Pergamon

Tetrahedron Letters 43 (2002) 2235–2238

TETRAHEDRON LETTERS

An improved 1,3-diene synthesis from alkyne and ethylene using cross-enyne metathesis

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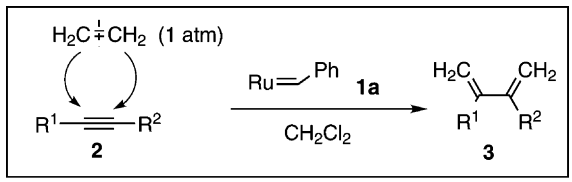
Received 28 December 2001; revised 21 January 2002; accepted 25 January 2002

Abstract—Synthesis of 1,3-diene from alkyne and ethylene (1 atm) was improved using ruthenium carbene complex **1b** having heterocyclic carbene as a ligand. In this reaction, the heteroatom at the propargylic position was not required, although the reaction of alkyne with the first-generation ruthenium carbene complex **1a** was affected by the substituent at the propargylic position. Various 1,3-dienes could be synthesized from alkynes and ethylene. © 2002 Published by Elsevier Science Ltd.

Although cross-enyne metathesis[1,2] is very interesting, it is difficult to use cross-enyne metathesis in synthetic organic chemistry because olefin metathesis,[3] enyne metathesis and diyne metathesis would occur simultaneously. During the course of our study on enyne metathesis,[4] we developed a novel method for synthesizing 1,3-diene **3** from alkyne **2** and ethylene using cross-enyne metathesis.[2] The reaction procedure is very simple: a CH_2Cl_2 solution of alkyne **2** and 3–10 mol% of ruthenium carbene complex **1a** reported by Grubbs[5] was stirred under ethylene gas (1 atm) for 1–2 days at room temperature to give 1,3-diene **3** in good to moderate yield (Scheme 1). This reaction was further extended using high pressure of ethylene gas.[6a]



Scheme 1. Novel synthesis of 1,3-diene from alkyne and ethylene.

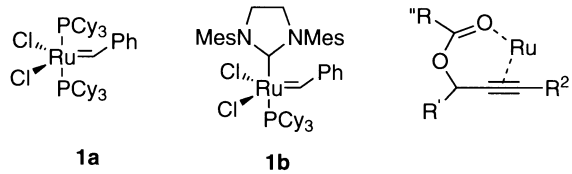


Figure 1.

In this reaction, if alkynes **2** have an acetoxy, benzoyloxy or tosylamide group at the propargylic position, 1,3-dienes **3** were obtained in good yields. However, alkynes **2** that did not have these groups at the propargylic position afforded 1,3-dienes **3** in poor yields.[2b] The effect of the heteroatom at the propargylic position is thought to arise because the carbonyl group of the acyl moiety coordinates with the ruthenium metal and then the reaction proceeds as shown in Fig. 1.[2c,7] During the synthetic study of anolignan A and anolignan B,[2c] we used the second-generation ruthenium carbene complex **1b**,[8] which has heterocyclic carbene as a ligand, and high reactivity of **1b** was observed in the synthesis of 1,3-dienes from alkynes. Thus, we decided to reinvestigate the synthesis of 1,3-dienes from alkynes and ethylene. Blechert has recently reported improved cross-enyne metathesis of alkyne and allylsilane using **1b**,[3d] and Diver has investigated cross-enyne metathesis of terminal alkynes having a heteroatom at the propargylic position under 60 psi of ethylene using **1b**.[6b,c]

At first, the effect of the acetoxy group at the propargylic position was examined. When a CH_2Cl_2 solution of alkyne **2a** with 5 mol% of first-generation Grubbs' catalyst **1a** was stirred under 1 atm pressure of ethylene (balloon) at room temperature for 48 h, the desired 1,3-diene **3a** was obtained in 16% yield (Table 1, run 1).

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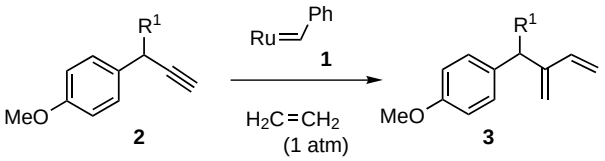
0040-4039/02/$ - see front matter © 2002 Published by Elsevier Science Ltd.
PII: S0040-4039(02)00215-0

Table 1. Effects of heteroatom at the propargylic position

Run		Reaction conditions						Yield (%)	
		R^1	Ru	(mol %)	Solvent	Temp. (°C)	Time (h)	**3**	**2**
1	**2a**	H	**1a**	5	CH_2Cl_2	rt	48	16	69
2	**2a**	H	**1a**	5	CH_2Cl_2	Reflux	24	—	84
3	**2b**	OAc	**1a**	5	CH_2Cl_2	rt	48	75	23
4	**2a**	H	**1b**	10	Toluene	80	5	91	—
5	**2a**	H	**1b**	5	Toluene	80	0.5	83	—
6	**2b**	OAc	**1b**	10	Toluene	80	0.5	100	—
7	**2b**	OAc	**1b**	5	Toluene	80	0.5	100	—



Scheme 2. Synthesis of 1,3-diene from terminal alkyne and ethylene.

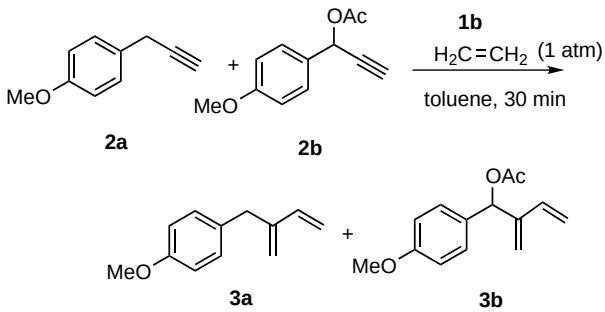
When the reaction was carried out in a similar manner upon heating, none of the product was obtained because **1a** was not stable under these reaction conditions (run 2).[9] However, alkyne **2b** having an acetoxy group at the propargylic position was treated with **1a** in a similar manner at room temperature to give desired 1,3-diene **3b** in 75% yield (run 3). It is clear that in the reaction of alkyne and ethylene with **1a**, the acetoxy group at the propargylic position is very important. On the other hand, when compound **2a** having no acetoxy group at the propargylic position was treated with 10 mol% of second-generation ruthenium carbene complex **1b** upon heating in toluene, the desired 1,3-diene **3a** was obtained in 91% yield after 5 h (run 4) (Scheme 2).

Using 5 mol% of **1b** in toluene, **3a** was obtained in 83% yield after only 30 min (run 5). In a similar manner, **2b** gave **3b** in quantitative yield after 30 min (runs 6 and 7). These results indicate that even in the absence of an acetoxy group at the propargylic position, ruthenium carbene complex **1b** is quite effective for the synthesis of 1,3-diene.

To confirm whether an acetoxy group at the propargylic position is effective for the synthesis of 1,3-diene, a competitive reaction was carried out. A toluene solution of a mixture of equal molar amounts of **2a** and **2b** and 2.5 mol% of **1b** was stirred upon heating at 80°C for 30 min. After the addition of ethyl vinyl ether and then the usual work-up, the crude product was purified by short column chromatography on silica gel to remove the catalyst. The ^1H NMR spectrum of the reaction mixture showed that 1,3-dienes **3a** and **3b** were formed in 77 and 66% yields, respectively, along with the recovered starting materials **2a** and **2b** in 17 and 34% yields, respectively (Table 2, run 1). The reaction was carried out at 50°C using 1 mol% of **1b**. After 30 min, **3a** and **3b** were obtained in 53 and 48% yields, respectively, along with the starting materials **2a** and **2b** in 33 and 46% yields, respectively (run 2). These results indicate that the reaction of **2a** with **1b** is slightly faster than that of **2b** with **1b**. It means that in the cross enyne metathesis with ethylene using **1b**, the electronic effect of the acetoxy group at the propargylic position is not important (Scheme 3).

Various alkynes **2** were treated with **1a** and **1b** under ethylene gas (1 atm), and the results are shown in Table 3. The reaction of terminal alkynes **2c** bearing a phenyl group or **2d** bearing an alkyl group proceeded smoothly to give 1,3-dienes **3c** and **3d** in high yields, respectively, after only 30 min. Internal alkynes **2e**, **2f** and **2g** also gave 1,3-dienes, **3e**, **3f** and **3g** in high yields. The effect of TMS group on alkyne was examined because in intramolecular enyne metathesis using **1a**, enyne having the TMS group on alkyne did not give a good result.[4a] The reaction of **2h** bearing TMS group on alkyne with ethylene using **1a** gave 1,3-diene **3h** in 21% yield after 16 h, while that using **1b** gave **3h** in 87% yield. The resulting 1,3-diene **3h** has a vinyl silane moiety, which would be a useful precursor in synthetic organic chemistry.

The reaction of alkyne **2i** having a carbomethoxy group with **1a** did not proceed at room temperature or upon

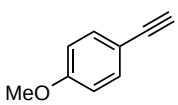
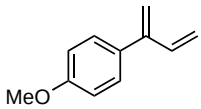
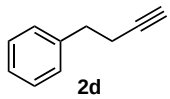
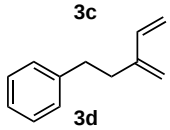
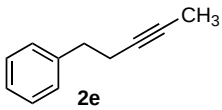
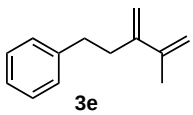
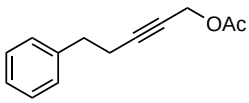
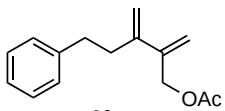
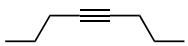
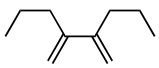
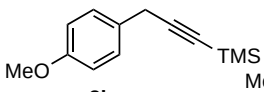
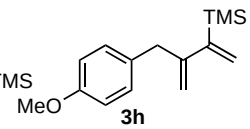
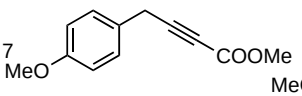
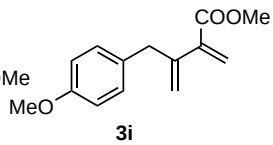


Scheme 3. Competitive reaction of **2a** and **2b** using **1b**.

Table 2. Competitive reaction of **2a** and **2b** with **1b**

Run	Ru (mol %)	Temp. (°C)	Yield (%)			
			3a	**3b**	**2a**	**2b**
1	2.5	80	77	66	17	34
2	1	50	53	48	33	46

Table 3. Synthesis of various 1,3-dienes

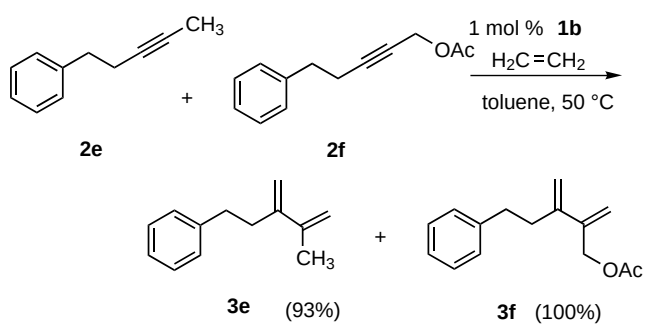
	alkyne	diene	"Ru"	mol %	temp. (°C)	time (h)	yield (%) 3	yield (%) 2
1	 **2c**	 **3c**	**1b**	5	80[a)]	0.5	88	—
2	 **2d**	 **3d**	**1b**	5	80[a)]	0.5	71	—
3	 **2e**	 **3e**	**1b**	5	80[a)]	0.5	85	—
4	 **2f**	 **3f**	**1b**	5	80[a)]	0.5	100	—
5	 **2g**	 **3g**	**1b**	5	reflux[b)]	24	80	—
6	 **2h**	 **3h**	**1a** **1b**	5 5	rt[b)] 80[a)]	16 16	21 87	78 10
7	 **2i**	 **3i**	**1a** **1a** **1b** **1b**	10 10 5 10	reflux [b)] rt[b)] 80[a)] 80[a)]	16 16 16 16	— — 33 43	93 70 67 34

a) in toluene. b) in CH_2Cl_2.

heating, and the starting material **2i** was recovered unchanged after 16 h (run 7). Although the reaction rate of **2i** with ethylene using **1b** was slow, the desired 1,3-diene **3i** was obtained in 43% yield along with **2i** in 34% yield after 16 h.

In the internal alkyne, competitive reaction between alkyne **2e** having no substituent at the propargylic position and alkyne **2f** having an acetoxy group at the same position was carried out. Since the reactions of these compounds with ethylene using **1b** were very fast, the reaction was carried at 50°C in toluene using 1 mol% of ruthenium catalyst. However, after only 15 min, the spots of the starting materials **2e** and **2f** were completely disappeared on TLC and both **3e** and **3f** were obtained in almost quantitative yields, respectively. It was confirmed that an acetoxy group at the propargylic position in the internal alkyne did not also affect the reaction rate in the cross-enyne metathesis (Scheme 4).

These results indicate that 1,3-diene synthesis from alkyne and ethylene (1 atm) was improved. The remarkable feature of the reaction using **1b** is as follows. The reaction procedure is very simple; that is, a solution of alkyne and **1b** (1–5 mol%) in toluene or CH_2Cl_2 is stirred at 50–80°C under ethylene gas, and 1 atm pressure of ethylene can be used. In this reaction,



Scheme 4. Competitive reaction of internal alkynes **2e** and **2f**.

functional groups such as a phenyl group, alkyl group, TMS group and even a carbomethoxy group on alkyne were tolerated and various 1,3-dienes were obtained in good to high yields. The presence or absence of an acetoxy group at the propargylic position did not affect the reaction rate to form 1,3-diene. Further studies are in progress.

General procedure for synthesis of 1,3-diene from alkyne using 1b. A solution of alkyne **2** and 1–5 mol% of **1b** was heated in CH_2Cl_2 or toluene at 50–80°C under ethylene gas (1 atm). After the spot of the starting material disappeared on TLC, ethyl vinyl ether (several drops) was added. The solvent was removed and the residue was purified by short column chromatography on silica gel to give 1,3-diene **3**.

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