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Note

Co(I)- *versus* Ru(II)-Catalyzed [2+2+2] cycloadditions involving alkynyl halides

Laura Iannazzo[a,1], Naoko Kotera[a,1], Max Malacria[a,1], Corinne Aubert[a,**], Vincent Gandon[a,b,1,*]

[a] *Institut Parisien de Chimie Moléculaire (UMR CNRS 7201)-FR 2769 UPMC univ Paris 06, C. 229, 4 place Jussieu, 75005 Paris, France*
[b] *ICMMO (UMR CNRS 8182), Université Paris-Sud 11, 91405 Orsay cedex, France*

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ABSTRACT

Alkynyl chlorides, bromides, and iodides have been tested as [2 + 2 + 2] cycloaddition partners using CpCo(CO)(dimethylfumarate) and Cp*Ru(cod)Cl as precatalysts. A series of cocyclizations between diynyl dihalides and alkynes, as well as intramolecular cycloadditions of triynyl dihalides, has been carried out. While this study confirmed the versatility of the ruthenium complex with all kinds of halides, the cheap air-stable cobalt complex proved nonetheless efficient with alkynyl bromides.

1. Introduction

The transition-metal-catalyzed [2 + 2 + 2] cycloaddition reaction has become an increasingly popular way to form functionalizable six-membered rings in the organic chemists' community [1]. Ever since the first total synthesis involving this reaction in 1980 [2], more than 30 natural products have been prepared owing to this strategy [3]. For instance, Nicolaou's approach to Sporolide B relies on a Ru(II)-catalyzed [2 + 2 + 2] cycloaddition between three alkyne partners including an alkynyl chloride [4]. Alkynyl chlorides [4,5], bromides [5,6], and iodides [6,7] have been only scarcely employed in transition-metal-catalyzed [2 + 2 + 2] cycloadditions, and these reactions have been strictly limited to the use of Cp*Ru(cod)Cl as precatalyst. Due to their higher tendency to insert into the C—X bond of alkynyl halides, materialized by the formation of homocoupling products (*i.e.* 1,2-diynes) [5,8], cobalt-based catalysts are notably absent in this chemistry. There is yet one exception in the bromide series: we have recently synthesized the air-stable cobalt complex **1** which allowed the cyclization of a triyne into the corresponding 1,2-dibromobenzene derivative in excellent yield (Scheme 1) [9]. Due to the potential importance of this methodology for the synthesis of complex molecules, we decided to study in detail the behavior of **1** toward alkynyl halides and to compare the results with those obtained with Cp*Ru(cod)Cl. The comparison between cobalt and ruthenium is particularly worthwhile since complex **1** is about 30 times cheaper than Cp*Ru(cod)Cl [10]. Besides, we have explored a new type of cyclization between diynyl dichlorides and alkynes.

2. Results and discussion

We started our investigation by a brief examination of the reactivity of monoalkynes. Because Ru-catalyzed cyclotrimerizations of alkynyl chlorides and bromides have been previously described [5], and because alkynyl chlorides are prone to homocoupling under cobalt-catalysis [8], we focused on the reactivity of a bromide and an iodide in the presence of **1** (Scheme 2). Homocoupling of iodide **2b** occurred highly selectively to afford 1,2-diyne **3** quantitatively. In contrast, neither cyclotrimerization nor homocoupling took place when using bromide **2a**.

The fact that alkynyl bromides apparently do not autotrimerize with **1** makes them potential candidates for cocyclization with other alkyne partners. We first focused on diynyl dihalides and compared cobalt with ruthenium catalysis (Table 1). In addition to the halide, the nature of the tether Z (carbon-, oxygen-, nitrogen-linkers) and of the R^1 and R^2 substituents (H, vinyl, aryl, alkyl, and ester) at the alkyne was also varied. Two experimental conditions were used: A (DCE, rt, 12 h) which are standard ones for Ru-

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* Corresponding author. ICMMO (UMR CNRS 8182), Université Paris-Sud 11, 91405 Orsay cedex, France. Tel.: +33 (0) 1 69 15 39 31; fax: +33 (0) 1 69 15 47 47.

** Corresponding author. Tel.: +33 (0) 1 44 27 70 68; fax: +33 (0) 1 44 27 73 60.

E-mail addresses: corinne.aubert@upmc.fr (C. Aubert), vincent.gandon@u-psud.fr (V. Gandon).

[1] Tel.: +33 (0) 1 44 27 70 68; fax: +33 (0) 1 44 27 73 60.

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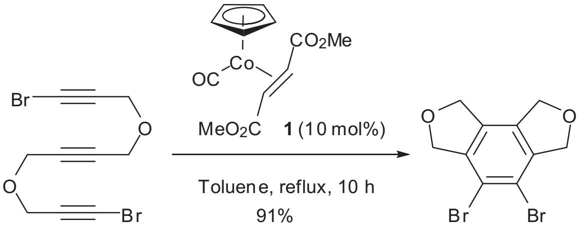
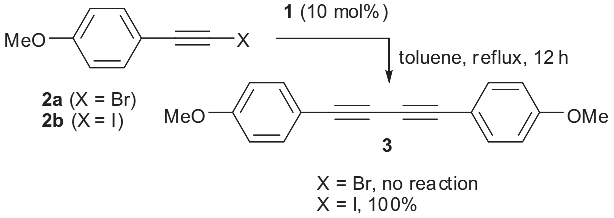
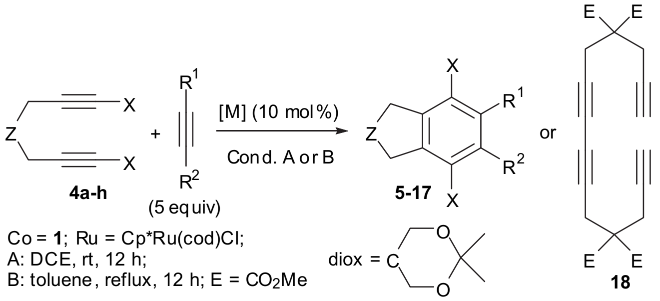


Scheme 1. Co(I)-catalyzed cyclization of a brominated triyne.



Scheme 2. Homocoupling of iodoalkyne **2a**.

Table 1
Cocyclizations of diynes and alkynes.



Entry	Diyne	Z	X	R^1	R^2	[M]	Cond.	Product	Yield (%)
1	**4a**	CH_2	Cl	H	CO_2Me	Co	A	–	0
2	**4a**	CH_2	Cl	H	CO_2Me	Co	B	**5**	20
3	***4a***	CH_2	*Cl*	*H*	CO_2Me	*Ru*	*A*	**5**	*87*
4	**4a**	CH_2	Cl	H	CO_2Me	Ru	B	**5**	65
5	**4a**	CH_2	Cl	H	Ph	Co	A	–	0
6	**4a**	CH_2	Cl	H	Ph	Co	B	**6**	18
7	**4a**	CH_2	Cl	H	Ph	Ru	A	**6**	90
8	***4a***	CH_2	*Cl*	*H*	*Ph*	*Ru*	*B*	**6**	*97*
9	**4a**	CH_2	Cl	H	CH_2OMe	Co	A	–	0
10	**4a**	CH_2	Cl	H	CH_2OMe	Co	B	**7**	10
11	***4a***	CH_2	*Cl*	*H*	CH_2OMe	*Ru*	*A*	**7**	*93*
12	**4a**	CH_2	Cl	H	CH_2OMe	Ru	B	**7**	82
13	**4b**	diox	Cl	H	C_4H_9	Co	A	–	0
14	**4b**	diox	Cl	H	C_4H_9	Co	B	**8**	52
15	***4b***	*diox*	*Cl*	*H*	C_4H_9	*Ru*	*A*	**8**	*100*
16	***4b***	*diox*	*Cl*	*H*	C_4H_9	*Ru*	*B*	**8**	*100*
17	**4c**	CE_2	Br	H	C_4H_9	Co	A	–	0
18	***4c***	CE_2	*Br*	*H*	C_4H_9	*Co*	*B*	**9**	*86*
19	**4c**	CE_2	Br	H	C_4H_9	Ru	A	**9**	79
20	**4c**	CE_2	Br	H	C_4H_9	Ru	B	**9**	69
21	**4c**	CE_2	Br	H	Ph	Co	B	**10**	70
22	**4c**	CE_2	Br	H	$C(Me){=}CH_2$	Co	B	**11**	53
23	**4c**	CE_2	Br	H	*p*-MeOPh	Co	B	**12**	48
24	**4c**	CE_2	Br	Et	Et	Co	B	**13**	40
25	**4d**	CH_2	Br	H	C_4H_9	Co	B	**14**	50
26	**4e**	$(CH_2)_2$	Br	H	C_4H_9	Co	B	–	0
27	**4f**	O	Br	H	C_4H_9	Co	B	**15**	46
28	**4g**	NTs	Br	H	C_4H_9	Co	B	**16**	88
29	**4h**	CE_2	I	H	C_4H_9	Co	A	–	0
30	**4h**	CE_2	I	H	C_4H_9	Co	B	**18**	38
31	**4h**	CE_2	I	H	C_4H_9	Ru	A	**17**	33
32	***4h***	CE_2	*I*	*H*	C_4H_9	*Ru*	*B*	**17**	*100*

Italics represents the optimal conditions.

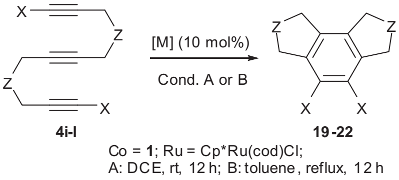
catalyzed [2 + 2 + 2] cycloadditions, and B (toluene, reflux, 12 h) which are typical for Co-catalyzed cyclizations. The cocyclization of diynyl dichlorides with alkynes was not studied before in any metal series. With such substrates, Cp*Ru(cod)Cl proved to be the best precatalyst (Entries 1–16). Excellent yields of cycloadducts **5-7** and **8** were reached using either A or B (Entries 3, 8, 11, 15, and 16). With **1**, conditions A did not allow the cocyclization to take place (Entries 1, 5, 9, and 13) and the diyne could be recovered in part [11]. On the other hand, the expected products could be obtained using conditions B, yet in low to moderate yields (Entries 2, 6, 10, 14).

We next examined the case of diynyl dibromides (Entries 17–28). Although conditions A still proved unproductive with **1** (Entry 17), conditions B provided the expected cycloadduct **9** in 86% yield (Entry 18). Of particular interest, **1** outperformed Cp*Ru(cod)Cl which led to 79 and 69% yield of **9** under conditions A and B respectively (Entries 19 and 20). To explore the scope of the Co-catalyzed reaction, various combinations of diynyl dibromides and alkynes were tested (Entries 21–28). Provided 1,6-diynes are used, the products could be isolated in each of the seven cases, in 40–88% yield. In contrast, no cocyclization took place when using the 1,7-diyne **4e** (Entry 26).

Lastly, the superiority of Cp*Ru(cod)Cl in achieving the cocyclization of diynyl diiodides with alkynes was clearly evidenced when using **4h** and 1-hexyne (Entries 29–32). With cobalt, homocoupling ensued to give tetrayne **18** in 38% yield (Entry 30), whereas **17** was isolated quantitatively with ruthenium (Entry 32). In order to verify whether the compatibility of **1** toward alkynyl bromides was inherent in its structure, some reactions of **4c** were carried out using the typical precatalysts $CpCo(CO)_2$ and $CpCo(C_2H_4)_2$ [12]. In each case, **4c** could be recovered in part, and no trace of cycloadduct could be detected among the degradation products.

The same conclusions could be reached in the triynyl dihalide series (Table 2). With chlorides and iodides, only ruthenium gave satisfactory yields of the expected tricyclic products (Entries 6 and 14). On the other hand, with bromides, complex **1** led to a slightly better result than Cp*Ru(cod)Cl (Entry 8). Again, the use of

Table 2
Cyclizations of triynes.



Entry	Triyne	Z	X	[M]	Cond.	Product	Yield (%)
1	**4i**	O	Cl	Co	A	–	0[a]
2	**4i**	O	Cl	Co	B	**19**	5
3	**4i**	O	Cl	Ru	A	**19**	47
4	**4i**	O	Cl	Ru	B	**19**	45
5	**4j**	NTs	Cl	Co	B	**20**	35
6	***4j***	*NTs*	*Cl*	*Ru*	*A*	**20**	*100*
7	**4k**	O	Br	Co	A	–	0[a]
8	***4k***	*O*	*Br*	*Co*	*B*	**21**	*91*
9	**4k**	O	Br	Ru	A	**21**	83
10	**4k**	O	Br	Ru	B	**21**	76
11	**4l**	O	I	Co	A	–	0[a]
12	**4l**	O	I	Co	B	**22**	5
13	**4l**	O	I	Ru	A	**22**	32[b]
14	***4l***	*O*	*I*	*Ru*	*B*	**22**	*100*

Italics represents the optimal conditions.

[a] No reaction.

[b] 60% reported with 15 mol% Ru in 24 h, see [6].

$CpCo(CO)_2$ and $CpCo(C_2H_4)_2$ did not allow the formation of the cyclization product.

3. Conclusion

This preliminary study shows that Cp*Ru(cod)Cl remains the best choice for $[2+2+2]$ cycloaddition of alkynyl chlorides and iodides. However, cobalt complexes may, under certain conditions, qualify as precatalyst for $[2+2+2]$ cycloaddition of alkynyl bromides. This feature is highly dependent on the nature of the ligands at Co. Mechanistic studies are underway to shed light on that matter.

4. Experimental section

*4.1. Procedure for the cocyclization of diynes with alkynes using the cobalt complex **1***

The alkyne (0.82 mmol) was slowly added over 10 min to a refluxing solution of CpCo(CO)(dimethylfumarate) **1** (0.04 mmol) and the diyne (0.16 mmol) in toluene (4 mL). The reaction mixture was refluxed overnight and then cooled to room temperature. The solvent was removed in vacuo and the residue purified by flash column chromatography using a gradient mixture of pentane and Et_2O.

*4.2. Procedure for the cyclization of triynes using the cobalt complex **1***

CpCo(CO)(dimethylfumarate) **1** (0.022 mmol) was added to a solution of the triyne (0.22 mmol) in toluene (4 mL) and the reaction mixture was refluxed overnight. After being cooled, the solvent was removed by rotary evaporation and the crude product was purified by flash column chromatography using a gradient mixture of pentane and Et_2O.

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Appendix. Supplementary material

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jorganchem.2011.08.041.

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[10] Complex **1** is prepared in one step in a 100% yield from CpCo(CO)*2* which costs ~ 3 €/mmol while Cp*Ru(cod)Cl is worth ~ 100 €/mmol.
[11] Although the structure of the side products could not be ascertained, we suspect a substantial amount of homocoupling.
[12] For a monograph on $CpCo(C_2H_4)_2$, see V. Gandon, C. Aubert, e-EROS (2008). doi:10.1002/047084289X.rn00943.pub2.