ORGANIC LETTERS

2006
Vol. 8, No. 5
907−909

Rhodium-Catalyzed [2+2+2] Cycloaddition of 1,6-Diynes with Isothiocyanates and Carbon Disulfide

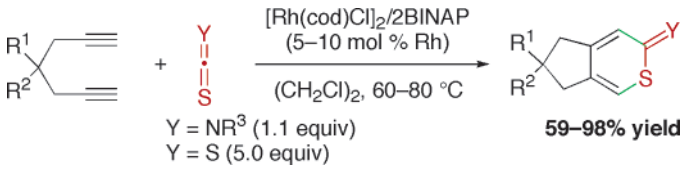
Ken Tanaka,*,† Azusa Wada,† and Keiichi Noguchi‡

Department of Applied Chemistry, Graduate School of Engineering, and Instrumentation Analysis Center, Tokyo University of Agriculture and Technology, Koganei, Tokyo 184-8588, Japan

tanaka-k@cc.tuat.ac.jp

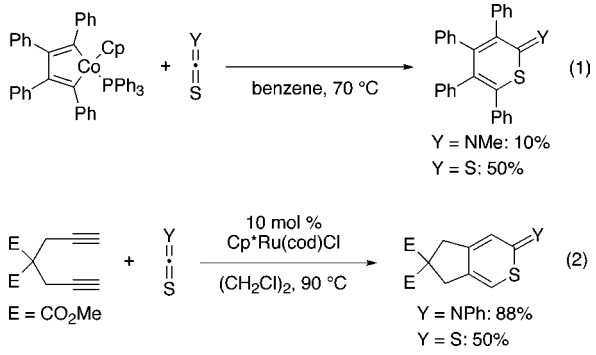
Received December 15, 2005

ABSTRACT



A neutral rhodium(I)/BINAP complex effectively catalyzed a [2+2+2] cycloaddition of 1,6-diynes with isothiocyanates to give bicyclic thiopyranimines in 59–98% isolated yield. The reaction with carbon disulfide also proceeded to give bicyclic dithiopyrones in 74–85% isolated yield.

Transition-metal-catalyzed [2+2+2] cycloaddition of alkynes with isocyanates leading to substituted 2-pyridones has been developed using a number of transiton-metal complexes,[1] such as Co, Ni, Ru, and Rh.[2−5] On the other hand, only a few examples have been reported for the corresponding reaction with isothiocyanates.[6−7] The pioneering work for such a transition-metal-catalyzed or mediated [2+2+2] cycloaddition of alkynes with isothiocyanates was first reported by Wakatsuki and Yamazaki using a stoichiometric amount of cobaltacyclopentadiene (eq 1).[6] Yamamoto, Itoh, and co-workers realized the catalytic version of this reaction using 10 mol % Cp*Ru(cod)Cl as catalyst (eq 2).[7] To the best of our knowledge, no example has been reported to date other than this Ru catalysis.



We recently reported the cationic rhodium(I)/H8-BINAP[8]-complex-catalyzed chemo-, regio-, and enantioselective

† Department of Applied Chemistry.
‡ Instrumentation Analysis Center.

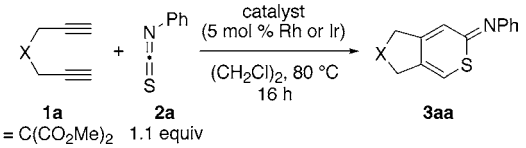
(1) For a review, see: Varela, J. A.; Saà, C. *Chem. Rev.* **2003**, *103*, 3787−3801.
(2) For Co, see: (a) Hong, P.; Yamazaki, H. *Tetrahedron Lett.* **1977**, 1333−1336. (b) Earl, R. A.; Vollhardt, K. P. C. *J. Org. Chem.* **1984**, *49*, 4786−4800. (c) Bonaga, L. V. R.; Zhang, H.-C.; Moretto, A. F.; Ye, H.; Gauthier, D. A.; Li, J.; Leo, G. C.; Maryanoff, B. E. *J. Am. Chem. Soc.* **2005**, *127*, 3473−3485.
(3) For Ni, see: (a) Hoberg, H.; Oster, B. W. *Synthesis* **1982**, 324−325. (b) Duong, H. A.; Cross, M. J.; Louie, J. *J. Am. Chem. Soc.* **2004**, *126*, 11438−11439.
(4) For Ru, see: (a) Yamamoto, Y.; Takagishi, H.; Itoh, K. *Org. Lett.* **2001**, *3*, 2117−2119. (b) Yamamoto, Y.; Kinpara, K.; Saigoku, T.; Takagishi, H.; Okuda, S.; Nishiyama, H.; Itoh, K. *J. Am. Chem. Soc.* **2005**, *127*, 605−613.
(5) For Rh, see: Flynn, S. T.; Hasso-Henderson, S. E.; Parkins, A. W. *J. Mol. Catal.* **1985**, *32*, 101−105.
(6) (a) Wakatsuki, Y.; Yamazaki, H. *J. Chem. Soc., Chem. Commun.* **1973**, 280. (b) Yamazaki, H. *J. Synth. Org. Chem. Jpn.* **1987**, *45*, 244−257.
(7) Yamamoto, Y.; Takagishi, H.; Itoh, K. *J. Am. Chem. Soc.* **2002**, *124*, 28−29.

10.1021/ol053044r CCC: $33.50 © 2006 American Chemical Society
Published on Web 02/04/2006

cross-cyclotrimerization of two different alkynes.[9] This catalyst was successfully applied to the chemo-, regio-, and enantioselective [2+2+2] cycloaddition of alkynes with isocyanates leading to substituted 2-pyridones.[10] In this paper, we describe a neutral rhodium(I)/BINAP-complex-catalyzed [2+2+2] cycloaddition of alkynes with isothiocyanates and carbon disulfide.

We first examined various rhodium catalysts to promote [2+2+2] cycloaddition of the malonate-derived 1,6-diyne **1a** with phenyl isothiocyanate (**2a**, 1.1 equiv) (Table 1).

Table 1. Screening of Catalysts for [2+2+2] Cycloaddition of 1,6-Diyne **1a** with Phenyl Isothiocyanate **2a**[a]



1a X = C(CO$_2$Me)$_2$ + **2a** 1.1 equiv → **3aa**

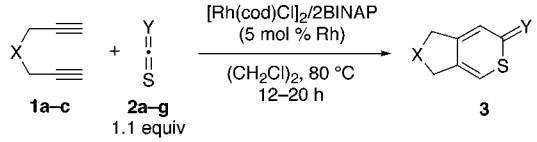
entry	catalyst	yield (%)[b]
1	[Rh(cod)$_2$]BF$_4$/BINAP	35
2	[Rh(cod)$_2$]BF$_4$/H8-BINAP	<2
3	[Rh(cod)Cl]$_2$/2BINAP	88[c]
4	[Rh(cod)Cl]$_2$/2H8-BINAP	71
5[d]	RhCl(PPh$_3$)$_3$	<2
6	[Ir(cod)$_2$]BF$_4$/BINAP	0
7	[Ir(cod)Cl]$_2$/2BINAP	0

[a] Reactions were conducted using catalyst (0.0025 or 0.0050 mmol), **1a** (0.10 mmol), **2a** (0.11 mmol), and $(CH_2Cl)_2$ (1.0 mL). The active catalysts were generated through hydrogenation (H_2, 1 atm, room temperature). [b] NMR yield. [c] Isolated yield. [d] Without hydrogenation.

Among the rhodium catalysts (5 mol % Rh based on **1a**) examined (entries 1−5), [Rh(cod)Cl]$_2$/2BINAP showed high catalytic activity at 80 °C to afford bicyclic thiopyranimine **3aa** in 88% yield (entry 3). Both a neutral and a cationic iridium(I) complex showed no catalytic activity (entries 6 and 7).

Next, the cycloaddition of **1a** with various isothiocyanates (1.1 equiv) was investigated using [Rh(cod)Cl]$_2$/2BINAP (5 or 10 mol % Rh) at 80 °C (Table 2). In general, both aryl and alkyl isothiocyanates were readily coverted to the corresponding bicyclic thiopyranimines in good to high yield. Sterically demanding *o*-tolyl isothiocyanate (**2b**) was also converted to the desired bicyclic thiopyranimine **3ab** in 74% yield (entry 2). Both aryl isothiocyanates bearing either an electron-donating group or an electron-withdrawing group readily reacted with **1a** (entries 3 and 4). Alkyl isocyanates

Table 2. Rhodium-Catalyzed [2+2+2] Cycloaddition of 1,6-Diynes with Isothiocyanates and Carbon Disulfide[a]



1a–c + **2a–g** 1.1 equiv → **3**

entry	diyne	isothiocyanate	product	yield (%)[b]
1	**1a**	**2a** Y = NPh	**3aa**	88
2		**2b** Y = N(2-MeC$_6$H$_4$)	**3ab**	74
3		**2c** Y = N(4-MeOC$_6$H$_4$)	**3ac**	73
4[c]		**2d** Y = N(4-ClC$_6$H$_4$)	**3ad**	89
5[c]		**2e** Y = NBn	**3ae**	87
6		**2f** Y = N*n*-Bu	**3af**	59
7[d]		**2g** Y = S	**3ag**	85
8[c]	**1b**	**2a** Y = NPh	**3ba**	81
9[d]		**2g** Y = S	**3bg**	74
10	**1c**	**2a** Y = NPh	**3ca**	87
11[d]		**2g** Y = S	**3cg**	75

[a] Reactions were conducted using [Rh(cod)Cl]$_2$ (0.0075 mmol), BINAP (0.015 mmol), **1a**−**c** (0.30 mmol), **2a**−**f** (0.33 mmol), and $(CH_2Cl)_2$ (1.5 mL). The active catalyst was generated through hydrogenation (H_2, 1 atm, room temperature). [b] Isolated yield. [c] 10 mol % Rh was used. [d] CS_2 (**2g**, 1.50 mmol) was used.

also gave the corresponding thiopyranimines (entries 5 and 6). The generality of this cycloaddition was subsequently examined with regard to the diyne substrates. Thus, the 1,3-diketone derivative **1b** and the 1,3-diol derivative **1c** gave the corresponding bicyclic thiopyranimines **3ba** and **3ca** in high yields (entries 8 and 10). On the contrary, tosylamide and ether-linked 1,6-diynes failed to undergo cycloaddition with **1a**.[11] Thus, rhodium-catalyzed [2+2+2] cycloaddition of alkynes with isothiocyanates cannot proceed without the aid of the Thorpe−Ingold effect induced by the tertiary center at the 4-position of 1,6-diynes.[12] In addition to isothiocyanates, carbon disulfide can be involved in the cycloaddition with 1,6-diynes. In the presence of [Rh(cod)Cl]$_2$/2BINAP (5 mol % Rh), 1,6-diynes **1a**−**c** reacted with carbon disulfide (5.0 equiv) at 80 °C to furnish the corresponding bicyclic dithiopyrones **3ag**−**cg** in 74−85% yields (entries 7, 9, and 11).

The asymmetric variant of this reaction, enantioselective desymmetrization of a 1,6-diyne, was briefly examined.

(8) For H8-BINAP = 2,2′-bis(diphenylphosphino)-5, 5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl, see: Zhang, X.; Mashima, K.; Koyano, K.; Sayo, N.; Kumobayashi, H.; Akutagawa, S.; Takaya, H. *Tetrahedron Lett*. **1991**, *32*, 7283−7286.

(9) (a) Tanaka, K.; Shirasaka, K. *Org. Lett*. **2003**, *5*, 4697−4699. (b) Tanaka, K.; Nishida, G.; Wada, A.; Noguchi, K. *Angew. Chem., Int. Ed*. **2004**, *43*, 6510−6512. (c) Tanaka, K.; Toyoda, K.; Wada, A.; Shirasaka, K.; Hirano, M. *Chem.−Eur. J*. **2005**, *11*, 1145−1156. (d) Tanaka, K.; Nishida, G.; Ogino, M.; Hirano, M.; Noguchi, K. *Org. Lett*. **2005**, *7*, 3119−3121.

(10) Tanaka, K.; Wada, A.; Noguchi, K. *Org. Lett*. **2005**, *7*, 4737−4739.

(11) In these cases, the homo [2+2+2] cycloaddition products of 1,6-diynes were generated as the sole product and isothiocyanates were recovered. 1,6-Diynes bearing substituents at terminal positions and 1,7-diynes also failed to undergo cycloaddition with **2a**.

(12) Beesley, R. M.; Ingold, C. K.; Thorpe, J. F. *J. Chem. Soc*. **1915**, *107*, 1080−1106. (b) Jung, M. E.; Gervay, J. *J. Am. Chem. Soc*. **1991**, *113*, 224−232.

When the reaction of the phenylacetate-derived 1,6-diyne **1d** with phenyl isothiocyanate (**2a**, 1.1 equiv) was conducted in the presence of [Rh(cod)Cl]$_2$/2(*R*)-BINAP (10 mol % Rh) at 60 °C, enantioenriched bicyclic thiopyranimine **3da** was obtained in 98% yield with 61% ee (eq 3). Enantiopure (+)-**3da** was easily prepared by recrystallization from CH_2Cl_2-pentane, the absolute configuration of which was determined to be *R* by an anomalous dispersion method (Figure 1). On

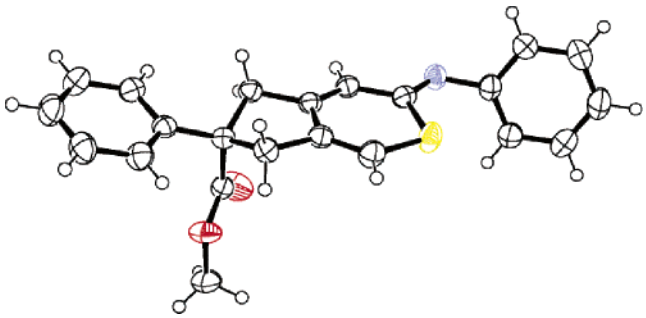
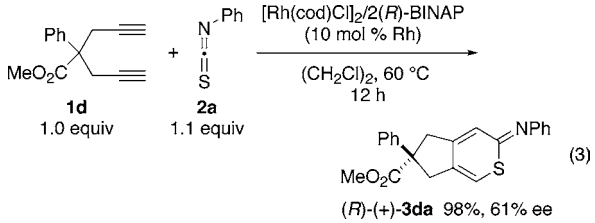


Figure 1. ORTEP diagram of (*R*)-(+)-**3da**.

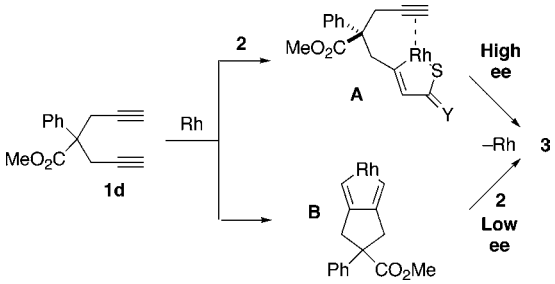
the other hand, the reactions using alkyl isothiocyanates **2e**,**f** gave the corresponding cycloaddition products with <10% ee.



(3)

Scheme 1 depicts a plausible mechanism of this rhodium-catalyzed [2+2+2] cycloaddition of 1,6-diynes with isothio-

Scheme 1



cyanates and carbon disulfide. In the case of phenyl isothiocyanate (**2a**), preferential formation of metallacycle **A** instead of **B** results in high enantioselectivity. On the other hand, preferential formation of metallacycle **B** instead of **A** results in low enantioselectivity in the case of alkyl isothiocyanates **2e**,**f**. Indeed, the homo [2+2+2] cycloaddition product of **1d** was generated as a byproduct other than the desired cross [2+2+2] cycloaddition products in the latter case.

In conclusion, we have developed a neutral rhodium(I)/BINAP complex-catalyzed [2+2+2] cycloaddition of 1,6-diynes with isothiocyanates and carbon disulfide leading to bicyclic sulfur heterocycles in high yield.

Acknowledgment. This work was supported by Uehara Memorial Fundation. We thank Takasago International Corporation for the gift of H8-BINAP.

Supporting Information Available: Experimental procedures, compound characterization data (PDF), and X-ray crystallographic files (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

OL053044R