
5	H	**3e**	29	15
6	COOMe	**3f**	9	25



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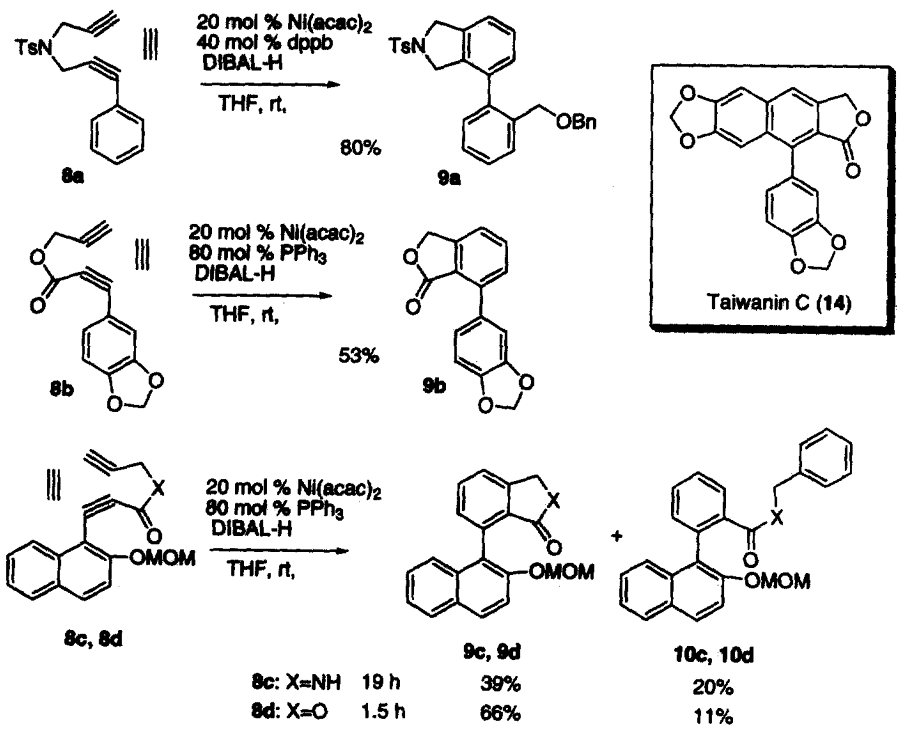
When diyne **3a** was reacted with acetylene in the presence of nickel catalyst, **5a** was obtained in 84% yield (Table 1, run 1), and neither biaryl **4a** nor **7** was obtained. The 1,3-diynes **3b**-**3e**, having various substituents, were used for this reaction, however, the desired biaryls **4** were not formed (Table 1), and in each case, the main product was benzyl alcohol **5**. When the alkyne **3f**, having a carbomethoxy group, was used, the main product was changed from **5** to **6** (run 6), and the result is consistent with that of the cyclization of **1a**. Although the construction of biaryl was unsuccessful in this system, the high reactivity of di-substituted alkyne **3** on [2+2+2] cocyclization was quite interesting.[6]

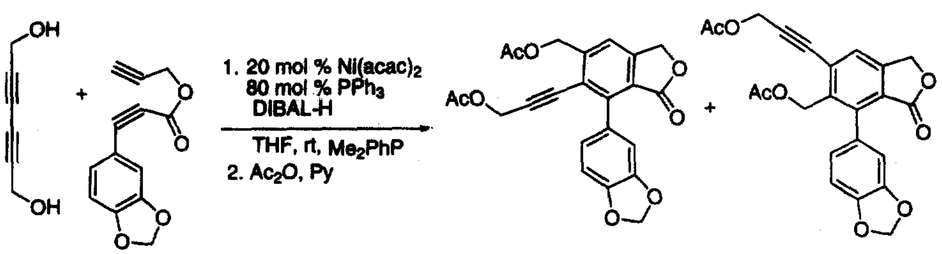
Subsequently, we examined the construction of biaryls from α,ω-diyne and alkyne (i.e. Type 2). When a THF solution of diyne **8a** having a phenyl group was stirred under acetylene gas in the presence of nickel catalyst derived from $Ni(acac)_2$, dppb, and DIBAL-H at room temperature, the desired biaryl **9a** was obtained in 80% yield.

Scheme 5. Synthesis of Biaryls from α,ω-Diyne and Alkyne



In the reaction of diyne **8b**, having a (methylenedioxy)phenyl group, with acetylene, the desired biaryl **9b** was obtained in 53% yield. The alkynes, **8c** and **8d**, having a naphthalene ring, gave biaryls **9c** and **9d** in 39% and 66% yields along with biaryls **10c** and **10d** in 20% and 11% yields, respectively. Since the reactivity of diyne **3** was quite interesting as a functionalized di-substituted alkyne, the reaction of diyne **3a** with **11** was also investigated. The reaction resulted in biaryls **12** and **13** being obtained in 64% and 12% yields, respectively. The biaryl **12** should be a good intermediate for the synthesis of natural products containing biaryl skeletons such as Taiwanin C (**14**). The results indicate that various biaryls having functional groups could be obtained from α,ω-diynes and alkynes, and that di-substituted alkyne **3a** can be used for the synthesis of biaryl as well as acetylene and DMAD.

Scheme 6



3a **11** **12** 64% **13** 12%

In conclusion, biaryls were constructed from alkyne and two equivalents of acetylene or from α,ω-diyne and alkyne using nickel-catalyzed [2+2+2] cocyclization in good to excellent yields. In this reaction, 1,3-diyne **3a** could be used as di-substituted alkyne. Further studies on the application of the synthesis of natural products as well as on the asymmetric synthesis of biaryls are in progress.

References and Notes

1. For [2+2+2] cycloaddition of alkenes and alkynes; (a) Schore, N. E. In *Comprehensive Organic Synthesis*; Trost, B. M.; Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 5, Chapter 9.4. (b) Grotjahn, D. B. In *Comprehensive Organometallic Chemistry II*; Abel, E. W.; Stone, F. G. A.; Wilkinson, G., Eds.; Pergamon Press: Oxford, 1995; Vol. 12, Chapter 7.3. (c) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49.
2. (a) Bhatarah, P.; Smith, E. H. *J. Chem. Soc. Perkin Trans. 1* **1990**, 2603. (b) Bhatarah, P.; Smith, E. H. *Chem. Commun.* **1991**. 277. (c) Bhatarah, P.; Smith, E. H. *J. Chem. Soc. Perkin Trans. 1* **1992**, 2169.
3. (a) Sato, Y.; Nishimata, T.; Mori, M. *J. Org. Chem.* **1994**, *59*, 6133. (b) Sato, Y.; Nishimata, T.; Mori, M. *Heterocycles* **1997**, *44*, 443.
4. For recent examples of Ni-catalyzed [2+2+2] cocyclization of alkenes and alkynes: (a) Ikeda, S.; Watanabe, H.; Sato, Y. *J. Org. Chem.* **1998**, *63*, 7026 and references cited therein. (b) Seo, J.; Chui, H. M. P.; Heeg, M. J.; Montgomery, J. *J. Am. Chem. Soc.* **1999**, *121*, 476.
5. For the synthesis of biaryls *via* aryl-aryl coupling reactions, see: Knight, D. W. In *Comprehensive Organic Synthesis*; Trost, B. M.; Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 3, Chapter 2.3.
6. (a) For Pd-catalyzed cyclotrimerization of 1,3-diynes; Takeda, A.; Ohno, A.; Kadota, I.; Gevorgyan, V.; Yamamoto, Y. *J. Am. Chem. Soc.* **1997**, *119*, 4547. (b) Very recently, Co(I)-catalyzed [2+2+2] cycloadditions of diyne 3 with two molecules of 5-hexynenitrile were reported, in which 3,3'-susbtituted 2,2'-bipyridine derivatives were obtained. See: Varela, J. A.; Castedo, L.; Saá, C. *J. Am. Chem. Soc.* **1998**, *120*, 12147.