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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.

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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-promoted² 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



Possible Reaction Course



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 %), PPh₃ (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.





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).









	Yield (%)				
Run	R		5	6	10
1	CH ₂ OH	3a	84	-	HU
2	TMS	3b	81	-	UH UH
3	Bu	3c	80	_	
4	Ph	3d	63		
5	н	30	29	15	И СН
6	COOMe	31	9	25	
					7

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

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



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

- 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.
- (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.
- (a) Sato, Y.; Nishimata, T.; Mori, M. J. Org. Chem. 1994, 59, 6133.
 (b) Sato, Y.; Nishimata, T.; Mori. M. Heterocycles 1997, 44, 443.
- 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.
- 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.
- (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 5hexynenitrile 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.